(8) K. Aldous, D. Mitchell, and F. Ryan, *Anal. Chem.*, **45**, 1990(1973).
(9) J. D. Winefordner and R. C. Elser, *ibid.*, **43**(4), 24A(1971).
(10) "Carbon Rod Atomizer," Varian Techtron Corp., Palo Alto, Calif., Dec. 1970, p. 4.
(11) "High Sensitivity Sampling Systems for Atomic Absorption," RG 67210, Perkin-Elmer Corp., Norwalk, Conn., 1972, p. 3.

ACKNOWLEDGMENTS AND ADDRESSES

Received November 12, 1973, from the *Applications Research Department, Quality Control Division, Syntex Laboratories, Inc., Palo Alto, CA 94304*

Accepted for publication February 12, 1974.

[x] To whom inquiries should be directed.

Factors Affecting Water Vapor Transmission through Polymer Films Applied to Solid Surfaces

ANTON H. AMANN*, RICHARD E. LINDSTROM, and JAMES SWARBRICK[x]

Abstract □ The permeation of water vapor through cellulose acetate phthalate polymer films applied in a variety of ways to hygroscopic solid surfaces was determined at several different temperatures. The systems investigated consisted of films: *(a)* placed against a flat solid surface, *(b)* sprayed onto a flat solid surface, and *(c)* sprayed onto tablets in a rotating coating pan. The data indicate that the activation energy of the absorption process is determined by the film, while the method of film application affects the actual rates of permeation at a given temperature. The physical properties of the material being coated also affect the water vapor absorption rate.

Keyphrases □ Films, cellulose acetate phthalate polymer—water vapor permeation on hygroscopic solid surfaces, comparison of application methods and temperatures □ Permeation, water vapor—polymer films applied to solid surfaces, effects of temperature and application method □ Absorption, water vapor—solid dosage forms, effects of film application method and film material

A previous paper (1) presented the relative characteristics of water vapor permeation through free-standing hydrophilic and lipophilic polymer films used to coat pharmaceutical solid dosage forms. It was shown that the permeation coefficients for the lipophilic films were unaltered by the presence of water vapor on the distal surface of the film. In contrast, water vapor permeation through the hydrophilic films was dependent on whether the vapor pressure gradient resulted from water vapor on one or both sides of the film. This behavior was rationalized on the basis of plasticization of the film by the permeating water vapor. With water vapor present on only one side of the film, dehydration was postulated to occur. This would reduce permeation, an effect noted in earlier work (2).

The present report extends previous work to include the water vapor permeation through hydrophilic cellulose acetate phthalate films when applied to the surface of solid systems having a potential to absorb moisture. In this manner, it was hoped to evaluate the relationship between free-standing films and those applied to solid dosage forms in terms of their water vapor permeability properties. Several model systems were thus established to create a series of conditions intermediate between permeation through a free film and one applied to a tablet. Accordingly, moisture permeation was studied in systems in which: *(a)* a film of cellulose acetate phthalate was simply placed in contact with a flat disk containing calcium chloride; *(b)* the same polymer, in solution, was sprayed onto one surface of a flat disk containing calcium chloride; and *(c)* the polymer solution was used to spray coat the entire surface of conventionally shaped convex tablets containing calcium chloride.

Table I—Water Vapor Permeation through Various Applied Films of Cellulose Acetate Phthalate[a]

System	Temperature	Permeability Coefficient P^0, g hr^{-1} cm^{-1} mm Hg^{-1} $\times 10^{-7}$
Cast film placed onto disk	20°	4.12 ± 0.71[b]
	30°	3.54 ± 0.83
	40°	2.37 ± 0.22
Sprayed film on disk	20°	2.64 ± 0.11
	30°	1.99 ± 0.18
	40°	1.52 ± 0.13
Film-coated tablet	20°	0.31 ± 0.06
	30°	0.18 ± 0.07
	40°	0.09 ± 0.02

[a] Vapor pressure of 16.5 mm Hg. [b] A 95% confidence interval.

