

# Effect of Absorbents on Water Vapor Transmission of Free and Applied Polymer Films

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**Abstract** □ The influence of different types of absorbents on moisture transmission through free (cast films) and applied (coated tablets) polymer films was investigated. In free film studies, lubricated granulations were considered to be the absorbent. The compressed tablet was considered to be the absorbent in applied film studies. The results suggested that, using the same film formulation and film thickness in all cases, the polymer film reduced moisture absorption to the same degree, independent of the absorbent used, suggesting a constant moisture permeation. The results of the free film studies also simulated those of the applied films, allowing the correlation of the data.

**Keyphrases** □ Polymer films—free and applied, effect of different types of absorbents on moisture transmission □ Absorbents—effect on moisture transmission through free and applied polymer films

Numerous techniques have been developed and published for studying water vapor transmission properties of free films. The methods employed the utilization of permeability cups (1) or vapor transmission cells (2). The data obtained from free film studies allowed for quantification of factors influencing water vapor transmission such as film thickness, types of polymers used, cross-linking and crystallinity (3), plasticizers (4), and conditions surrounding the film as well as the method of film preparation (5).

In applied film studies, when tablets were coated with a polymer film, the rates of moisture uptake of tablet matrixes containing calcium chloride were determined as a function of film coat thickness and calcium chloride content of the matrix (6). These tablets were film coated with various lipophilic, hydrophilic, and mixed lipophilic-hydrophilic polymer systems. The results indicated that the water vapor transmission characteristics of applied films were different from those of free films. Recently (7), several model systems created a series of conditions intermediate between permeation through a free film and one applied to a tablet. It was shown that the physical characteristics of the absorbent influence the rate of water vapor transmission through the polymer film.

The objective of free film evaluation is to predict what may happen in the applied state. Therefore, one is confronted with certain limitations if free film studies are to exemplify the applied state. Two important considerations are: (a) solid dosage form or granulation on one side of the film, and (b) water vapor having a finite equilibrium level of absorption onto granules, powders, or tablets at any one temperature and vapor pressure.

In the past (2, 5-7), when data were evaluated using Fick's law in combination with Henry's law, the vapor pressure gradient was held constant and water vapor was to diffuse through a film and be absorbed into or by an infinite sink. Thus, a linear relationship was established when the transmitted water vapor

was plotted *versus* time. If a finite equilibrium condition can be reached and the vapor pressure gradient changes with time, then a deviation from linearity might be expected.

The purposes of this paper are to present data showing what influences different types of absorbents have on water vapor transmission through free and applied polymer films and to establish a relationship between free and applied polymer films.

## EXPERIMENTAL

**Preparation of Cast Films**—Twenty milliliters of hydroxypropyl methylcellulose<sup>1</sup> polymer solution was poured onto glass plates. Glass rings, with a diameter of 13.3 cm, were used to control the area of spreading. The composition of the polymer solution was: hydroxypropyl methylcellulose NF, 15 cps, 4.5 g; absolute alcohol USP, 45.0 ml; and methylene chloride, *q.s.*, 100.0 ml.

After the solvents were allowed to evaporate overnight, films were placed into a 40° chamber for 24 hr. Prior to using these films in water vapor transmission studies, they were equilibrated for at least 24 hr in a humidity chamber. Film thickness was determined by a micrometer and was found to be  $8.0 (\pm 0.5) \times 10^{-3}$  cm.

**Water Vapor Transmission Studies through Free Polymer Films**—Permeability cups<sup>2</sup> were used to hold 25 g of various pharmaceutical granulations (hereafter referred to as absorbents). These absorbents represented six different dosage forms. The pre-treated film was placed onto the cup and sealed with melted white ceresin wax<sup>3</sup>. The seal was allowed to cool before using the cell. The area of transmission was 41.7 cm<sup>2</sup>.

Water vapor uptake was measured by placing these cups in a desiccant jar containing saturated sodium chloride solution. This procedure resulted in a vapor pressure condition of 17.8 mm Hg at 25° (8). The desiccant jar was placed in a controlled room at  $25 \pm 1^\circ$ .

