DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 17(14), 2005-2016 (1991)

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

PART III: EXPOSURE TO TEMPERATURES AND RELATIVE HUMIDITIES WHICH MIMIC THE FILM COATING PROCESS

E. OKUTGEN,[1] J.E. HOGAN[2] and M.E. AULTON[1]

1Department of Pharmacy, Leicester Polytechnic,
Leicester, LE1 9BH, UK
2Colorcon Ltd, Murray Road, St Pauls Cray,
Orpington, Kent, BR5 3QY, UK

ABSTRACT

Dimensional changes of tablets compressed from maize starch were measured by means of a free-armature transducer rig under three possible simulated film coating conditions (30°C and 45%RH, 40°C and 33%RH, and 45°C and 20%RH) for one hour and then during re-equilibration to ambient temperature and relative humidity until no further significant changes were detected. It was found that these changes were normally greater at the stage of re-equilibration of the tablets to ambient conditions rather than at the stage of exposure itself. Tablet expansions were observed to be greatest in cores which had been exposed to higher temperatures and lower relative humidities. The volume increase of freshly coated tablets due to moisture uptake is of great interest since it may produce high internal stress within the coat and cause coating defects such as cracking, edge splitting and peeling and/or bridging of the intagliations. Estimates have been made to emphasise the importance of the role played by these volume increases on the total internal stress created within the film coat. Some practical implications to reduce the internal stress caused by swelling of tablet core is also discussed.

INTRODUCTION

Film coating defects, such as cracking, edge splitting, peeling and bridging of intagliations are known to be caused by the build up of stress within the film (1,2). It is suggested that the total internal stresses within a film coat, P, is the summation of P_S (the stress which develops as a result of film shrinkage following solvent loss by evaporation (3)), P_T (the stress which arises from changes in temperature during the coating process as a result of differences in the thermal expansion coefficients of the film coat and the tablet substrate (4)) and P_V (the stress resulting from volume changes of the tablet core as a result of water sorption (5) and viscoelastic strain recovery). If the stress created in the film by these factors exceeds the tensile strength of the film, cracks (either micro or macroscopic in nature) and edge splitting can occur and destroy the integrity of the film. If the internal stress exceeds the forces of adhesion holding the film to the substrate, local detachments and bridging of the intagliations can appear (6,7).

Banker et al. (8) demonstrated that the swelling of hydroxypropyl cellulose film coated tablet cores containing microcrystalline cellulose and calcium carbonate in various proportions caused the coat to break after approximately 6 hours whereas this effect was not observed with cores containing dicalcium phosphate dihydrate whose total moisture uptake was insignificant and complete within 2-3 hours. This could be attributed to differences in core expansion.

In recent work (9), it was observed that tablets exposed to temperatures which mimic the film coating process undergo extensive dimensional changes due to temperature and moisture variations. The most significant dimensional changes occur on re-equilibration of the tablets to room temperature; a stage that corresponds to the completion of the film coating process. In the present work, the significance and consequences of the dimensional changes of tablet cores exposed to the influence of changes in both humidity and temperature which simulate the conditions of a tablet bed during and after a typical film forming process are studied. The contribution of these factors in creating internal stress within the film coat is also discussed. The experimental conditions were based upon the results obtained from temperature and humidity measurements carried out within a bed of tablets during an actual aqueous film coating run in a Manesty Accela-Cota (10).

MATERIALS AND METHODS

Materials and Apparatus:

Maize starch, B.P. was used as the tabletting material in this work due to its highly pronounced response to temperature and moisture variations, and to the extensive viscoelastic expansion undergone by tablets formed from this material after compression (9). A Monsanto Tensometer 10 (Monsanto, Swindon, UK) was employed for the compaction of 10mm diameter and 3.1mm thick, flat-faced

tablets. Dimensional changes of these tablets were measured by a free-armature transducer rig. The details of this apparatus is given elsewhere (9). The readings for temperature and relative humidity were taken with a Humidity and Temperature Indicator HMI 31 (Vaisala, Sweden). In order to produce the required temperature and relative humidity conditions which simulate a typical aqueous film coating process, a Controlled Environment Cabinet (Fisons, UK) was used.