EXPERIMENTAL

Preparation of Disks and Tablets Containing Calcium Chloride—The powder mixture used for compression contained calcium chloride USP (33%) in microcrystalline cellulose[1]. Magnesium stearate (1%) was present as a lubricant. The compressed disks were prepared using flat-faced punches and die, 1.60 cm in diameter, and a press[2] set at 1816 kg (4000 lb). Under these conditions, the formation pressure was approximately 13,000 psi. The average weight of the disks was 1.586 ± 0.001 g.

Tablets were prepared from the same powder mixture using a single-punch tablet press[3] fitted with deep concave punches, 0.96

[1] Avicel, F.M.C. Corp.
[2] Carver.
[3] Stokes model E.

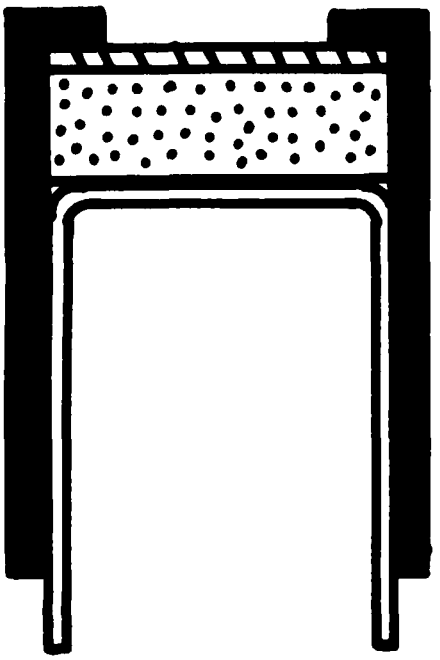

Figure 1—*Cross section of device for determining permeation through film applied to solid disk. Key:* ▧, *polymer film;* ▨, *calcium chloride disk;* ■, *rubber sleeve; and* □, *inverted glass cup.*

cm in diameter. The compression pressure was approximately 35,000 psi, the average weight was 0.281 ± 0.007 g, and the average tablet hardness was 6.2 ± 1.6 kg.

Preparation of Cellulose Acetate Phthalate Films—The compositions of the polymer solutions used in the formation of cast and sprayed films were as reported previously (1).

Spray Coating of Disks and Tablets—The flat calcium chloride disks were mounted onto glass plates by means of adhesive tape on the back of the disk. With the plate in a vertical position, the entire plate was sprayed with polymer solution from a distance of 15 cm. A forced-air spray gun was used, with the spray nozzle adjusted to give a pattern 2.54 cm wide at a distance of 15 cm when operating at a pressure of 2 psi. In this manner, a uniform film coat was applied to one surface of the disks as well as to the exposed surface of the glass plate between the disks. After drying overnight, the disks were removed.

One thousand calcium chloride tablets were placed in a 20-cm diameter coating pan, rotating at 35 rpm. Cold air was blown over the tablet bed to remove any surface dust. With the spray gun orifice set at "wide" and under a pressure of 2 psi, sufficient coating solution was sprayed on until "twinning" of the tablets was observed. Hot air was then blown into the pan to aid in the removal of solvent. This sequence was repeated until the desired thickness of film coat had been applied.

Determination of Film Thickness and Exposed Area—Film thickness was determined by means of calipers. With the disks, this was taken as the increase in thickness before and after spraying. With the tablets, half of the increase in overall thickness was held to be equivalent to the thickness of the film coat.

With the disks, the diameter of the circular aperture of the device shown in Fig. 1 was measured prior to uptake studies. The surface area of the film-coated tablets was computed from the dimensions (wheel diameter, height of curved surface, diameter, and height of flat edge) of the tablet.

Moisture Permeation of Cellulose Acetate Phthalate Films—A calcium chloride disk, with either an applied cast film or a sprayed film, was placed in the device shown in Fig. 1 and positioned in a temperature-controlled oven containing a single-pan analytical balance. Five disks were used for each run. The vapor pressure within the oven was maintained at 16.5 mm Hg. The steady-state rate of water uptake was determined as described elsewhere (1). Blank runs were undertaken using aluminum disks in place of the polymer film to confirm that weight increases were due solely to water permeation across the exposed area of the film.