To ensure that moisture was not absorbed by, or transmitted through, the wax, a metal template was placed onto the cup and sealed with the wax. No weight changes occurred under the same conditions as were used for the free films.

At specified time intervals (*i.e.*, 8-12 hr), these cups were weighed on a top-loading balance having a precision of  $\pm 1$  mg.

**Tablet Preparation**—Six different types of absorbents (pharmaceutical granulations) were compressed into tablets. A 16-station rotary tablet machine, fitted with four deep cup punches, was employed. Hardness, tablet weight, and size of punches depended on the type of absorbent used. The tablets were coated by a continuous spray technique. Film thickness was determined by measuring, with a micrometer, 50 tablets before and after coating. Actual film thickness was  $8.0 (\pm 0.5) \times 10^{-3}$  cm for all six coating runs.

The exposed surface area of the tablets was calculated from the punch specifications and height of the sidewall surface.

The coated tablets, along with uncoated tablets, were placed in a 40° oven for 1 week prior to moisture uptake studies.

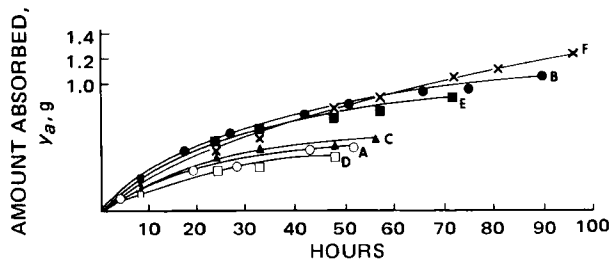
**Moisture Uptake Studies of Applied Polymer Films**—Three sets of 20 coated tablets, as well as uncoated tablets, were placed in a petri dish and subjected to the same experimental design as free films.

**Measurement of Water Vapor Transmission**—As anticipated, in the presence of a polymer film a nonlinear relationship

<sup>1</sup> Shinetsu Chemical Co.

<sup>2</sup> Thwing Albert Instrument Co., Philadelphia, Pa.

<sup>3</sup> Strahl and Pitch, West Babylon, Long Island, N.Y.



**Figure 1**—Amount of moisture absorbed onto granules as a function of time in the presence of a polymer film. Key: O, Formulation A; ●, Formulation B; ▲, Formulation C; □, Formulation D; ■, Formulation E; and X, Formulation F.

was found when the amount of moisture absorbed,  $y_a$  (considered to be a function of amount of moisture transmitted), was plotted versus time,  $t$  (Fig. 1). When the reciprocal functions were plotted ( $1/y_a$  versus  $1/t$ ), linearity was seen (Fig. 2). A possible explanation for this relationship is as follows.

If the vapor pressure gradient is held constant, then water vapor transmission follows the equation (9):

$$y_t = PA(p_0 - p)t \quad (\text{Eq. 1})$$

where  $y_t$  is the concentration of moisture transmitted at time  $t$ ,  $A$  is the area of transmission,  $P$  is the average permeability coefficient as a function of the distance or length of the concentration gradient (usually film thickness), and  $(p_0 - p)$  is the difference in vapor pressure between both sides of the film.

Should no moisture be present on one side of the film and should a limited space be available for moisture to occupy, then Henry's law would apply in that:

$$p = Sy_t \quad (\text{Eq. 2})$$

where  $S$  is a proportionality constant, relating pressure to the concentration of moisture. Equation 2 can be substituted into Eq. 1 when at  $t = 0$ ,  $y = 0$ ; then:

$$y_t = PA(p_0 - Sy_t)t \quad (\text{Eq. 3})$$

or:

