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DEGRADATION KINETICS OF THIAMINE HYDROCHLORIDE IN DIRECTLY COMPRESSED TABLETS III

WATER VAPOUR TRANSMISSION THROUGH FREE AND APPLIED EUDRAGIT FILMS

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ABSTRACT

Water vapour transmission through free and applied film of four Eudragit resins namely, E_{100}, L_{100} and RS_{100} to directly compressed thiamine hydrochloride tablets was investigated. The type of Eudragit film influenced both water vapour transmission and moisture absorption characteristics of the tablets compressed with either single or binary blend of vehicles. The moisture absorption rate constant K_a, for a given batch was found to be a function of vapour pressure, P, and film thickness, L. The relationship between K_a and either of these parameters is exponental and may be expressed as $K_a = A \exp(x/P)$ and $K_a = K_a^* \exp(-x^* L)$. In general, film coating with Eudragit resins affected the physical characteristics of the tablets. The rate of drug release, K has an exponentially relationship as $K_e = K_o \exp(-c/L)$.

INTRODUCTION

The pathways by which drugs decompose have been categorised by Mollica et al (1) into hydrolytic, oxidative and miscellaneous reactions. The effect of atmospheric moisture on the hydrolysis of drugs has been the subject of investigations (2-4). The investigation carried out by Lesson and Mattocks (3) supports the general conclusion on the role of absorbed moisture on the degradation of solid dosage forms. Thus, the stability of tabletted drugs may be enhanced not only by ensuring that there is a low moisture content in the matrices used for manufacturing but also by limiting the access of moisture to the solid dosage form after manufacturing. The latter may require the application of film coating as a means of enhancing the stability of some solid dosage forms. Lehmann and Dreher (5) reported that stable formulations of vitamin tablets could be prepared by the application of film coating of Eudragit resin. This resin, which is methacrylic acid and methacrylate ester polymers, has been fully investigated (5). The resins availabel are categorized by the manufacturer (6) according to their solubility, pH profiles and permeability characterisitcs. Water vapour transmission through polymer films has been a subject of intensive investigations (7-10). It has been reported by different workers that the permeability characteristics of a polymer film may be affected by plasticizers and /or solid loading material incorporated while the film is being cast (7,8). While film coating may delay the chemical decomposition of drugs by acting as a barrier against atmospheric moisture, it may affect the physical properties of the coated particles and/or tablets. The physical properties that may be affected include hardness, disintegration time and dissolution rate (11,12).

The objective of this work was to evaluate the permeability characteristics of free and applied films of different Eudragit resins. This may throw light on the effect of film coating on the stability of directly compressed thiamine hydrochloride tablets. The effect of different Eudragit resins on the physical properties of the tablets was also investigated.

EXPERIMENTAL

Materials: The direct compression excipients used were Avicel (PH101)[1], Anhydrous lactose,[2] and Celutab,[3] Eudragit resins namely, E_{100}, L_{100}, RL_{100} and RS_{100}[4] were respectively used for casting films and tablet coating. Dibutyl phthalate[4] was incorporated as a plasticizer where necessary. Thiamine hydrochloride,[5] the active material was used as received from the manufacturer.

Methods:

Preparation and Evaluation of Vitamin Tablets

Thiamine hydrochloride in 90.46% w/w of either single or binary blend of direct compression vehicles was compressed into tablets. The compression of the tablets and the evaluation of their physical characteristics were carried out to methods which have been reported previously (13).

Study of Moisture Adsorption By Thiamine Hydrochloride Tablets:

Moisture adsorption isotherm and moisture uptake-time profiles for thiamine hydrochloride tablets were studied as described in an earlier work in this series (14). The different relative humidity conditions were achieved by using saturated solutions of different salts, contained in a Gallenkamp humidity oven.[I]

Preparation of Free Eudragit Films

A 20% w/w solution of a given Eudragit resin was prepared using a 1:1 alcohol/acetone system as solvent. In order to ensure the elasticity of the film, a 10% w/w of dibutyl phthalate was incorporated into each solution of Eudragit L_{100}, RL_{100} and RS_{100}. The amount of an Eudragit resin required to cast a film of required thickness, L, was calculated from the area of the surface used for casting and the concentration of the resin in solution. The films were cast on a highly polished galss plate of 63.6 mm^2 surface area. A 5 ml aliquot of a given Eudragit solution was carefully delivered onto the glass surface such that no air bubbles were trapped. The solvent was allowed to evaporate at room temperature during 24 h. The cast films were later equilibrated for 24 h at 80% RH in the humidity oven adjusted to a temperature of 30°C. The thickness of the film produced was measured using a precision digital micrometer[III].

Preparation of Film Coated Tablets:

Thiamine hydrochloride tablets directly compressed with 90.46% w/w of either Avicel, Anhydrous lactose, Celutab or a 1:1 binary blend of these vehicles were film coated in a 57.25 mm diameter tablet coating pan[III] by continuous spray technique. The amount of a given Eudragit resin required to impart a film thickness of 2 x 10^{-2} mm to the tablets, was calculated on the basis of tablet surface area. The solution of a given Eudragit resin was sprayed onto the tablets contained in the revolving coating pan. The adherence of tablets to the wall of the coating pan was prevented by dusting the tablets lightly with talc. In order to ensure even coating of all tablets, those adhering to each other were manually separated. The coated tablets were then dried and transfered to screw-capped bottles which were stored in a desiccator containing calcium chloride as desiccant, until required for use.

Study of Water Vapour Transmission:

A diagramatic representation of the permeability cell adapted for the investigation is shown in Fig. 1. The cell used is a 30 ml capacity vaccine bottle carrying a screw cap, through which 3 mm diameter hole was drilled. A rubber ring was placed between the inner portion of the cap and the mouth of the glass bottle. A film of Eudragit resin was interposed between the cap and the rubber ring with the latter acting as a support for the film. The positioning of the film over the 3 mm hole thus ensured that vapour transmission into the bottle was entirely through the film. The area of contact between the cap and the shoulder of the glass vessel was sealed with hard paraffin wax. The area of the film exposed to vapour transmission was 7.01 mm^2.

Coated or uncoated tablets being investigated were placed in different permeability cells. The samples were stored at 50°C, 47% RH 40°C, 100% RH and 35°C, 80% RH. The moisture transmission through the film was assessed by determining the weight of moisture absorbed by the tablets.

