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EFFECTS OF TABLET CORE DIMENSIONAL INSTABILITY ON THE GENERATION OF INTERNAL STRESSES WITHIN FILM COATS

PART I: INFLUENCE OF TEMPERATURE CHANGES DURING THE FILM COATING PROCESS*

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ABSTRACT

Commercial-sized (10mm diameter and 3.1mm thick) flat-faced tablets, formed from three direct compression bases (Avicel PH101, Emcompress and Starch 1500) and from maize starch, were stored at ambient conditions for 1, 24, 48 and 72 hours following their compression, then exposed to temperatures of 30 and 40°C for two hours, and afterwards allowed to re-equilibrate to room temperature for another two hours. The aim of this was to simulate temperature variations experienced during a typical film coating process. During this time, dimensional changes of the tablets were measured by means of a free-armature transducer rig. The dimensional changes occurring during the preliminary ambient storage due to viscoelastic strain relaxation were found to be significant, but were much smaller in magnitude compared to those occurring during the subsequent heating/cooling cycle which is part of the tablet coating process. Tablets of Avicel,maize starch and Starch 1500 decreased in size during heating and expanded during cooling whereas tablets of Emcompress exhibited the opposite behaviour. The exposure temperatures were found to influence the magnitude of these strain changes. The results were evaluated in terms of subsequent relative humidity changes causing loss and gain of water from the tablets during this temperature cycle. Possible consequences of these dimensional changes relate to the creation of internal stress within the film coat which could result in coating defects (eg. cracking, edge splitting and bridging of intagliations).

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INTRODUCTION

Cracking and edge splitting of the film coat or bridging of the intagliations are problems that film formulators often encounter during tablet film coating. It is well acknowledged that these coating defects are a manifestation of inherent high residual stresses distributed within the plane of the film coat (1-4). These coating defects are important not only because they destroy the integrity and elegance of the film, but also because they affect the shelf-life and durability of the product. Additionally, and more seriously, they may affect the release kinetics of the drug in the case of enterosoluble and/or sustained release films.

The possibility of splitting of sugar coats by high viscoelastic strain relaxation of tablet cores following sugar coating was suggested by Aulton et al. (5). Tablets undergoing unloading following the application of a maximum pressure, spring back towards their final dimensions resulting in both an expansion in volume and a distortion in shape (6,7). However, long periods of time are required for the tablets to attain their final dimesions (5,8). This duration depends on the viscoelastic characteristics of the tabletting materials and on compact size (9).

On the other hand, significant volume increases occur due to swelling when certain tablets are exposed to humid conditions (10-12). The importance of moisture uptake in high humidity conditions on the dimensional stability of the compacts was discussed by White (13) who obtained volume changes of up to 21% when tablets of ibuprofen granules were stored in saturated conditions. Porter (14,15) and Rowe (16) have suggested that this kind of dimensional change occurring in tablet cores would affect the build up of internal stress within the film coats.

The Origin of Internal Stress In the Film:

One source of internal stress developed within the film coat is solidification of film due to solvent evaporation and subsequent shrinkage of the film coating around the tablet substrate to which it is attached by adhesive bonds, as suggested by Croll (17). No stress is developed during the early stages of solvent evaporation (i.e. before the solidification point) where the polymer chains are mobile and any resulting stress is relieved by polymer flow.

Another origin of residual internal stress in film coatings is proposed by Sato (18) and is based on differences in the coefficient of thermal expansion between the coating and the substrate; this results in thermal strain during changes in temperature of the coating process. This strain is reversible with temperature as it occurs during cooling from the glass transition temperature of the film to ambient and it decreases with increased temperature.

Rowe (3) suggested the total internal stress (P) in a film coat applied to a tablet substrate to be composed of the stress created by film shrinkage during solvent evaporation (P_S) and the stress caused by thermal strain due to temperature changes during film coating process (P_T). Modifying and combining the equations derived by Croll (17) and Sato (18), Rowe (16) obtained Equation 1 for the calculation of total stress:

$$P = E/3(1-\nu)\,[(\phi_s-\phi_r)/(1-\phi_r) + \Delta\alpha\,\Delta T] \qquad \text{(Eq. 1)}$$

where E and ν are the Young's modulus and the Poisson's ratio of the film, respectively; ϕ_s

is the volume fraction of solvent at the solidification point; ;ϕ_r is the volume fraction of the solvent remained in the dry film at ambient conditions; $\Delta\alpha$ is the difference between the cubic thermal expansion coefficients of the film coat (α_c) and the tablet substrate (α_s); ΔT is the difference between the Tg of the film and the test temperature (T).