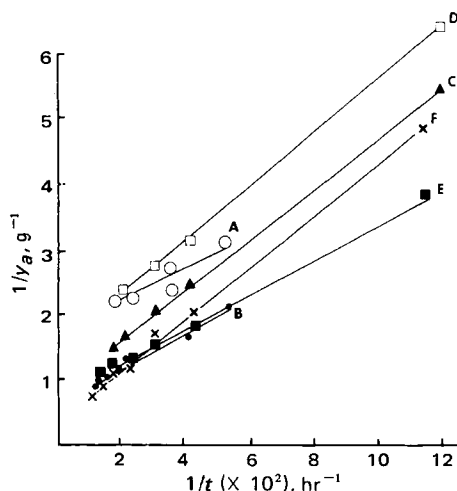
$$y_t = PAp_0t - PASy_tt \quad (\text{Eq. 4})$$

Solving for  $y_t$  then gives:

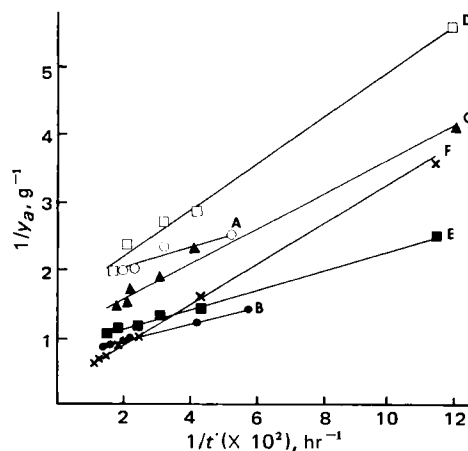
$$y_t = (PAp_0t)/(1 + PAST) \quad (\text{Eq. 5})$$

Since the amount of moisture absorbed,  $y_a$ , is measured, a relationship can be established between the amount transmitted and the amount absorbed in the following manner. The rate of moisture transmission,  $(dy/dt)_t$ , can be expressed as:

$$(dy/dt)_t = -k_1Ap \quad (\text{Eq. 6})$$



**Figure 2**—Amount of moisture absorbed onto granules as a function of time in the presence of a polymer film. Data plotted according to Eq. 17. Key: see Fig. 1.



**Figure 3**—Amount of moisture absorbed onto granules as a function of time in the absence of a polymer film. Data plotted according to Eq. 17. Key: see Fig. 1.

where  $k_1$  can be considered the moisture transmission constant. The absorption rate,  $(dy/dt)_a$ , can be expressed as:

$$(dy/dt)_a = k_2Ap - k_3x_a \quad (\text{Eq. 7})$$

where  $k_2$  and  $k_3$  are the absorption and desorption rate constants, respectively; and  $x_a$  is the amount of moisture absorbed,  $y_a$ , per unit weight of absorbent,  $m$ . If one assumes a steady-state condition, then the rate of moisture transmitted is equal to the rate of moisture absorbed. Thus,  $(dy/dt)_t = (dy/dt)_a$  and:

$$-k_1Ap = k_2Ap - k_3x_a \quad (\text{Eq. 8})$$

Solving for the vapor pressure,  $p$ , then gives:

$$p = (k_3x_a)/(k_1 + k_2)A \quad (\text{Eq. 9})$$

By definition, the equilibrium constant,  $K_e$ , is equal to:

$$K_e = (k_1 + k_2)/k_3 \quad (\text{Eq. 10})$$

Then Eq. 9 can be expressed as:

$$p = x_a/K_eA \quad (\text{Eq. 11})$$

As mentioned before, when at  $t = 0$ ,  $p = 0$  and  $y_a = 0$ , then Henry's law (Eq. 2) can be applied and Eq. 11 can be written as:

$$y_t = x_a/K_eSA \quad (\text{Eq. 12})$$

Substitution of Eq. 12 into Eq. 5 then gives:

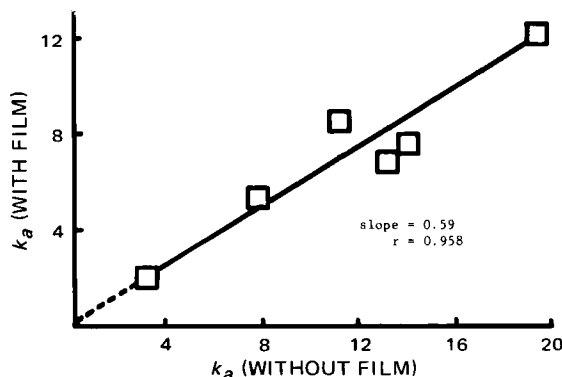
$$x_a/K_eSA = (PAp_0t)/(1 + PAST) \quad (\text{Eq. 13})$$