Evaluation of Film Coated Tablets:

The effect of coating with different Eudragit resins on weight, thickness, hardness, disintegration time and disso-

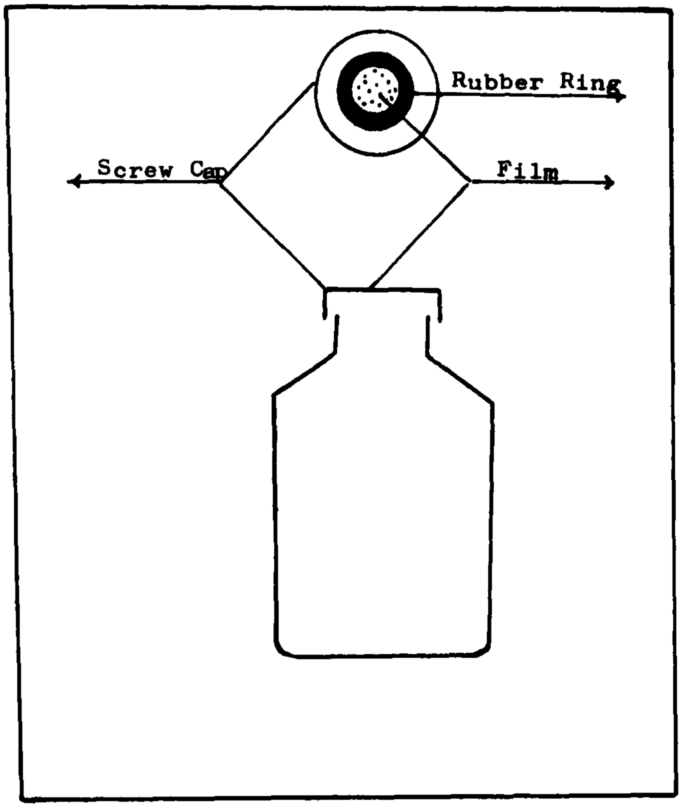


Fig. 1 Permeability Cell for Water Vapour Transmission Study.

lution of thiamine hydrochloride tablets was investigated. The effect of film thickness on the physical properties of thiamine hydrochloride tablets coated with a given Eudragit resin was also studied.

RESULTS AND DISCUSSION

The use of direct compression in place of the wet granulation technique eliminates water which is usually present in the granulating solution and the heat necessary for drying. These two factors may contribute to drug

Table 1: Some Physical Characteristics of Thiamine Hydrochloride Tablets compressed with 90.46% w/w of Single and Binary Blends of Named Vehicles

Vehicle	Weight (g)		Thickness (mm)		Hardness MN m^{-2}		Friability		Disint. T.	
	Mean	C.V.%	Mean	C.V.%	Mean	C.V.%	Mean	C.V.%	Mean	C.V.%
Avicel (A)	0.25470	1.53	2.96	0.722	21.26	4.23	0.474	3.88	1.24	48.8
Anhydrous lactose USP (B)	0.2558	3.19	2.72	1.33	9.135	6.43	0.568	3.22	10.25	2.9
Celutab (C)	0.2489	2.32	2.768	1.336	11.26	10.83	0.35	128.3	11.12	25.29
1:1 Binary Blends										
A + B	0.2688	5.06	2.91	1.90	16.86	6.98	1.12	9.03	23.25	5.0
A + C	0.2586	5.06	2.95	1.159	16.06	7.73	0.106	11.61	23.58	7.73

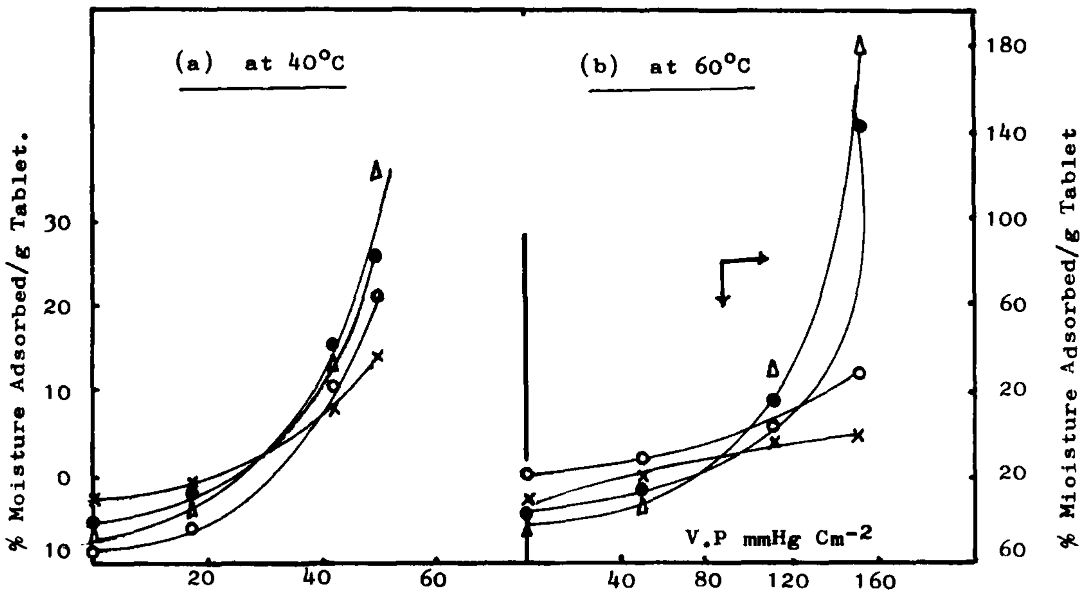


Fig. 2(a,b) Van der waal-type Moisture Adsorption Isotherm Exhibited by Thiamine Hydrochloride Tablets Compressed with 90.46% w/w of ΔCelutab,● Anhydrous lactose,O Avicel and X Emcompress.

decomposition. The application of direct compression technique to tabletting however, does not solve the problems of drug instability due to moisture since the solid dosage forms can also adsorb moisture from the surrounding atmosphere. The physical characteristics of the directly compressed tablets are presented in Table 1.