Considering the mechanical swelling of tablets containing hygroscopic materials at humid conditions due to moisture uptake, Rowe (16) also derived a new equation to estimate the stress created within the film due to volume changes of the tablet core (P_V):

$$P_V = (E/1-v)(\Delta V/3V) \qquad \text{(Eq. 2)}$$

where ΔV is the volume change of the tablet core and V is the volume of the core before storage.

Coating defects such as cracking, and edge splitting and peeling will occur when the total internal stress generated within the plane of the film exceeds the tensile strength of the film (19). Similarly, bridging of the intagliations will be observed when this stress is high enough to cause a reaction stress which exceeds the adhesion forces acting at the tablet substrate/film coat interface in the opposite direction (4).

Temperature Variations During Film Coating Process :

In the manufacture of film coated tablets, prior to the actual coating process, freshly compressed tablet cores are usually stored at ambient conditions for a few hours or days. A typical aqueous film coating time for 150kg of cores in a perforated drum coater (e.g. Accela-Cota) can take up to two hours (20). Although the tablet bed temperature is influenced by many factors, (such as drying air temperature, the duration of the spraying and drying periods, the rate of rotation of coating pan, the temperature of the coating solution and the kind of solvent applied (21)), during the aqueous film coating process itself, it should be maintained at a constant value of approximately 37-40°C (20). This range can be reduced to 30-40°C in the case of using organic solvents (21).

In the present study, the dimensional changes of tablets on extended storage at ambient conditions and the influence of temperature cycles which mimic those occuring in a typical film coating process were investigated and possible effects of these dimensional changes on the internal stress within the film coat are discussed. The temperature and relative humidity variations within a tablet bed during an actual aqueous film coating process and the dimensional changes of tablet cores exposed to these conditions are investigated in the second and the third parts of this work, respectively (22, 23).

MATERIALS AND METHODS

Materials and Equipment:

Avicel PH101 (FMC Corporation), Emcompress (Edward Mendell Co., Inc.), Starch 1500 (Colorcon Ltd.) and maize starch BP were used as received from the suppliers after being stored at room conditions (23°C and 40%RH) for at least two weeks before experimentation. A Monsanto Tensometer 10 (Monsanto, Swindon, UK) was used for tablet compression. Dimensional changes of tablets were measured by means of a free-armature transducer rig (Figure 1). The output of the linear variable displacement transducer (LVDT) was sent via a transducer conditioner to a Y-t chart recorder which

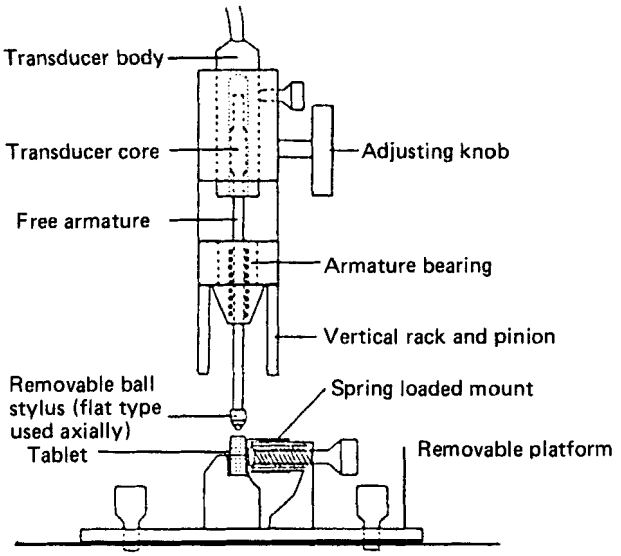

FIGURE 1
Diagram of the Free-armature Transducer Rig With a Sample Mounted for Radial Testing.

had been calibrated with respect to the LVDT, by means of a screw micrometer. In order to record the temperature of the test environment simultaneously, a thermometer was also connected to this two-pen chart recorder. The moisture content of the tablets was measured by an Infrared Moisture Determination Apparatus (Mettler LP12, Mettler Instrumente AG, CH). The readings for relative humidity were taken by a Humidity and Temperature Indicator HMI 31 (Vaisala, Sweden).