Since:

$$x_a = y_a/m \quad (\text{Eq. 14})$$

then:

$$y_a/mK_eSA = (PAp_0t)/(1 + PAST) \quad (\text{Eq. 15})$$



**Figure 4**—Comparison of absorption rate constants from free film studies.

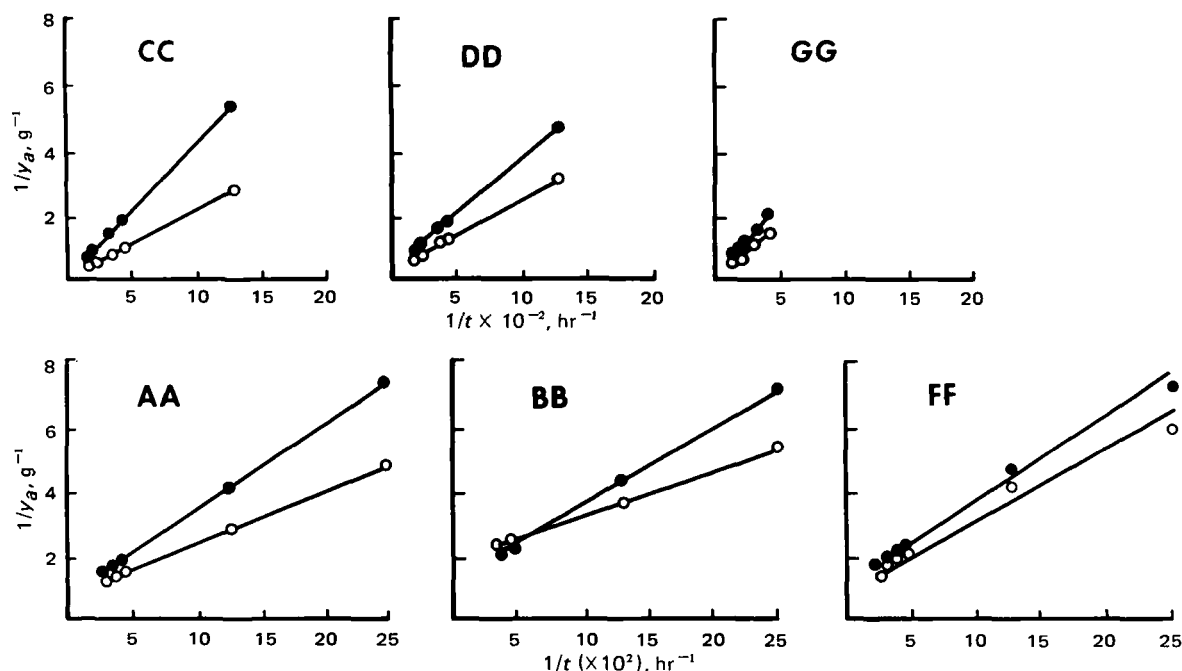


Figure 5—Data for coated (O) and uncoated (●) tablets plotted according to Eq. 17.

or:

$$mK_eSA/y_a = 1/(PAp_0t) + S/p_0 \quad (\text{Eq. 16})$$

and, therefore:

$$1/y_a = 1/(SPK_eA^2mp_0)t + 1/K_eAmp_0 \quad (\text{Eq. 17})$$

A plot of  $1/y_a$  versus  $1/t$  should yield a straight line. The following were calculated by plotting the data according to Eq. 17. The quantity  $SP$  was considered to be the apparent absorption rate constant,  $k_a$ :

$$k_a = 1/(\text{slope})K_eA^2mp_0 = (\text{intercept})/(\text{slope})(A) \quad (\text{Eq. 18})$$

$$K_e = 1/(\text{intercept})Amp_0 \quad (\text{Eq. 19})$$

The absorption in the absence of a polymer film was also plotted according to Eq. 17.