Fig. 2(a,b) shows the type of moisture adsorption isotherms exhibited by the drug/vehicle tablet system used in the present investigation. It can be seen in this figure that the degree of moisture adsorption is dependent on the vapour pressure under which the experimental work

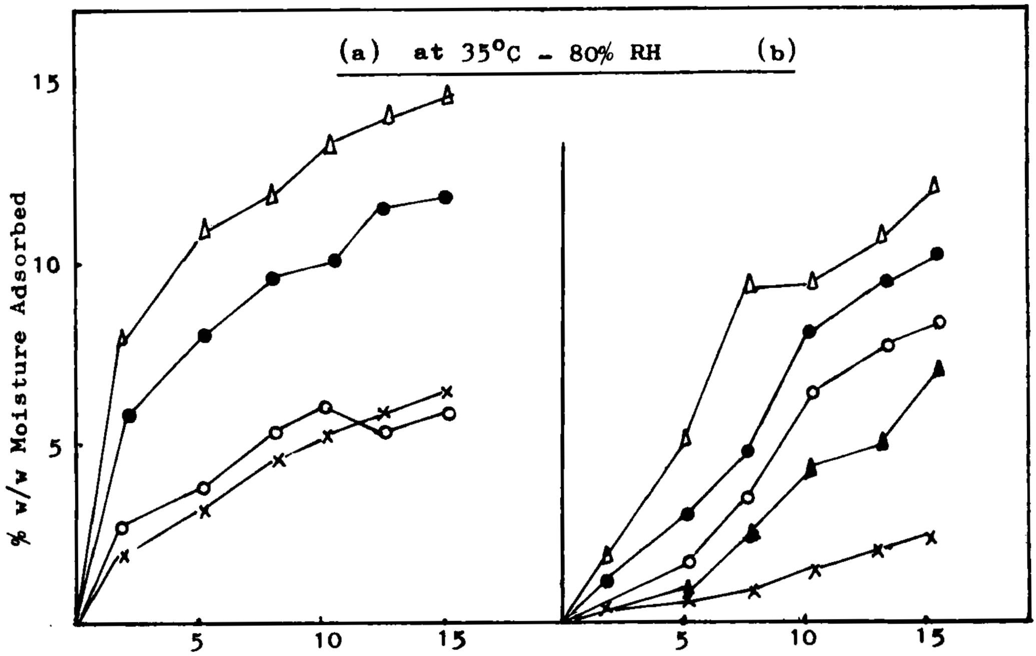


Fig. 3(a,b) Moisture Adsorption-TIME Profile of Thiamine hydrochloride Tablets Compressed with 90.46% w/w of (a) △ Celutab, ● AHL, ○ Avicel and X Emcompress and (b) 1:1 Binary Blends of △ Celutab/Avicel, ● Celutab?AHL, ○ Celutab/Emcompress ▲ Avicel/AHL and X Avicel/Emcompress.

was carried out. The type of tabletting vehicle is equally important. Thus the tablets prepared with Celutab, a hygroscopic vehicle showed the highest moisture uptake. The data obtained for the moisture uptake-time profiles of t the batches investigated are in agreement with those obtained from the study of moisture adsorption isotherm. Figs. 2 and 3 respectively show that the batches formulated with Celutab or its binary blend with Avicel or Anhydrous lactose showed a greater capacity for moisture adsorption than those formulated with single vehicles.

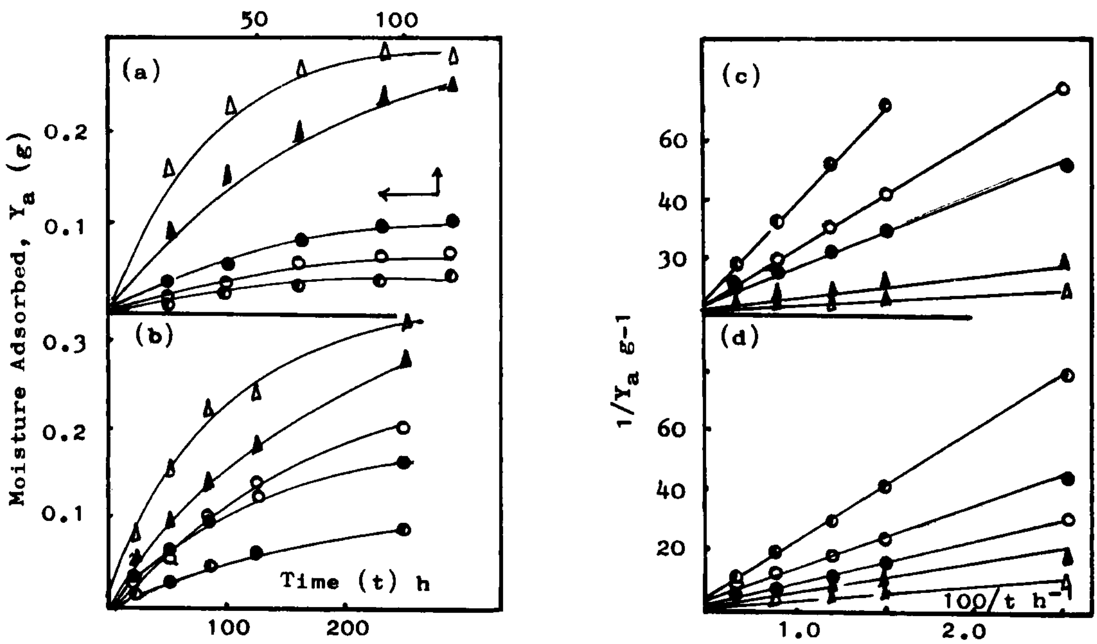


Fig. 4 Water Vapour Transmission Through Applied (a) and Free (b) Films of Eudragit RS100 onto Thiamine Hydrochloride Tablets Compressed with 90.46% w/w of △ Celutab, ▲ Avicel/Celutab 1:1 Blend, ● Avicel, ○ AHL and ◐ Avicel/AHL 1:1 Blend Fig. 4(c,d) Represent $1/Y_a$ vs 1/t plot.

The rate of water vapour transmission through free Eudragit films onto thiamine hydrochloride tablets is shown in Fig. 4 (a,b). The films, free or applied functioned as barriers and thus decreased water absorption by the tablets. The film cast with Eudragit L100 and RS100 respectively were the least permeable to water. The films cast followed by the films cast with RL100 and E100 respectively showed moderate impermeability to moisture. The water vapour transmission data were analysed using an expression proposed by Ammann (15):

$$1/Y_a = 1/(SPK_e\ A^2mP^o)t + 1/K_eAmP^o \qquad \text{Eq. 1}$$

where Y_a is the weight in grams of moisture absorbed by m grams of adsorbent; A is the surface area of the film through which vapour is transmitted after t hours and P^o is the vapour pressure in mm Hg/cm^2. The parameters, S,P and K_o are proportionality constants relating vapour pressure to the concentration of moisture, the average permeability coefficient which is a function of film thickness and equilibrium rate constant respectively. A plot $1/Y_a$ vs 1/t should, according to Eq. 1, yield a straight line as shown in Figs. 4(c,d).