Methods:

Prior to each test, the compressed tablets were stored at ambient laboratory conditions (23.2±3°C and 31.4±7%RH) for 24 hours after their compression. This period allowed the tablets to release the major component of their viscoelastic strain recovery. This has been found not to influence the subsequent dimensional changes of tablets during the film coating process (9).

The free-armature transducer rig was placed in the environment cabinet together with a thermocouple and the humidity indicator. Based upon the results of mean equilibrium values of relative humidity obtained at certain temperatures at the centre of the tablet bed (10), the environment cabinet was set to provide temperatures of 30, 40 and 45°C at relative humidities of 45, 33 and 20%, respectively. Prior to each run, the cabinet was left to operate for at least four hours to ensure that the transducer rig and the cabinet itself equilibrated to these conditions before the initiation of the experiments.

The tablets, which had been maintained at ambient conditions for 24 hours, were placed underneath the transducer armature and exposed to the controlled temperature and relative humidity environment for one hour. At the end of this period, the environment cabinet was turned off and the sealed doors were opened to allow the air in the cabinet to equilibrate back to ambient laboratory conditions, again to simulate typical film coating procedures. Measurements were recorded until no further significant dimensional change of the tablets was detected. The same procedure was repeated at each test conditions and for both axial and radial settings of the free-armature transducer rig on replicate tablets.

Measurements of the movements undergone by the rig alone were also taken during 'blank' runs under the same conditions in order to compensate for thermal expansion/contraction of the rig; thus the net magnitude of tablet dimensional changes could be calculated. The readings for temperature and relative humidity within the cabinet were taken before the test was started, during exposure to test conditions, then at 5 minutes intervals during the re-equilibration to ambient conditions until no further significant change was detected.

RESULTS AND DISCUSSION

The plots in Figures 1 to 6 illustrate the axial and radial dimensional changes undergone by the tablets of maize starch during exposure to three possible film

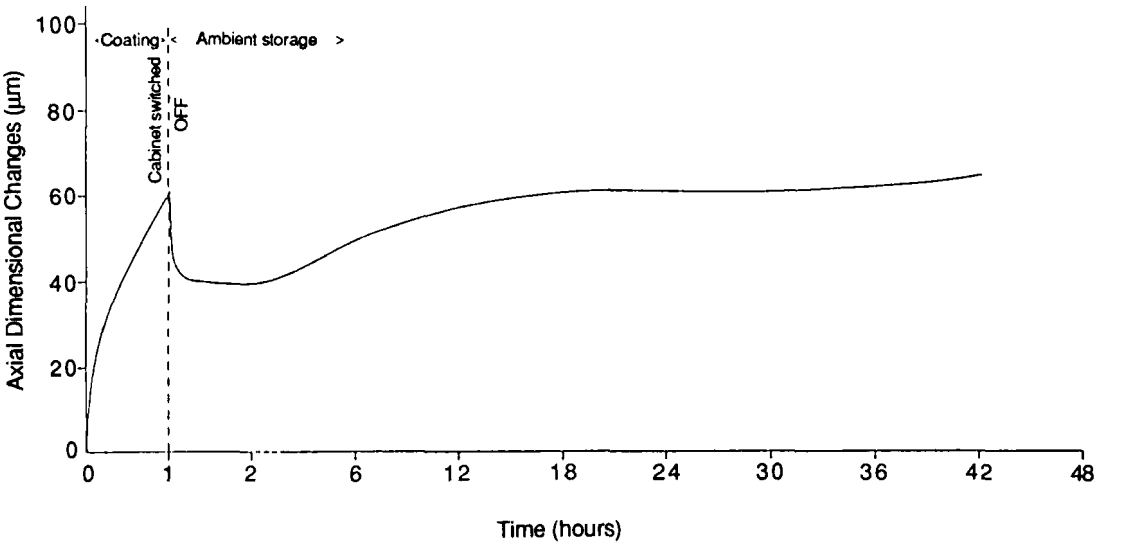

FIGURE 1

Axial dimensional changes of maize starch tablets during exposure to 30°C-45%RH test conditions for one hour and re-equilibration to ambient conditions