Batches of tablets were also studied under similar conditions of temperature and vapor pressure over the requisite period of time. In this case, however, the tablets were simply placed in the oven.

The permeability coefficient, P, was calculated as described previously (1), as was P^0, the permeability coefficient at zero film thickness.

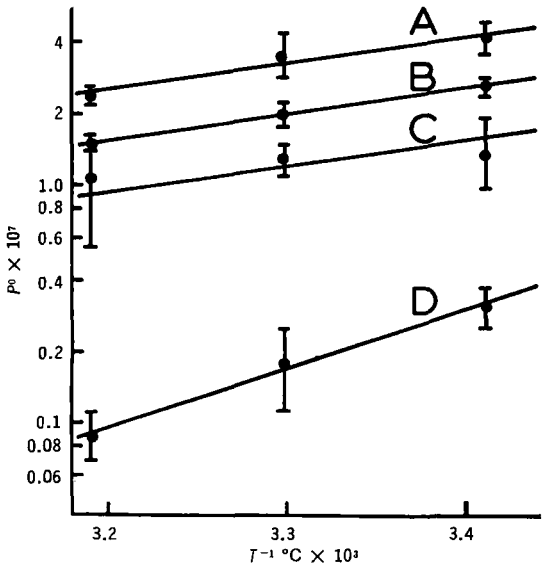

Figure 2—*Semilogarithmic plot of* P^0 versus $1/T$ *for the systems studied. Key: A, cast film placed against disk; B, film sprayed onto disk; C, free film with moisture on one side (1); and D, film sprayed onto tablets.*

Table II—Water Vapor Absorption of Uncoated Disks and Tablets Containing Calcium Chloride (33%) in Microcrystalline Cellulose[a]

System	Temperature	Rate of Water Vapor Absorption, g hr^{-1} cm^{-2} mm $Hg^{-1} \times 10^{-4}$
Uncoated disks	20°	14.8
	25°	9.8
	30°	5.3
Uncoated tablets	20°	0.29
	30°	0.25
	40°	0.18

[a] Vapor pressure of 16.5 mm Hg.

RESULTS AND DISCUSSION

The permeation results obtained with the three systems investigated are listed in Tables I and II. Permeation coefficients are plotted *versus* $1/T$ in Fig. 2. Data from free films (1) are included for comparison. Of interest in Fig. 2 is the degree of parallelism between the permeability of precast films placed against disks (A), spray-coated disks (B), and free precast films with moisture on one side (C). These Arrhenius-type plots suggest that: *(a)* the activation energy for the absorption process, *Ea*, is determined by the film, and *(b)* the actual rates of permeation at any given temperature depend on the method of film application. This latter contention is compatible with the observation made with free-standing hydrophilic polymer films, namely that the rate of water vapor permeation increases with the amount of moisture on the distal film surface (1). With systems where the film is applied to a solid surface, the distal surface is the internal one. Thus, while the permeating vapor is able to diffuse from the distal surface of the free-standing film, it is less able to do so when the film is applied to the tablet or disk surface. As a result, variations in the

method of film application may lead to differences in the steady-state accumulation of moisture at the distal surface. This, in turn, would alter the film's permeation characteristics through plasticization. The data in Fig. 2 suggest that the more intimate the contact between the film and the tablet and/or disk, the less the degree of moisture accumulation and the lower the plasticizing effect.

A second important factor relating to moisture uptake by films coated on disks or tablets is seen in Fig. 2. When contrasting the plot for the film sprayed onto the disk made with the press (B) with that for the tablet (D) made on the single-punch tablet press, it is apparent that the energy of activation varies with the character of the material being coated. Thus, the disks were prepared under approximately 13,000 psi pressure while the tablets were formed under 35,000 psi pressure. This difference is further emphasized in Table II, which gives the rate of water vapor uptake by the uncoated disks and tablets. The rate of water vapor uptake is approximately 20–50 times faster and obviously more temperature dependent for the disks than for the tablets.