The values of absorption and equilibrium rate constants K_a and K_e respectively may be calculated from the graph since.

$$K_a = 1/(\text{Slope})\ K_e\ A^2mP^o \qquad \text{Eq. 2}$$

$$\text{and}\quad K_e = 1/(\text{intercept})\ AmP^o \qquad \text{Eq. 3}$$

The lowest absorption rate constant, K_a was obtained for a film prepared with Eudragit RS100 and L100. The data presented in Table 2 shows that the absorption rate constant, K_a for the compressed tablet is lower than K_a^* obtained for uncoated tablets. This was generally the cast whether the film was free or applied. Figs. 5(a,b) show that a plot of absorption rate constant, K_a of given thiamine hydrochloride batch in the presence of Eudragit film (free or applied) vs absorption rate constant K_a^* of the corresponding uncoated batch exposed to the experimental conditons. There is a linear relationship between the two rate constants which implies that

$$K_a = XK_a^* \qquad \text{Eq. 4}$$

where X is the slope which is a measure of the degree of reduction in K_a. The values of X and the regression of K_a on K_a^* are given in Table 3. The free films prepared with Eudragit L100 and RS100 showed excellent performance and

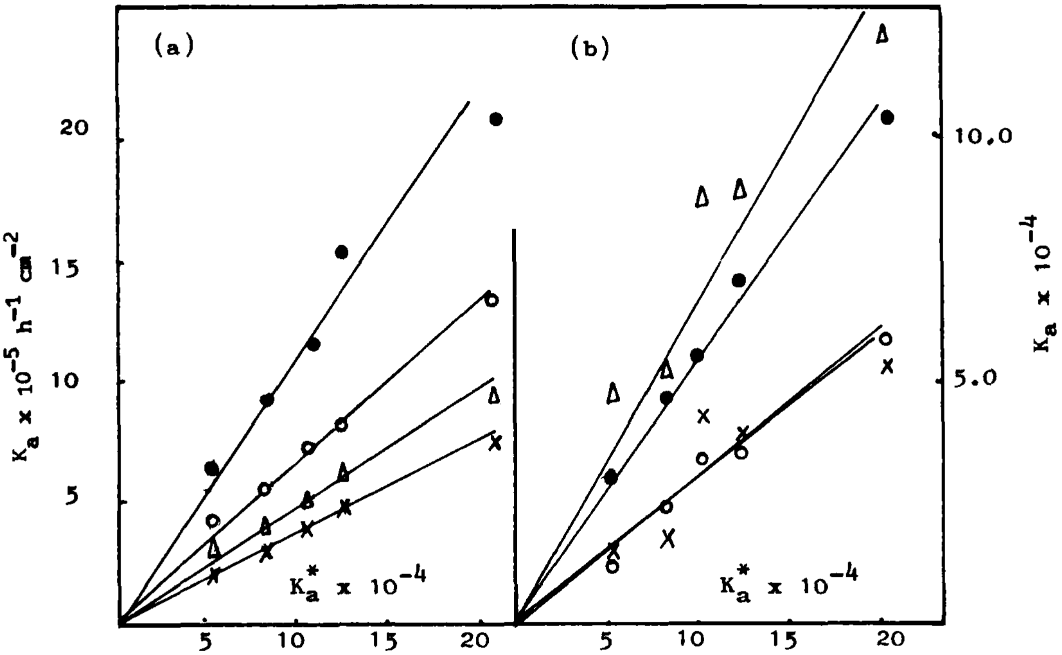
Table 2: Absorption Rate Constant for water vapour Transmission at 50°C and 47% RH Through Different Eudragit Film (Applied & Free) onto Thiamine Hydrochloride Tablets Directly Compressed with 90.46 % w/w of a Named Vehiclesor Blend

Vehicle	K_a^*	Applied Film$^+$			
	No Film	E100	L100	RL100	RS100
Avicel (A)	11.25	0.62	0.43	0.95	0.66
AHL (B)	11.76	0.54	0.422	1.34	0.68
Celutab (C)	20.39	0.86	0.69	1.96	1.058
(A+B) 1:1	6.63	0.38	0.0725	0.77	0.39
(A+C) 1:1	9.166	0.46	0.198	1.16	0.56
		Free Film$^+$			
(A)		8.00	4.68	5.44	3.3
(B)		6.16	3.52	5.40	2.85
(C)		11.73	5.33	8.8	5.55
(A+B) 1:1		2.37	1.43	2.24	0.821
(A+C) 1:1		4.40	1.76	5.30	2.36

+ $Ka/h/cm^2 \times 10^{-4}$, Film Thickness was 2.0×10^{-2} cm

were less permeable than films cast with Eudragit E100. The films cast with the latter resin were the most permeable.

The vapour transmission through free and applied Eudragit film was influenced by vapour pressure P^o, under which the experiment was carried out. Fig. 6(a) shows that the absorption rate constant K_a increased as the vapour pre-



Figs. 5(a,b) Absorption Rate Constant K_a in the presence of Eudragit films (a) applied (b) free vs K_a^* in the absence of Eudragit film for water vapour transmission onto thiamine Hydrochloride Tablets compressed with 90.46% of different Direct Compression Vehicles and Coated with Eudragit ● E100, O RS100, △ RL100 and X L100.

Table 3: The Degree of Reduction X, in Absorption Rate Constant K_a^* in water vapour Transmission Through Applied and Free Films of Eudragit resins onto thiamine hydrochloride Tablets

Eudragit Resin	Applied		Free	
	X	Corr. Coeff.	X	Corr. Coeff.
E_{100}	96.5	0.816	40.31	0.949
L_{100}	95.5	0.954	71.65	0.8399
RL_{100}	91.35	0.836	52.0	0.9491
RS_{100}	95.14	0.997	65.6	0.985

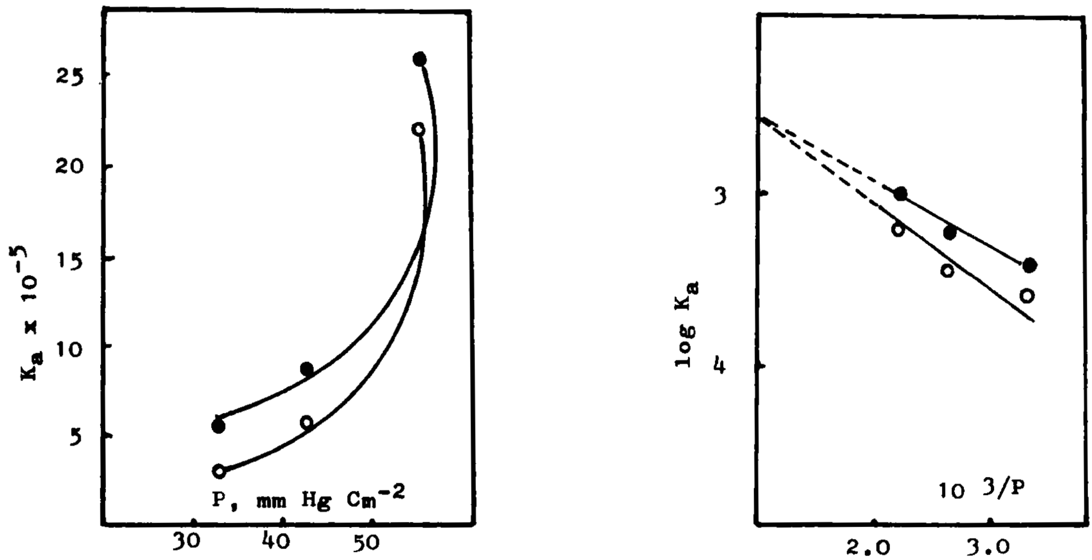


Fig. 6 Absorption Rate Constant as a Function of Water Vapour Pressure for Thiamine Hydrochloride Tablets Compressed with 90.46% Celutab and Coated with Eudragit ● E_{100} and O L_{100}