## RESULTS AND DISCUSSION

The results of the absorption studies in the presence and absence of a polymer film are plotted in Figs. 2 and 3 according to Eq. 17. From the slopes and intercepts, the apparent absorption rates and equilibrium constants were calculated according to Eqs. 18 and 19 (Table I).

The presence of a polymer film (when the same formulation is compared) has no impact on the equilibrium constant (Table I).

Table I—Computation of the Rate Constants Derived from Eqs. 18 and 19, Using Pharmaceutical Granulations<sup>a</sup>

Formulation <sup>b</sup>	$k_a, \text{hr}^{-1}$ $\text{cm}^{-2} \times 10^{-4}$		$K_e, \text{cm}^{-2} \text{mm Hg}^{-1} \times 10^{-5}$	
	With-out Film	With Film	Without Film	With Film
	D	10.97	9.01	3.50 (0.35) <sup>c</sup>
F	2.92	2.16	15.40 (2.64)	13.47 (1.68)
C	7.79	5.61	5.99 (1.33)	6.49 (0.78)
A	19.40	12.20	3.39 (0.17)	3.59 (0.19)
E	13.92	7.57	6.26 (1.29)	7.59 (0.64)
B	13.52	6.98	7.48 (0.21)	7.81 (0.57)

<sup>a</sup> Area of transmission ( $A$ ) = 41.70  $\text{cm}^2$ , weight of powders ( $m$ ) = 25.00 g, and vapor pressure ( $p_0$ ) = 17.8 mm Hg. Film thickness was  $8.0 \times 10^{-3}$  cm. <sup>b</sup> See Figs. 2 and 3 for corresponding graph. <sup>c</sup> Represents  $\pm 95\%$  confidence interval.

Because there is no difference in  $K_e$ , it appears that the limiting factor in the absorption process is the absorption of moisture onto granules and not diffusion through the polymer film. At equilibrium conditions, diffusion must occur at a much faster rate than absorption. Should the film be more of a controlling factor, a shift in  $K_e$  could be expected.

Comparison of the absorption rates shows that differences exist not only from one formulation to another but also when absorption is compared in the presence or absence of a polymer film. In all cases, absorption is much slower in the presence of a polymer film. The data appear to show that the polymer film has a variable diffusion rate. If the controlling factor is the polymer film and if the absorption rate is much greater than the permeation rate, no differences would be seen in the absorption rate when all of the different absorbents are compared in the presence of a polymer film. If this is the case, the vapor pressure differential would be constant on both sides of the film and linearity would be seen when  $y_a$  is plotted versus  $t$ , simulating a condition whereby moisture can be absorbed by, or diffuse into, an infinite sink.

The polymer film also can reduce absorption by acting as a barrier, which causes a change in vapor pressure with time. This method is ruled out since the slopes would be equal and independent of the absorbent, because  $(dy/dp)$  would be constant for any one film thickness at a given temperature and vapor pressure. The fact that the vapor pressure would probably change at a different rate, depending on the absorbent, would not cause a difference in  $k_a$ , because the slope would be a function of the average permeability coefficient.

Another alternative would be that the diffusion process has already occurred and that the polymer film actually presents an obstacle in absorption. This postulate is not unrealistic for several reasons. First, the polymer film is a relatively permeable species, and diffusion would be expected to occur much faster than the time required to reach equilibrium conditions. To reach equilibrium levels of absorption<sup>4</sup> took as long as 1 month. Second, the space between the granulation and the polymer film is very small, and a large concentration of water vapor would not be required to have a vapor pressure differential between both sides of the film of zero. The assumptions of this last alternative were used in developing Eq. 17. Therefore, at any given temperature and vapor pressure, the polymer film should be a constant barrier in reducing absorption.

<sup>4</sup> Equilibrium levels of moisture were determined for each granulation. However, the data are not included since no relationship existed between the total amount of moisture absorbed and  $K_e$  or  $k_a$ .