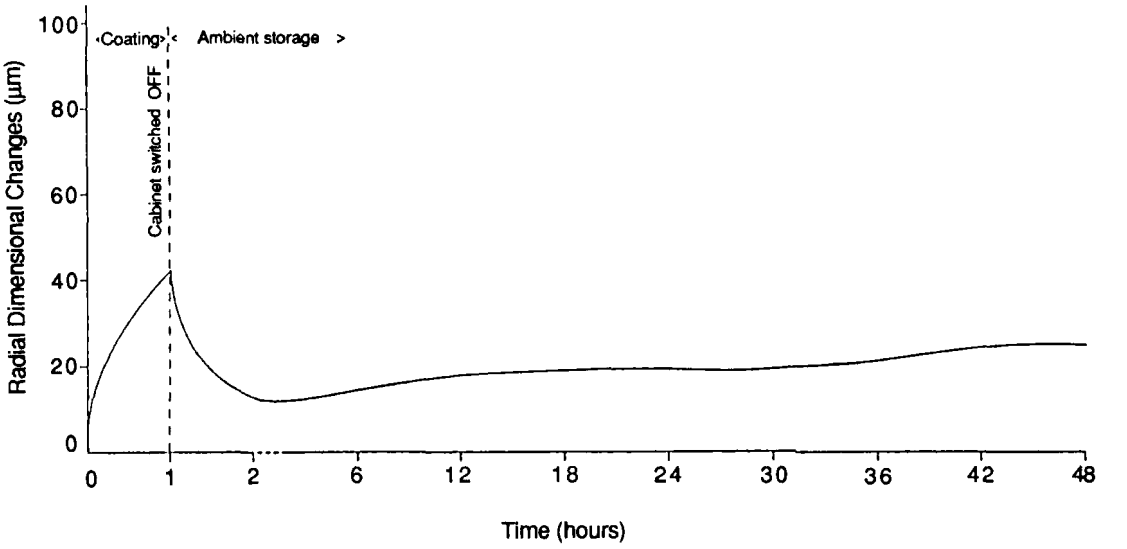

FIGURE 2

Radial dimensional changes of maize starch tablets during exposure to 30°C-45%RH test conditions for one hour and re-equilibration to ambient conditions