Over the pressure range studied, it is reasonable to expect that the disks would have a higher porosity and specific surface than the tablets. This would account for the more rapid uptake of moisture by the disks. Assuming that the specific surface and porosity of the compressed tablet are critical and, hence, rate limiting, one would expect the moisture uptake by the disks to become related increasingly to the temperature-dependent rate of water vapor condensation. When a film is applied, however, the situation changes. The rate of water absorption by the disks, which in the uncoated state are able to absorb water considerably faster at all temperatures, is largely controlled by the film. Thus the activation energy for the spray-coated disks (B) is the same as that for the free films (C).

The coated tablets, however, present two barriers to the water permeation and absorption process. The first is due to the film. The second is the relatively low specific surface and low porosity interface of the compressed tablet. In comparison to the disk, the passage of water molecules into the tablet is restricted and the activation energy becomes a function of both factors. In support of this argument, the energy of activation for the water vapor absorption process with coated tablets is 11.9 kcal/mole, in reasonable agreement with the sum of the activation energies for permeation of the film (5.3 kcal/mole) and the rate of water uptake by the uncoated tablet (5.5 kcal/mole).

In conclusion, the results of this study indicate that the rate of water vapor absorption by solid dosage forms, film coated with a hydrophilic powder, is determined by the method of film application and the physical characteristics of the coated material. The data suggest that, with this type of film, the rate of absorption may be decreased by ensuring that the film is in intimate contact with the dosage form and by compressing the tablet to the maximum degree feasible compatible with disintegration considerations.

REFERENCES

(1) J. Swarbrick, A. H. Amann, and R. E. Lindstrom, *J. Pharm. Sci.*, **61**, 1645(1972).

(2) J. Swarbrick and A. H. Amann, *J. Pharm. Pharmacol.*, **20**, 886(1968).

ACKNOWLEDGMENTS AND ADDRESSES

Received January 10, 1974, from the *Pharmaceutics Section, School of Pharmacy, University of Connecticut, Storrs, CT 06268*

Accepted for publication February 26, 1974.

* Present address: Abbott Laboratories, North Chicago, IL 60064

ˣ To whom inquiries should be directed. Present address: Sterling-Winthrop Research Institute, Rensselaer, NY 12144

Flexure Test for Determination of Tablet Tensile Strength

S. T. DAVID* and L. L. AUGSBURGERˣ

Abstract □ A new method for determining the tensile strength of tablets is proposed utilizing two fulcrums and a knife edge. The fulcrum and knife edge pieces were affixed to the platens of a motorized tablet hardness tester. The new method was found to give rapid, reproducible results which agreed well with tensile strength values obtained from diametral compression. In contradistinction to diametral compression, tablets invariably failed in tension using the new method, as evidenced by uniform splitting into halves.

Keyphrases □ Tensile strength, tablets—new flexure test, apparatus and equations □ Tablets, tensile strength—new flexure test for determination, apparatus and equations □ Flexure test—determination of tablet tensile strength, compared to diametral compression method, apparatus and equations

Several approaches have been utilized in the evaluation of tablet strength. Some of the more popular designations for values relating to the strength of tablets are bending resistance (1), crushing force (2), and tensile strength (3–7). Of these, tensile strength is of more fundamental importance because it is independent of tablet dimensions and provides a measure of the inherent strength of the compacted material (6, 7).

DISCUSSION

Fell and Newton (3, 4) determined tensile strength using a diametral compression test similar to that commonly used to determine tablet crushing strength where tablets are compressed between two flat platens. If the tablets fail in tension, tensile strength may be computed from:

$$\sigma_0 = \frac{2P}{\pi D t} \qquad \text{(Eq. 1)}$$

where σ_0 is the tensile strength, P is the applied load, D is the tablet diameter, and t is the tablet thickness. Based on elastic theory, the derivation of this equation may be found in standard texts (8–10). In general, this involves a consideration of radial pressures and concentrated loads acting along a diameter of a circular disk and an analysis of the state of stress in the circular disk in terms of rectangular stress components. The principal assumptions are that the disk obeys Hooke's law, that the disk is isotropic, and that the modulus of elasticity in tension and compression is the same. For the vertical central section, which would represent the section in a flat-faced tablet where failure takes place, compressive stresses are at a minimum at the center of the load diameter and infinite at the extremities where the