Fig. 6(b) Shows Linear Relation Between log K_a and 1/P

ssure increased. There exists an Arrhenius-type relationship between K_a and 1/P; thus,

$$\log K_a = A - x/P \qquad \text{Eq. 5}$$

A plot of log K_a vs 1/P is linear and is presented in Fig. 6(b). The pre-exponential factor A, represents the absorption rate constant at infinite vapour pressure while the slope x is a measure of the permeation force which can be defined as the force needed for a molecule of water to permeat a unit area of a given film. The values of A and x given in Table 4 are in agreement with results obtained earlier which showed that a high permeation force would a needed for the less permeable film of Eudragit E100 film.

Table 4: Values of the Pre-exponential A, and Permeation Force (x) Factor for water vapour Transmission Through Eudragit

Eudragit	A x 10^{-4} x h^{-1} cm^{-2}	(x) mm Hg cm^{-2}	Corr. Coeff.
E100	3.98	115.15	0.9562
L100	3.55	138.18	0.9595

Water vapour transmission through Eudragit films to thiamine hydrochloride tablets was affected by the thickness of the film, L. Figs. 7 (a,b) show that absorption rate constant K_a decreased as the film thickness increased. The relationship between K and film thickness L, is exponential and may be mathematically represented as

$$K_a = K_a^* \exp(-X^* L) \qquad \text{Eq. 6}$$

A plot of log K_a vs L is presented in Fig. 8(a,b). The values of X* which represents the transmission resistance (cm^{-1}) of an Eudragit film to water molecule are given in Table 5. The correlation coefficient of K_a on L is also given in the same table. The permeability coefficient P, of a given film was calculated from the expression (7):

$$q = PAt\ P^o/L \qquad \text{Eq. 7}$$

where q is the weight of water in grams transmitted through the free film of Eudragit resin at a given temperature; A, the surface area in cm^2 and L is the film thickness in cm. The P^o is the vapour pressure difference under which the experiment was carried out. It is shown in Fig. 9(a) that

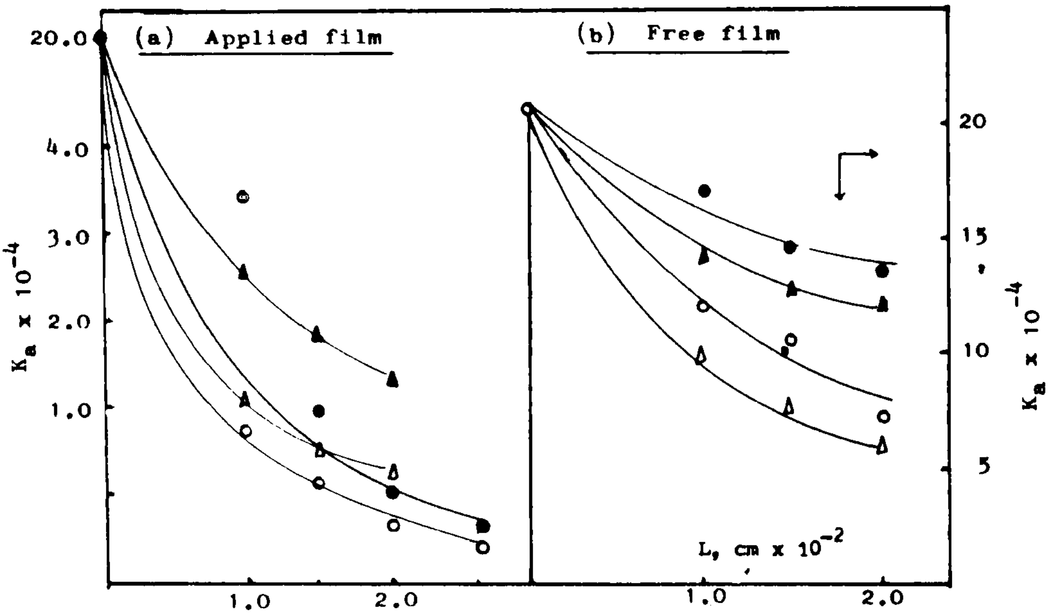
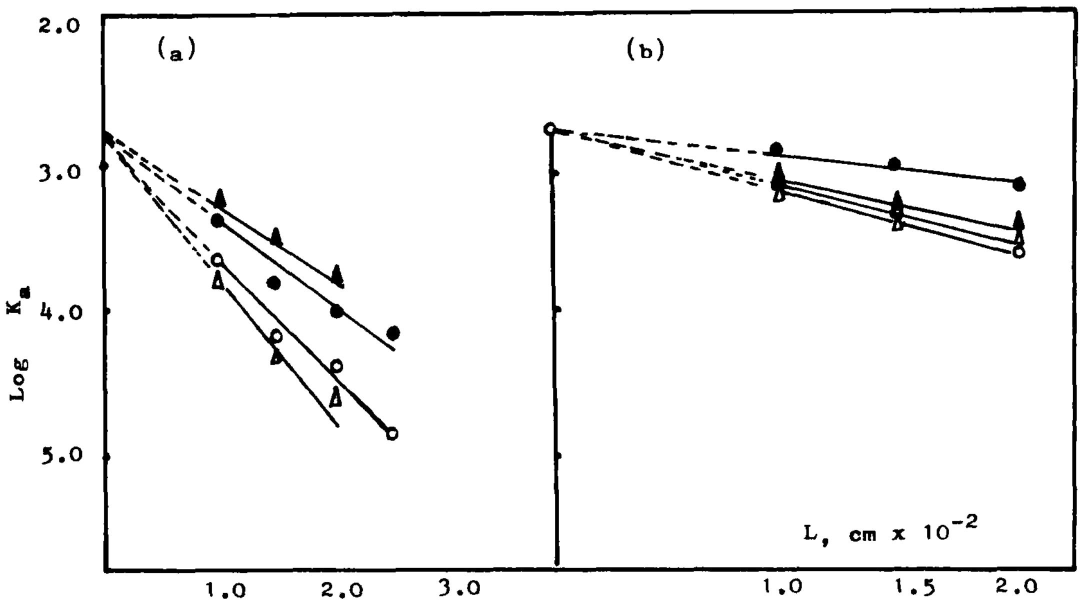


Fig. 7(a,b) Absorption Rate Constant K_a as a function of film Thickness L, for Thiamine Hydrochloride Tablets Compressed with 90.46% w/w of Celutab.