Methods:

10mm diameter, 3.1mm thick flat-faced tablets were compressed under 100MPa pressure applied at an upper punch speed of 25mm/min. Prior to compression of tablets of Emcompress (only), it was necessary to pre-lubricate the die and punch surfaces. Lubrication was affected by compressing a mixture of 50%w/w magnesium stearate and 50%w/w Emcompress.

The newly compressed tablets were stored in ambient conditions for 1, 24, 48 and 72 hours, then exposed to temperatures of 30 or 40°C (22±6%RH and 14±4%RH, respectively) for two hours and then allowed to re-equilibrate to room temperature for another two hours. The aim of this was to simulate temperature cycling based on data for typical commercial film coating systems. This cycle was begun exactly two minutes after decompression to allow the tablet to release all of its elastic and most of its rapid viscoelastic strain since it was not the aim of this study to examine this behaviour as these rapid, post-compression dimensional changes are not relevant to the practice of film coating.

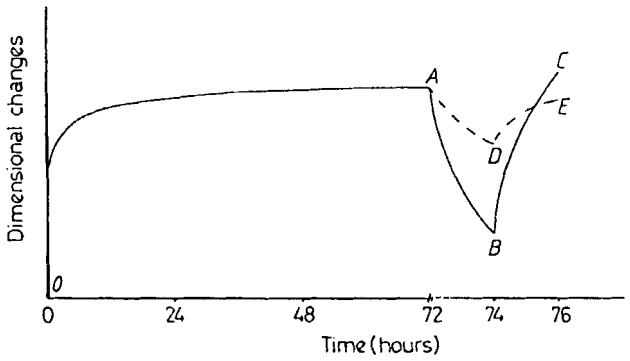

FIGURE 2
Dimensional Changes of Tablets During Simulated Storage and Coating Temperature Cycles of 30 and 40°C (Schematic).

Maintaining both the free-armature transducer rig and the sample in a controlled temperature environment, dimensional changes of the tablets were measured during the temperature cycling. In order to increase the accuracy of the rig, it was designed so that it was not possible to measure axial and radial movements simultaneously (Figure 1). Therefore measurements were taken for each direction independently on replicate tablets. The lack of spring in the LVDT and the low mass of the aluminium free-armature minimised the possibility of indentation of the transducer tip into the sample.

The moisture content of the replicate tablets prepared from the same materials under the same conditions were measured on completion of each storage stage as well as on ejection of the tablets from the die. The tablets were dried at power selection of 6 by the Infrared Moisture Determination Apparatus which provided temperatures of 100-110°C. Drying process was carried out until no further changes in their weights were recorded.

RESULTS AND DISCUSSION

Figure 2 represents a characteristic schematic profile of dimensional changes undergone by a tablet during the complete temperature cycles. On the curve, (O) corresponds to the moment that the measurement was started two minutes after decompression. The tablet releases its viscoelastic strain and expands during its storage in ambient conditions (line OA). The major part of the release is generally completed in the first 24 hours. At the next stage where the tablet is exposed to higher temperatures simulating a coating run for two hours (beginning at Position A), as a result of heat, the tablet possibly looses water and contracts considerably at a high rate (Position B for 40°C and D for 30°C). This rate of contraction always greater at the higher temperature of exposure. On allowing the tablet to re-equilibrate to room temperature for another two hours, it then swells, possibly due to the gradual regaining of moisture. This occurs at a higher rate when recovering from higher temperature exposures (line BC for 40°C and line DE for 30°C, respectively).