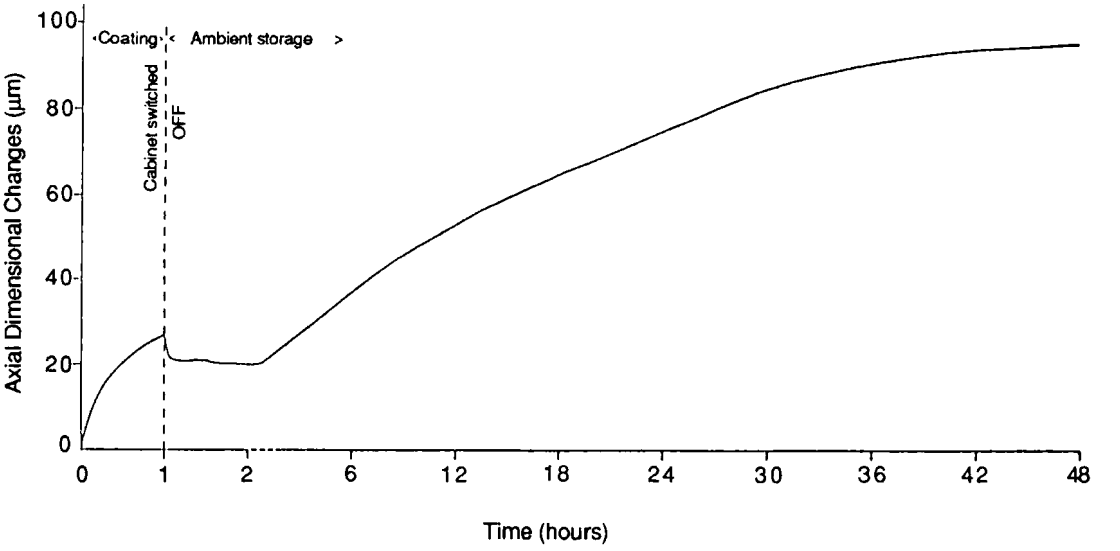

FIGURE 3

Axial dimensional changes of maize starch tablets during exposure to 40°C-33%RH test conditions for one hour and re-equilbration to ambient conditions

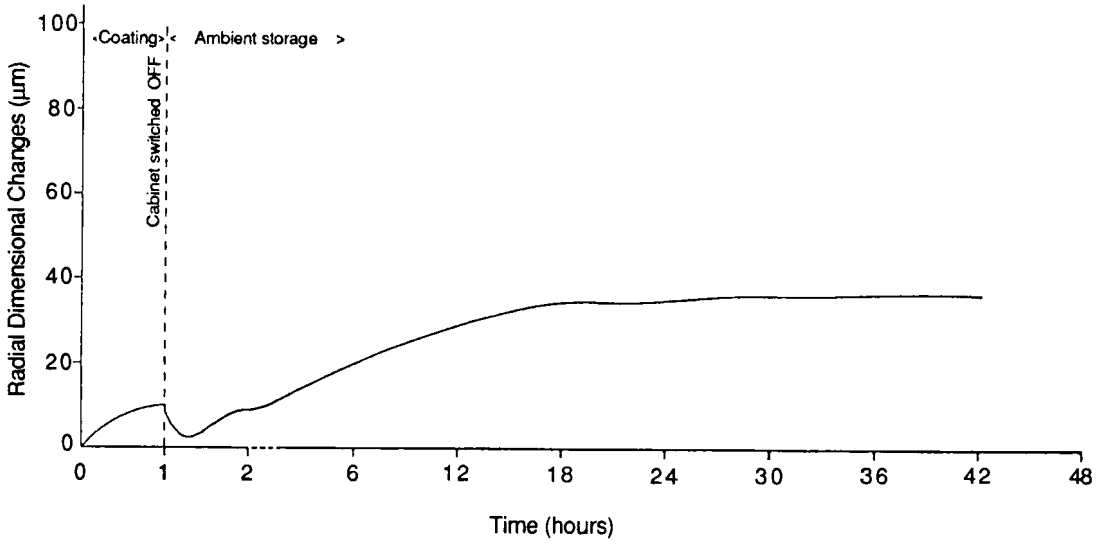

FIGURE 4

Radial dimensional changes of maize starch tablets during exposure to 40°C-33%RH test conditions for one hour and re-equilibration to ambient conditions