Key: ○ E_{100}, ▲ Rl_{100}, △ RS_{100}, ● L_{100}

there was no correlation between the permeability coefficient P, and the film thickness, L. This is in agreement with the results obtained by Deege and Froch (16). These investigators interpreted their results on the assumption that a thick film of cellulose acetate has the same permeation characteristics as a film cast from polystyrene. Kuriyama et al (17) did not consider Eq. 7 valid and therefore suggested that permeability resistance 1/Q should have a linear relationship with film thickness. Permeability resistance is in fact the



Figs. 8(a,b) Log K_a vs L, plot for Water Vapour Transmission Through Applied (a) and Free (b) Eudragit Films onto Thiamine Hydrochloride Tablets Compressed with 90.46% w/w Celutab and Coated with ● E_{100}, ▲ RL_{100}, O L_{100} and Δ Rs_{100}.

Table 5: Values of Transmission Resistance X^*, of Different Applied and Free Eudragit Films and Correlation Coefficient of log K_a on L

Eudragit	Transmission Resistance cm^{-1}		Corr. Coeff.	
	Applied	Free	Applied	Free
E100	44.6	16.3	-0.888	-0.9725
L100	73.19	30.00	-0.966	-0.9929
RL100	53.38	20.58	-0.86	-0.943
RS100	80.21	33.33	-0.9926	-1.15

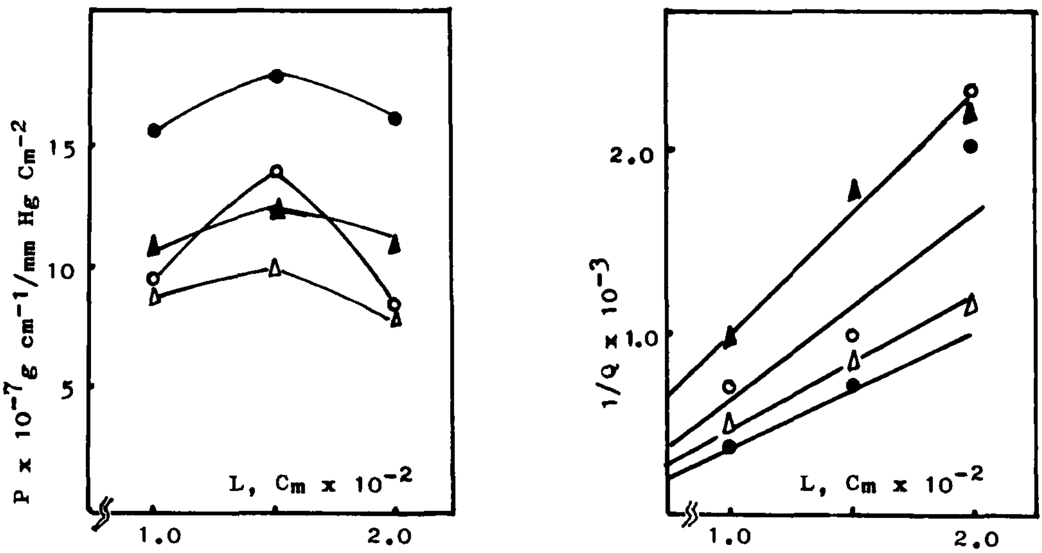


Fig. 9(a) Permeability Coefficient P as a Function of Film Thickness L, for Water Vapour Transmission Through Different Eudragit Resins Applied onto Thiamine Hydrochloride Tablets Prepared from 90.46% Celutab

Key: ● E_{100}, O L_{100}, ▲ RS_{1000} and △ RL_{100}.

Fig. 9(b) Permeability Resistance 1/Q as a function of Film Thickness L, for Water Vapour Transmission Through Different Eudragit Resins onto Thiamine Hydrochloride Tablets Prepared from 90.46% Celutab

Key: as in Fig. 9(a).

reciprocal of permeability, which is defined by the equation (17).

$$Q = q/At \ (g/m^2 . \ 24 \ h) \qquad \text{Eq. 8}$$

where g is the amount of water in grams transmitted through a film of surface area $A(m^2)$ within 24 h. The permeability data obtained in the present investigation was analysed by assuming that a linear relationship existed between permeability resistance 1/Q and film thickness, L, Fig. 9(b) does indeed show that there is linearity. From the foregoing it is obvious that the use of Eudragit resin in the film coating of thiamine hydrochloride tablets would of course decrease water vapour transmission to the tablet. Thus it would enhance the stability of the tablets. On the basis of permeability to water vapour the Eudragit films can be arranged in the sequences.

$$RS100 = L100 > E_{100} > RL_{100}$$

The film coating of thiamine hydrochloride tablets with Eudragit resins would also affect some of its physical properties. The applied film would be expected to retard the release of drug from tablets formulated with direct compression vehicles. Table 6 also shows that film coating increased the disintegration time Dt, of the tablets. The effect was more pronounced for tablets coated with Eudragit RS100 and RL100. The solubility of Eudragit E100 in the dissolution medium (0.1NHCl) would account for the little or no change obtained in the release of the vitamin from tablets film coated with it. This can be seen in the dissolution profiles shown in Fig. 10. The degree of reduction DR, in dissolution rate produced by film coating was calculated from

$$DR = 100\ (1-K_e/K_o) \qquad \text{Eq. 9}$$

where K_e is the dissolution rate constant of tablets film coated with a given Eudragit resin and K_o is the dissolution rate constant for the corresponding uncoated control tablets. Table 7 shows that tablets film coated with Eudragit RS100 or L100 offered the highest degree of change while Eudragit E100 showed the least change in dissolution rate.