When the axial dimensional changes of the tablets formed from four different test materials were compared, during the storage period at ambient conditions for 72 hours, tablets of Avicel, maize starch and Starch 1500 underwent great axial viscoelastic strain relaxation (Figures 3a and 3b). For the tablets of maize starch and Starch 1500 the expansion of tablets continued at a reducing rate until the end of the storage period whereas tablets of Avicel reached a relatively steady stage after the first 24 hours. However, during the entire ambient storage stage, tablets formed from Emcompress which is a non time-dependent material, exhibited no axial dimensional changes (Figure 3b). At the end of this long period of viscoelastic strain recovery (72 hours in Figures 3a and 3b), the maximum axial expansion of the tablets were 47μm, 36.5μm, 36.0μm and 0.4μm for the tablets of maize starch, Avicel PH101, Starch 1500 and Emcompress, respectively.

Radial viscoelastic strain recovery of the tablets of Avicel, maize starch (Figure 4a) and Starch 1500 (Figure 4b) exhibited rather an unsteady line due to slight occasional contractions. Radially, following a different rank order, at the end of 72 hours the maximum radial expansion of the tablets reached the values of 12.3μm, 4.0μm, 3.5μm and 1.3μm for the tablets of maize starch, Emcompress, Starch 1500 and Avicel, respectively. These values were much lower than the maximum axial expansion for the tablets of Avicel, maize starch and Starch 1500.

On exposure of the tablets to a heating/cooling cycle, all of them, except those of Emcompress, underwent contraction when heated and expansion when cooled to room temperature in both directions. Tablets of Emcompress exhibited the opposite, but possibly more expected, pattern by expanding during heating and contracting during cooling phases (Figures 3 and 4b). However, the dimensional changes taking place on those tablets were small; especially on exposure to 30°C.

In order to elucidate the quantitative difference between axial and radial deformation, the data obtained from tablets of maize starch and Emcompress (representatives of elastically deforming and brittle materials, respectively) are presented in Figures 5a and 5b in terms of change in percentage strain with time. The percentage of viscoelastic strain relaxation on ambient storage and the dimensional changes occurring on exposure to temperatures which mimic the film coating process are always greater in the axial direction of the tablets of Avicel, maize starch and Starch 1500. Only the expansion of tablets formed from Emcompress following their compression was greater in the radial direction during ambient storage (Figure 5b). This may be attributed to the different compact structure formed by this material. On exposing the tablets of Emcompress to the temperature cycles, axial dimensional changes were much higher than the radial changes at 40°C.

Ambient storage for 1, 24, 48 and 72 hours prior to the coating cycle did not have any effect on the magnitude of subsequent dimensional changes of tablets, except at short durations. The tablets of Avicel, maize starch and Starch 1500 which were exposed to 40°C after 1 hour (also after 24 hours for samples of Avicel) of ambient storage underwent spontaneous axial expansion prior to contraction. Similar behaviour was observed on exposure to 30°C with tablets of maize starch and Starch 1500 after 1 hour ambient storage. The data of axial dimensional changes for Avicel PH101 tablets is shown as a representative in Figure 6. It is believed that this is due to a combination effect of temperature and unreleased viscoelastic strain occurring at the early stages of

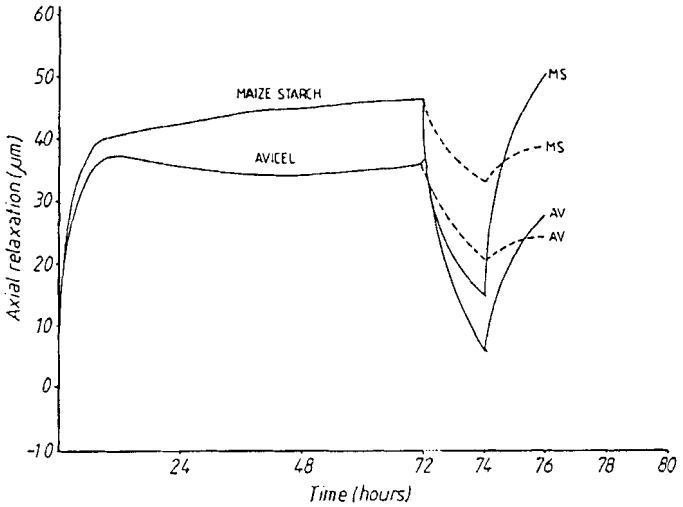

FIGURE 3a
Axial Dimensional Changes of Tablets During Simulated Storage and Coating Temperature Cycles. Comparison of Avicel PH101 and Maize Starch.