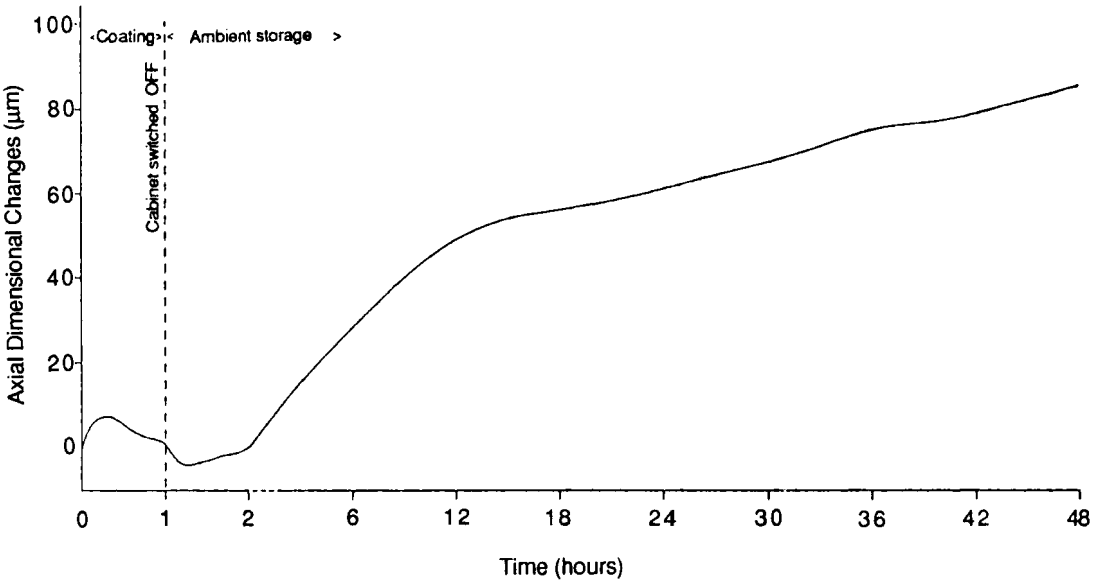

FIGURE 5

Axial dimensional changes of maize starch tablets during exposure to 45°C-20%RH test conditions for one hour and re-equilibration to ambient conditions

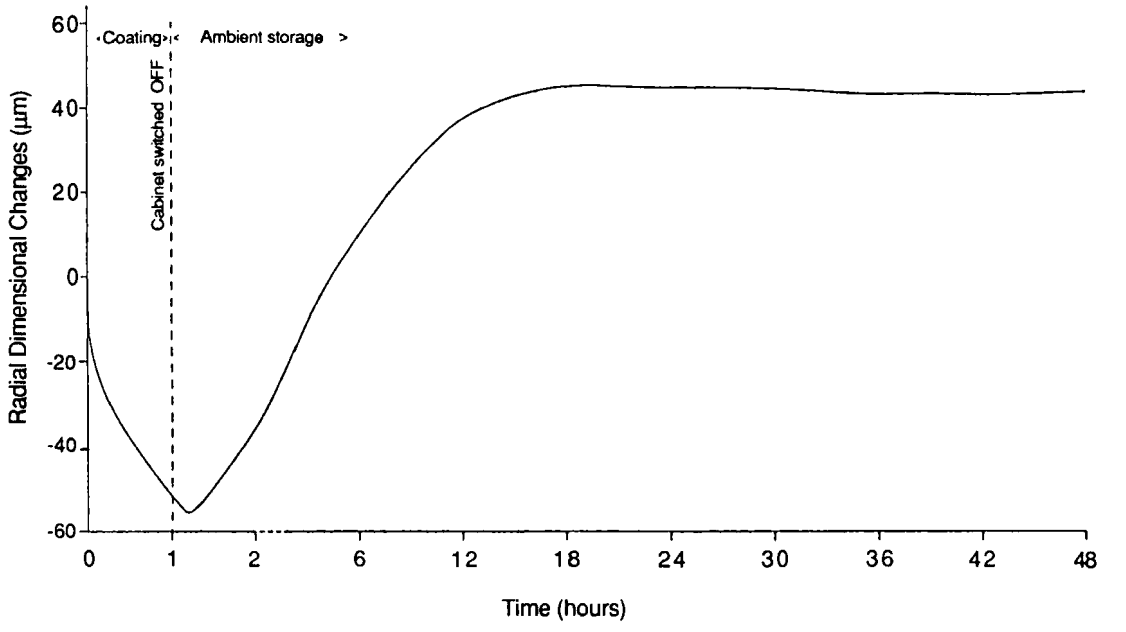

FIGURE 6

Radial dimensional changes of maize starch tablets during exposure to 45°C-20%RH test conditions for one hour and re-equilibration to ambient conditions

coating conditions for one hour and then, during their re-equilibration to ambient conditions.