The effect of film thickness of a given Eudragit resin on the dissolution of thiamine hydrochloride tablets compre-

Table 6: Effect of Film Coating with Different Eudragit Resins on Hardness H*, and Disintegration Time Dt+, of Thiamine Hydrochloride Tablets Prepared from 90.46% w/w of the Named Vehicles

Vehicle	Applied Eudragit Film**							
	E_{100}		L_{100}		RL_{100}		RS_{100}	
	H MNm^{-2}	Dt (min)	H MNm^{-2}	Dt (min)	H MNm^{-2}	Dt (min)	H MNm^{-2}	Dt (min)
Avicel	21.4(3.07)	11.5(2.8)	22.86(2.7)	18.5(3.8)	23.5(2.2)	15.15(3.3)	22.15(2.5)	22.2(3.8)
AHL	11.02(1.9)	13.71(3.05)	9.98(2.4)	21.6(2.9)	23.5(2.2)	15.15(3.3)	22.15(2.5)	22.2(3)
Celutab	23.28(4.0)	8.95(1.82)	22.81(2.9)	25.8(2.1)	23.5(2.2)	8.99(2.2)	36.15(3)	18.2(4.0)

*Mean of 10 Determinations ± (SD)

+Mean of 6 Determinations in 0.1N HCl ± (SD)

**Film Thickness is 2.0 x 10^{-2} cm.

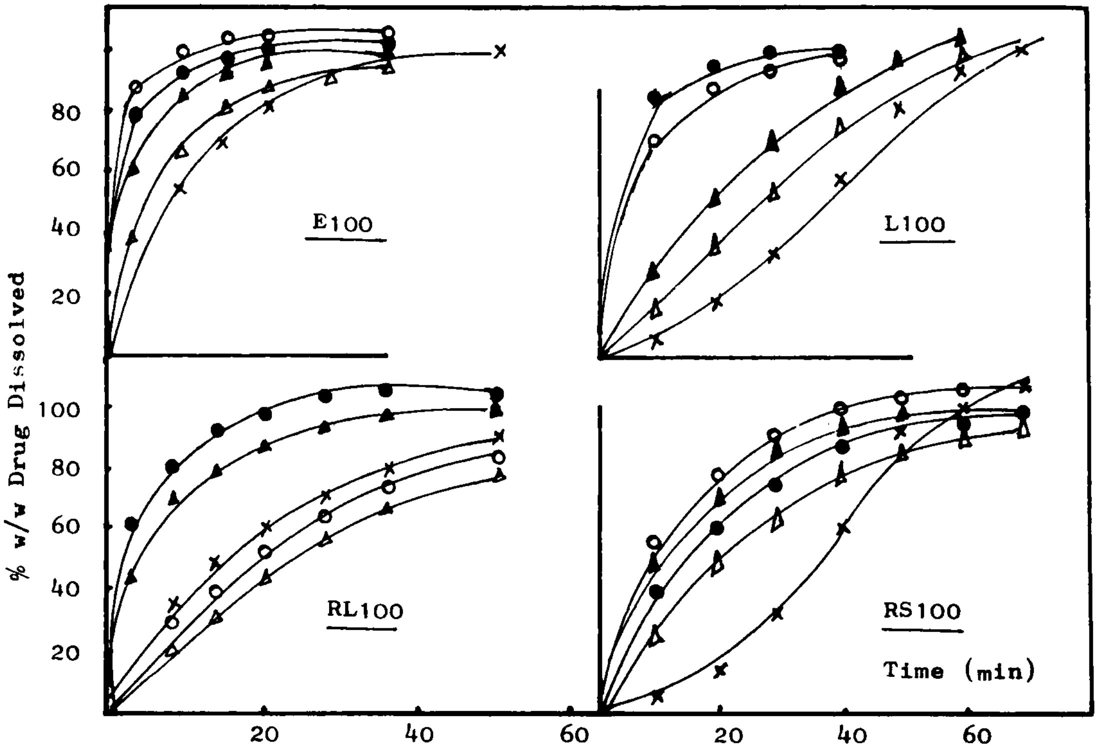


Fig. 10 Dissolution Profiles of Thiamine Hydrochloride Tablets Compressed with 90.46% w/w of AHL, Avicel, Avicel/Celutab 1:1, Celutab and Avicel/AHL 1:1 and Film Coated with 2.0×10^{-2} different Eudragit Resins.

ssed with 90.46% w/w of Celutab is shown in Fig. 11 (a,b). There is a semi-log relationship between dissolution rate constant K_e and film thickness, L; thus

$$\log K_e = \log K_o - cL/2.303 \qquad \text{Eq. 10}$$

where K_o, K_e and L are dissolution rate constants of thiamine hydrochloride (min-1) for uncoated and coated tablets respectively and film thickness. The slope c, of Eq. 10 may be defined as diffusion resistance of the film (cm^{-1}) to the molecules of thiamine hydrochloride. This follows from Eq. 7

Table 7: Degree of Reduction in Dissolution Rate Constant K_o^*, of Thiamine Hydrochloride Tablets Compressed with 90.46% w/w of the Named Vehicles and Film Coated with 2×10^{-2} cm of Different Eudragit Resins

Vehicle	$K_o \times min^{-1}$	$(1-K_e/K_o)$ 100			
		Applied Eudgragit			
		E_{100}	L_{100}	RL_{100}	RS_{100}
Avicel (A)	0.335	58.38	71.05	83.28	86.86
AHL (B)	0.180	40.00	69.44	71.11	79.44
Celutab (C)	0.184	29.89	61.90	67.98	72.28
A + B (1:1)	0.056	14.28	51.79	51.79	54.82
A + C (1:1)	0.048	33.33	50.00	50.00	52.08

*Determined in 0.1N HCl

used for calculating permeability coefficient, P. During dissolution, the molecules of the dissolution medium (0.1N HCl) would diffuse through the film and reach the core of the tablet. Some thiamine hydrochloride in the core would dissolve in the medium. The dissolved thiamine hydrochloride would then diffuse out of the tablet core through the film barrier. If P^o is substituted with the term $(C_r - C_s)$ where C_r and C_s are the concentrations of thiamine hydrochloride in the core and bulk solution respectively, Eq. 7 becomes

$$q = PAt\,(C_r - C_s)/L \qquad \text{Eq. 11}$$

The concentration C_s in the bulk solution is small compared with C_r, the concentration in the core of the tablets; C_s can be neglected and Eq. 11 take the form

$$q = Pat\;\; Cr/L \qquad \text{Eq. 12}$$

The permeability coefficient of the film, P is then given by

$$P = q.L/At\,C_r \qquad \text{Eq. 13}$$

At finite time t , C_r becomes equal to q and hence

$$P = L/At \qquad \text{Eq. 14}$$

But the diffusion resistance of thefilm of thiamine hydrochloride is Pt which is equal to c which is given as