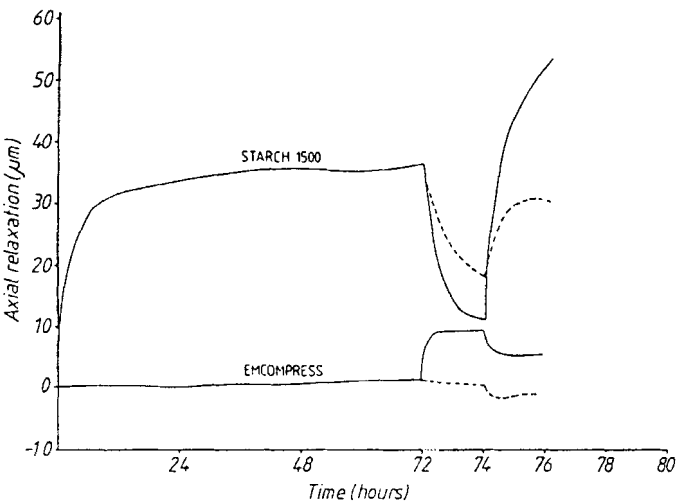

FIGURE 3b
Axial Dimensional Changes of Tablets During Simulated Storage and Coating Temperature Cycles. Comparison of Emcompress and Starch 1500.

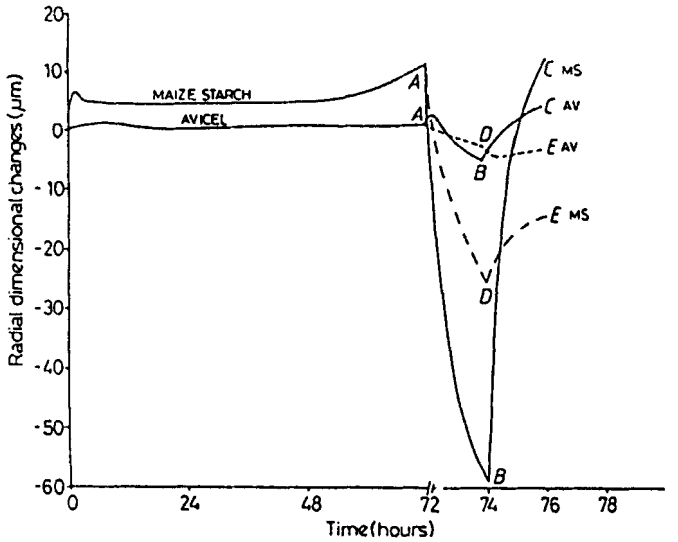

FIGURE 4a
Radial Dimensional Changes of Tablets During Simulated Storage and Coating Temperature Cycles. Comparison of Avicel PH101 and Maize Starch.

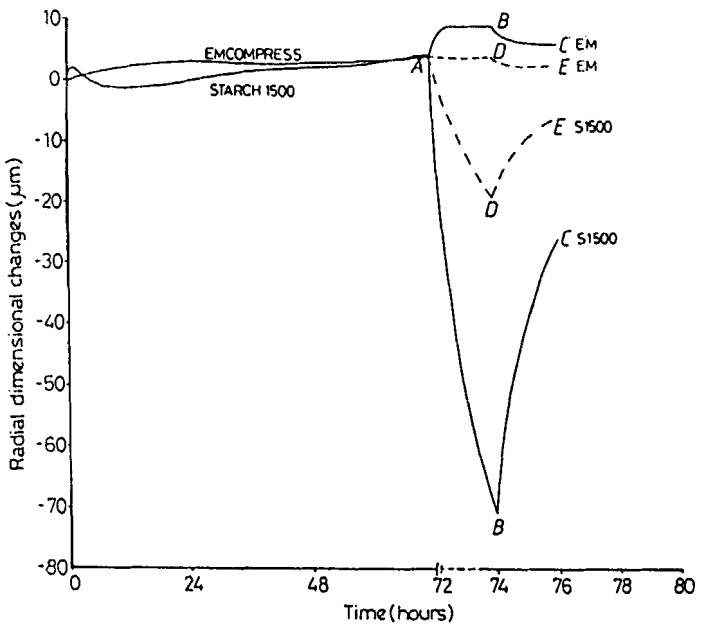

FIGURE 4b
Radial Dimensional Changes of Tablets During Simulated Storage and Coating Temperature Cycles. Comparison of Emcompress and Starch 1500.