Dimensional Changes Occurring During a Film Coating Process:

The characteristic patterns exhibited at the stage where the tablets of maize starch were exposed to temperatures and relative humidities simulating a film coating process depended to a great extent on the test conditions. The tablets exposed to test conditions of 30°C and 45%RH (Figures 1-2), and 40°C and 33%RH (Figures 3-4) for one hour expanded at high rates, being greater in the former case. The expansion in the axial direction was greater than in the radial direction. The tablets exposed to the test conditions of 45°C and 20%RH (Figures 5-6), however, underwent a gradual axial contraction during the one hour exposure after a rather insignificant expansion which took place in the first 15 minutes. Radially, only contraction was observed.

It can be suggested that the moisture absorption and desiccation characteristics of maize starch tablets at different test conditions is responsible for this behaviour. If the tablets are exposed to these test temperatures, without controlling the relative humidity (9), only contraction is observed both axially and radially due to loss of water from the tablets at low humidity levels during that stage. In the present work, however, the relative humidities in the test environment were higher than ambient conditions normally expected at those temperatures. In the case of the 30°C and 45%RH test condition, both the relative humidity and the temperature are higher than the pre-test storage conditions. Thus, the expansion observed in Figures 1 and 2 over the first hour is a result of two components; (i) due to thermal expansion and (ii) due to moisture absorbtion. At the 40°C and 33%RH test conditions, the expansion over this time is lower (Figs. 3 and 4), because the test relative humidity is similar to the storage relative humidity, thus only thermal effects are observed. At the 45°C and 20%RH test conditions, the relative humidity is lower than pre-test storage conditions and therefore there are two contrasting effects; (i) thermal expansion, (ii) contraction due to water loss. This is reflected in the data shown over the first hour in Figures 5 and 6. In the case of the radial measurements, the tablets have a nett contraction over the test period showing that shrinkage due to water loss overcome any radial thermal expansion.

Dimensional Changes Occurring After a Film Coating Process:

As soon as the humidity cabinet was turned off and the sealed doors were opened, the tablets underwent an abrupt contraction in all cases (Figures 1-6) due to the rapid drop in the relative humidity and consequent water loss from the compacts. This was followed by expansion of the tablets soon after. The most pronounced contraction (when the cabinet was turned off) occurred after 30°C and 45%RH storage (Figure 1-2) due to the greatest drop in relative humidity of the

TABLE 1

Mean Percentage Maximum Nett Expansion of Maize Starch Tablets on Re-equilibration to Ambient Conditions

Test Conditions	Maximum Net Linear Expansion(%)	
	Axial	Radial
30°C-45%RH	0.72	0.12
40°C-33%RH	2.45	0.34
45°C-20%RH	2.53	0.98

environment. It took up to one hour for the test environment to approach ambient conditions and at about this time the tablets begin to expand. The major part of the tablet expansion took place in the first 5 hours of equilibration, but it still continued at a reducing rate for much longer. It has also been noticed that when the tablets had been exposed to the test conditions of higher temperatures and lower relative humidities, they underwent a higher rate of subsequent expansion. This is again due to greater amount of water-loss taking place during exposure to these conditions than the conditions of lower temperatures and higher relative humidities. Therefore, the tablets are capable of absorbing more moisture at the re-equilibration stage. It is assumed that the tablets themselves would be re-equilibrated to ambient room conditions before 5 hours, thus the continued expansion suggests that the temperature and humidity cycles undergone during this simulated film coating process have precipitated further viscoelastic strain.

The percentage axial and radial expansion of tablets on completion of each storage period at ambient conditions is presented in Table 1.

General Discussion:

Dimensional changes undergone by tablets during the phase of exposure to certain test conditions corresponding to the spraying stage of an actual film coating process are significant, but they are not as important as the extensive swelling of tablet cores taking place during the ambient storage of the freshly film coated tablets. At this stage the tablets are fully film coated and large volume increase will create large internal stresses (P_V) within the film coat which, by that time, has dried and has a lower flexibility. Additionally, following the spraying cycle, film

coated tablets are sometimes subjected to a short post-spraying stage where only the inlet and the exhaust air ducts operate. At that stage, the relative humidity in the coating chamber will drop to lower values than those presently observed (10). It can be easily predicted from the results that this would cause more moisture loss, more initial contraction of the tablet and thereby, greater volume changes as the tablets return to ambient room conditions.