Table II—Computation of the Rate Constants Derived from Eqs. 18 and 19, Using Coated and Uncoated Tablets<sup>a</sup>

Formulation <sup>b</sup>	Area (A) of 20 Tablets, cm <sup>2</sup>	Weight (m) of 20 Tablets, g	$k_a$ , hr <sup>-1</sup> cm <sup>-2</sup> × 10 <sup>-4</sup>		$K_e$ , cm <sup>-2</sup> mm Hg <sup>-1</sup> × 10 <sup>-5</sup>	
			Uncoated	Coated	Uncoated	Coated
FF	76.30	22.14	9.97	7.93	4.72 (0.80) <sup>c</sup>	4.92 (0.76) <sup>c</sup>
GG	58.60	17.86	2.67	1.87	2.20 (0.21)	2.47 (0.27)
DD	73.20	17.03	3.60	2.23	2.39 (0.14)	2.21 (0.23)
BB	77.60	23.26	18.05	11.45	6.04 (1.31)	4.94 (0.31)
AA	65.20	13.38	11.91	7.08	7.60 (0.32)	6.38 (1.64)
CC	59.20	11.82	4.91	2.37	3.77 (1.60)	3.77 (1.60)

<sup>a</sup> Vapor pressure ( $p_0$ ) = 17.8 mm Hg, and film thickness =  $8.0 \times 10^{-3}$  cm. <sup>b</sup> See Fig. 5 for corresponding graph. <sup>c</sup> Represents ±95% confidence interval.

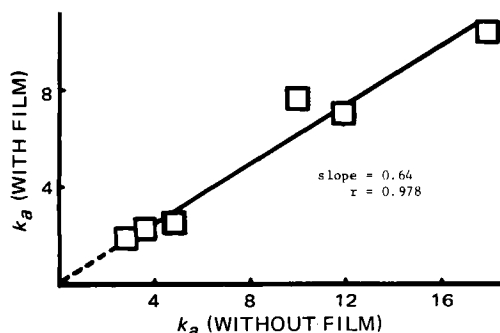


Figure 6—Comparison of absorption rate constants from applied film studies (coated and uncoated tablets).

To demonstrate this, the apparent absorption rates were plotted in Fig. 4. A good relationship appears to exist in that a reduction in the absorption rate of about 40%<sup>5</sup> can be attributed to the polymer film. This finding suggests that the total moisture and the amount absorbed at a given time interval are functions of the absorbent and that the degree to which a polymer film reduces absorption is constant and, apparently, independent of the absorbent.

As to film-coated tablets, the data obtained from these studies were treated as with free films (Fig. 5). As can be seen, linearity is obtained by plotting  $1/y_a$  versus  $1/t$  and common intercepts are obtained for each common tablet, with or without film coating.

The calculated equilibrium constants and absorption rates are given in Table II. The absorption rates are plotted in Fig. 6.

It appears that the same holds true for film-coated tablets as for free films in that the film retards moisture absorption by about 40% and is independent of the tablet formulation. Only the rate of absorption and the total amount absorbed are influenced by the tablet formulation.

When the results obtained with tablets and granules are considered, the mechanism by which a polymer film retards moisture apparently must be by altering or hindering the rate at which mois-

<sup>5</sup> Calculated on the basis that:

$$\frac{[k_a(\text{without film}) - k_a(\text{with film})]/k_a(\text{without film}) \times 100\%}{100\%} = (1 - \text{slope}) \times 100\%$$

can be considered as the decrease in absorption attributed to the polymer film.

ture diffuses to the absorption site. The presence of the film presents a constant barrier which slows the diffusion of moisture, resulting in a relationship such as that shown in Figs. 4 and 6. Therefore, the degree to which the polymer film retards absorption would be independent of the tablet or granule formulation and also independent of the physical nature of the solid matrix.

In conclusion, the absorbent does not influence moisture permeation through the film but, instead, the polymer film slows the absorption process. The results show that a very good correlation is obtained between free and applied films when subjected to this experimental design and treated according to Eq. 17.

Further investigation is needed to test the influence of film thickness, film formulation, vapor pressure, temperature, and tablet formulation factors, all of which can cause changes in moisture absorption.

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