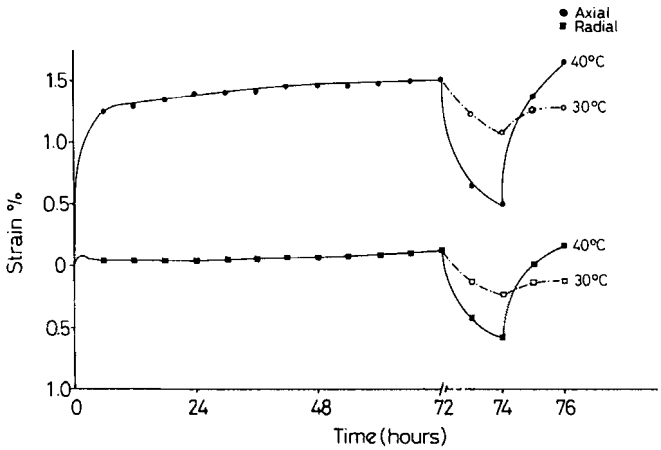

FIGURE 5a
Comparison of Changes in Axial and Radial Strain of Maize Starch Tablets During a Simulated Storage and Temperature Cycle.

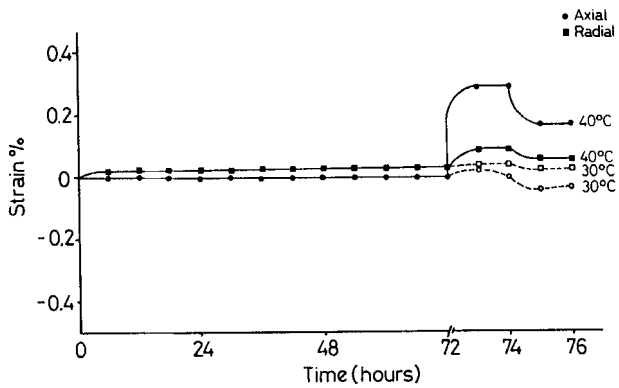

FIGURE 5b
Comparison of Changes in Axial and Radial Strain of Emcompress Tablets During a Simulated Storage and Temperature Cycle.

ambient storage period. In the following minutes the effect of water loss became more dominant causing contraction of the tablet. This kind of behaviour was not observed on the tablets of Emcompress axially and on any of the samples radially. Apart from this effect no overlying trend has been observed as an influence of ambient storage period on the subsequent axial and radial dimensional changes of tablets.

On allowing the tablets to cool back to room temperature, their dimensional stability had not returned at the end of two hours. Thus, it can be proposed that whilst

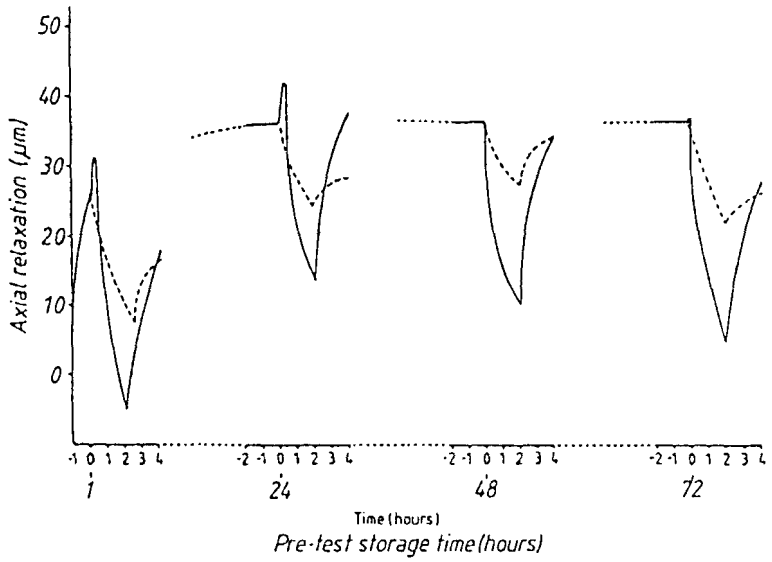

FIGURE 6
Effect of Initial Storage Time on Axial Dimensional Changes of Avicel PH101 Tablets During a Simulated Storage and Temperature Cycle.

thermal equilibration occurred during these two hours, the heating/cooling cycle had precipitated further isothermal viscoelastic expansion., Absorbed moisture could also have had a lubrication action within the compacted material at grain boundaries (13).