Aulton et al. (11) reported that the maximum rate of volumetric expansion occurred at the edges of their compacts on prolonged storage at high humidities. Since Chow (12) and Hoffman (13) showed that the largest stresses were also found near the edges of a film when measured along the substrate/film interface and since the edges of a film coated tablet are often the thinnest part of the coating, it can be proposed that this area would be an especially favourable spot for the beginning of a failure leading to edge splitting and subsequent peeling of the film coat.

In order to estimate the internal stress (P_V) created within the film coat as a result of tablet core expansion due to moisture uptake on storage, Rowe (5) suggested Equation 1:

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

where E and ν are the Young's modulus and the Poisson's ratio of the film, respectively; ΔV is the volume change of the tablet core during storageand V is the volume of the core before storage. Employing Equation 1 and taking the example of a film coating with an E value of 10^3MPa and a ν of 0.35, Rowe (5) estimated a P_V value of 5.13MPa for a 1% volume increase in the tablet core on storage, while a 10% volume increase gave 51.3MPa which was considered to be very close to the tensile strength of such a film.

Table 2 shows calculated P_V values (based on the example of film discussed above) for actual core expansions observed in this work. During the calculations, the volume of the tablet before the moisture absorption (V) is calculated by considering the previous dimensional changes undergone by the tablet (i.e. following ejection during 24 hours ambient storage - data from (9)-, during coating process, and during sudden contraction due to moisture loss after the coating process). These P_V values are significant enough to play an important part in the development of a final effective internal stress within all film coatings.

There is no doubt that the role of P_V would be more capable of creating coating defects in the case of the presence of a more hygroscopic excipient/drug in the tablet core formulation, a hydrophilic polymer that forms films with high water permeability (14-17), and under the circumstances of storing the finished products at higher humidities.

TABLE 2

Mean Percentage Volume Increase of Maize Starch Tablets on Re-equilibration to Ambient Conditions and Resulting Internal Stress Created within a Film Coat

Test Conditions	Volume Increase(%)	P_V(MPa)
30°C-45%RH	0.946	4.853
40°C- 33%RH	3.095	15.877
45°C-20%RH	4.520	23.188

It is proposed that the total internal stress created within the film coat applied to a tablet core is the sum of three major stresses, i.e.:

$$P = P_S + P_T + P_V \qquad \text{(Eq. 2)}$$

P can be calculated by combining the equations derived by Croll (3), Sato (4) and Rowe (5) and the resulting equation is shown below:

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

In Equation 3, ϕ_S and ϕ_r are the volume fraction of solvent at the solidification point and remaining in the dry film at the ambient condition, respectively, $\Delta\alpha$ is the difference between the cubic thermal expansion coefficients of the film coat (α_c) and the tablet substrate (α_s) and ΔT is the difference between the glass transition temperature of the film (T_g) and the ambient temperature (T).

Practical Implications to Reduce P_V:

The main control of P_V is to limit volumetric changes (ΔV) and therefore to minimise water loss and gain by the tablet core. Hence, the control of the permeability of a film coat to water is of prime concern. These results have shown that greater expansion of the tablet core occurs on completion of the coating process when the tablet bed temperature is higher (i.e at higher inlet air temperature and/or lower spray rate) due to the consequent lower tablet bed relative humidity. Allen et al. (18) reported that films formed at lower spray rate were more permeable to water vapour. Since this would result in even more subsequent moisture absorption,

especially if the drug/excipient core has a great affinity for moisture, it will aggravate the development of the internal stress within the film due to volume changes of the core and may eventually cause the film coat to break.