Change in Moisture Content of Tablets:

Throughout the discussion of the results, a concept concerning the contraction of tablets due to moisture loss at high temperatures and expansion of them due to moisture uptake when they were cooled to ambient temperature has been put forward to explain the characteristic behaviour of the tablets of Avicel, maize starch and Starch 1500 when exposed to temperatures which mimic the film coating process. In order to verify this suggestion, as well as to find out why the tablets of Emcompress differ from the others, the moisture content of tablets which had been exposed to the same simulated conditions were quantified. Measurements were taken on completion of each storage stage (i.e. at O, A, B, C, D and E in Figure 2). Percentage moisture content of tablets was expressed as a percentage of weigth of dry tablets.

The results for samples of Starch 1500 and Emcompress are presented in Tables 1 and 2; the moisture content changes in tablets formed from other materials exhibited similar characteristics. Their moisture content remained the same from the time of compression (O) and during storage under ambient conditions until subjected to heat (at A). It was observed that the tablets, indeed, lost moisture during exposure to heat and water loss was greater at 40°C (B) than at 30°C (D). Once the tablets were allowed to re-equilibrate to room temperature, the water was regained and the moisture content of the

TABLE 1

Ambient Air Humidity and Corresponding Moisture Content of Starch 1500 Tablets During Storage and Temperature Cycles.

Stage* During Simulated Coating Run	Ambient Air Temp.(C°)	RH (%)	Tablet Moisture Content (%)
O	23	40	10.3
A	23	40	10.4
B	40	14	7.1
C	23	40	9.3
D	30	22	8.5
E	23	40	10.0

(*) see Figure 2

TABLE 2

Ambient Air Humidity and Corresponding Moisture Content of Emcompress Tablets During Storage and Temperature Cycles.

Stage* During Simulated Coating Run	Ambient Air Temp.(C°)	RH(%)	Tablet Moisture content (%)
O	23	40	21.0
A	23	40	20.5
B	40	14	19.0
C	23	40	20.5
D	30	22	19.0
E	23	40	19.6

(*) see Figure 2

tablets had reached almost the same value as the beginning (C and E). The changes in percentage moisture content during the temperature cycle were the greatest for the tablets of maize starch and Starch 1500, and followed by the tablets of Avicel. The high ability for moisture uptake of these materials with increasing percentage of relative humidity is well known.

Similar characteristics were observed on the samples of Emcompress, too. However the changes in percent moisture content of these tablets as relative humidity changed were insignificant and apparently did not influence the thermal expansion and contraction of the material. It is well documented that Emcompress does not lose moisture easily at low temperatures and shows no moisture uptake at low relative humidities (11,24,25).

CONCLUSIONS

The results presented in this work have shown that the dimensional changes which take place due to viscoelastic recovery during an extended ambient storage are

significant and a major part of them is completed in about 24 hours after the ejection of the tablet from the die. During the film coating process, however, tablets are exposed to a temperature cycle (i.e. heating and cooling phases) which promotes *greater and more important* dimensional changes as a result of temperature and moisture variations. Besides, the magnitude of these dimensional changes is not dependent on the preliminary ambient storage time, but on the inlet air temperature of the coating run and the percentage relative humidity of the tablet bed. The most significant dimensional changes occur when the fully coated tablets are allowed to re-equilibrate to room temperature on completion of the process and onwards. It is during this stage that the tablet swells due to moisture uptake and subsequent greater expansion occurs. Thus, a high internal stress within the film coat is created by this factor which may exceed the tensile strength of the film or the adhesion force acting at the film/tablet interface and cause major film coating defects such as cracking, edge splitting and peeling or bridging of the intagliations.

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