Patel et al. (14) reported that plasticisers could enhance or retard moisture permeation through a polymer film, depending upon their concentration and type. The use of hydrophobic plasticisers often may result in a decrease in film permeability (19,20). Inclusion of pigments may decrease permeability as a consequence of particles serving as a barrier to the diffusing moisture. However, there is a level at which the polymer can no longer hold all the pigment particles together and voids are created leading to increase in moisture permeation (21,22). This point is described as 'critical pigment volume concentration' (CPVC) by Chatfield's theory (23). Film thickness is another important factor influencing the permeability of the films. Patel et al. (14), Banker et al. (15) and Parker et al. (21) reported increasing water vapour transmission rates of films with decreasing film thickness. Patel et al. (14) pointed out that this effect increased as the hydrophilicity of the film increased.

Amann et al. (24) emphasised the importance of the contact between the film and the tablet. They proposed that the lower the porosity and specific surface of the tablet, the more intimate this contact and the less the degree of moisture uptake.

Thus, in conclusion, processing variables of the coating run, storage conditions of final product, water permeability characteristics of the film coat and hygroscopicity of the content of tablet cores can be considered as the factors which have major importance on controlling the generation of internal stress within a film coat as a result of expansion of the tablet core and subsequent film coating defects.

ACKNOWLEDGEMENTS

The authors wish to thank Sandoz, Turkey for financial support to EO, Colorcon Ltd. for materials and Richard Webster for his invaluable technical assistance.

REFERENCES

1. R.C. Rowe, J. Pharm. Pharmacol., 33, 423 (1981).
2. R.C. Rowe, J. Pharm. Pharmacol., 33, 610 (1981).
3. S.G. Croll, J. Appl. Polym. Sci., 23, 847 (1979).
4. K. Sato, Prog. in Org. Coat., 8, 143 (1980).
5. R.C. Rowe, J. Pharm. Pharmacol., 35, 112 (1983).
6. S.C. Porter, Drug Cosm. Ind., Sept, 50 (1981).
7. R.C. Rowe and S.F. Forse, Acta Pharm. Technol., 28(3), 207 (1982).

8. G.S. Banker, A.Y. Gore and J. Swarbrick, J. Pharm. Pharmacol., 18, Suppl. 205S (1966).
9. E. Okutgen, J.E. Hogan and M.E. Aulton, Drug Dev. and Ind. Pharm., 17 (9), (1991).
10. E. Okutgen, M Jordan J.E. Hogan and M.E. Aulton, Drug Dev. and Ind. Pharm., 17 (9), (1991)
11. M.E. Aulton, D.N. Travers and P.J.P. White, J. Pharm. Pharmacol., 25, Suppl. 79P (1973).
12. T.S. Chow, In "Adhesion Sciences and Technology", Vol. 9B, L.H. Lee, (ed.), Plenum Publishing Corp., New York, London, 1975, p. 687.
13. R.W. Hoffman, Surf. Int. Analysis, 3(1), 62 (1981).
14. M. Patel, J.M. Patel and A.P. Lemberger, J. Pharm. Sci., 53, 286 (1964).
15. G.S. Banker, A.Y. Gore and J. Swarbrick, J. Pharm. Pharmacol., 18, 457 (1966).
16. J. Swarbrick, A.H. Amann and R.E. Lindstrom, J. Pharm. Sci., 61, 1645, (1972).
17. A.O. Okhamafe and P. York, Pharm. Acta Helv., 60(3), 92 (1985).
18. D.J. Allen, J.D. de Marco and K.C. Kwan, J. Pharm. Sci., 61, 106 (1972).
19. S.C. Porter, Pharm. Technol., 4, 67 (1980).
20. S.C. Porter, Int. J. Pharm. Technol. Prod. Manuf., 3(1), 21 (1982).
21. J.W. Parker, G.E. Peck and G.S. Banker, J. Pharm. Sci., 63, 119 (1974).
22. S.C. Porter and K. Ridgway, J. Pharm. Pharmacol., 34, 5 (1982).
23. H.W. Chatfield, "Science of Surface Coatings", Van Nostrand, New York, 1962.
24. A.H. Amann, R.E. Lindstrom and J. Swarbrick, J. Pharm. Sci., 63, 931 (1974).