$$C = L/A = cm^{-1} \qquad \text{Eq. 15}$$

The values of c for Eudragit film on a tablet could be calculated from the slopes of the curves presented in Fig. 11 (b). Table 8 shows that the highest value of diffusion resistance was obtained with the films of Eudragit RS100; This is followed by RL100. The correlation coefficient of log K_e on L is given in Table 8. Eqs. 6 and 10 have a common parameter which is film thickness, L. If the expression for film thickness as given in Eq. 6 is substituted in Eq. 100 the expression becomes:

$$\log K_a = \log K_a^{*} - X^{*}/c \log \frac{K_o}{K_e} \qquad \text{Eq. 16}$$

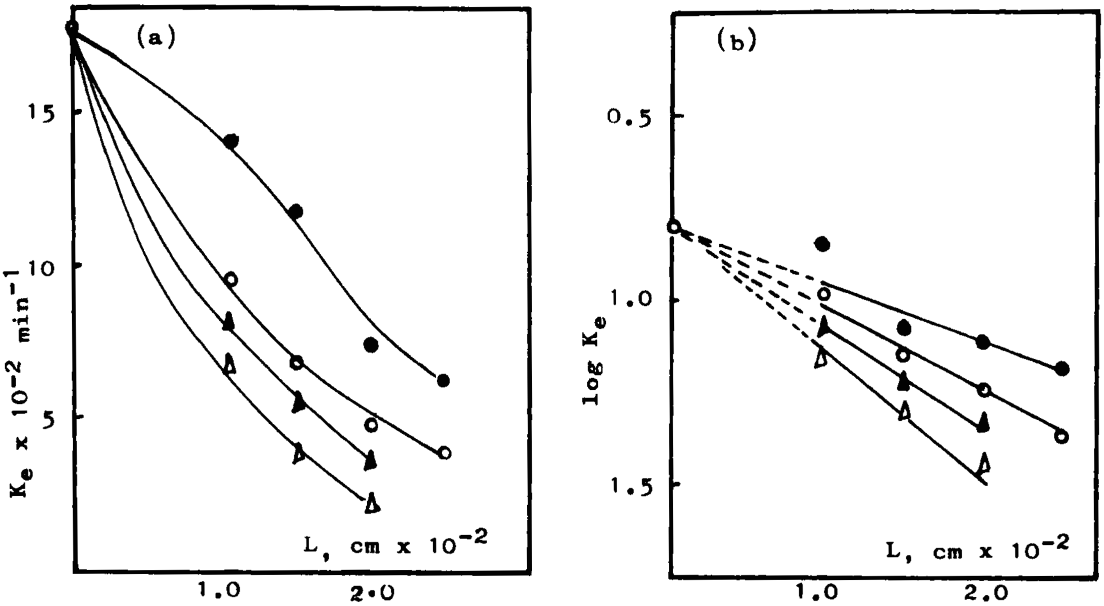


Fig. 11(a) Dissolution Rate Constant K_e (0.1N HC_1) as a function of Film Thickness L, for Thiamine Hydrochloride Tablets Compressed with 90.46% w/w of Celutab and Film Coated with ● E_{100}, ○ L_{100} ▲ Rl_{100} and △ Rs_{100}.

Fig. 11(b) log K_e vs L plot.

In other words a log linear relationship exists between absorption rate constant K_a and dissolution rate constant K_e. Table 9 shows the statistical analysis of the curves presented in Fig. 12.

The result obtained for the effect of film thickness on hardness of thiamine hydrochloride tablets is in agreement with that reported by Stern (11). Fig. 13(a) shows that, there is linearity between the hardness of the tablets coated

Table 8: Least Square Fits of K_e on L According to Eq. 10 for the Release of Thiamine Hydrochlor* from Tablets Film Coated with Different Eudragit Resins

Applied Resin	Slope (C) cm^{-1}	Corr. Coeff. r
E_{100}	-13.3	-0.9998
L_{100}	-17.20	-0.99355
RL_{100}	-25.50	-0.9889
RS_{100}	-31.57	-0.874

*In 0.1N HCl

Table 9: Least Square fits of log K_a on log K_e/K_o According to Eq. 16 for Thiamine Hydrochloride Tablets Compressed with 90.46% w/w of Celutab and Film Coated with Different Eudragit Resins

Applied Resins	Slope X^*/C		Corr. Coeff. (r)
	Experimental	Estimated	
E_{100}	4.00	3.35	0.935
L_{100}	3.86	4.26	0.79
RL_{100}	2.105	2.09	1.10
RS_{100}	2.50	2.54	0.9675

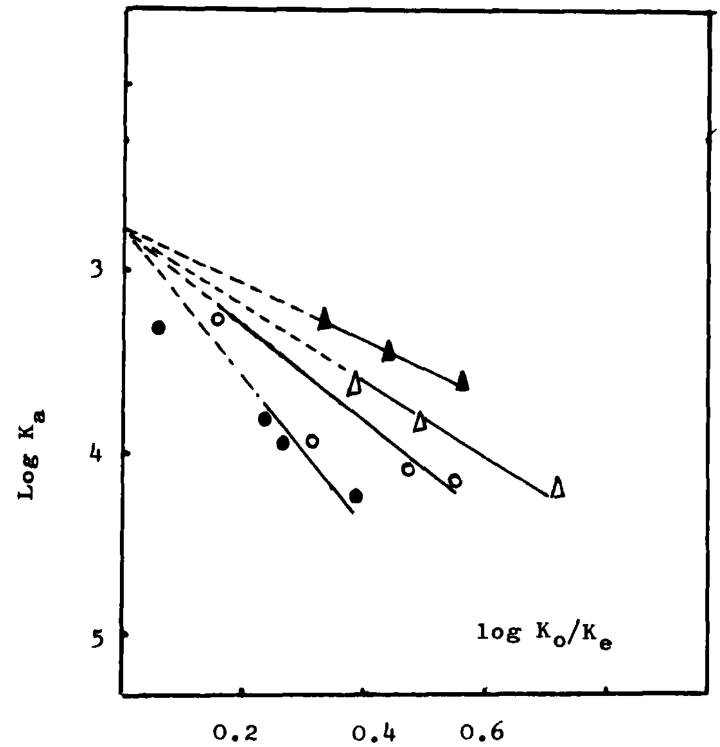


Fig. 12 Log K_a vs K_o/K_e According to Eq. 16 for Thiamine Hydrochloride Tablets Compressed 90.46% w/w of Celutab and Film Coated with ▲ RL_{100}, △ RS_{100}, ○ L_{100} and ● E_{100}.

with Eudragit resin and the film thickness. The effect of film thickness on the disintegration time of coated thiamine hydrochloride was also investigated. No simple correlation was obtained between disintegration time, Dt and film thickness, L. But generally as shown in Fig. 13(b) an increase in film thickness caused a marked increase in disintegration time.

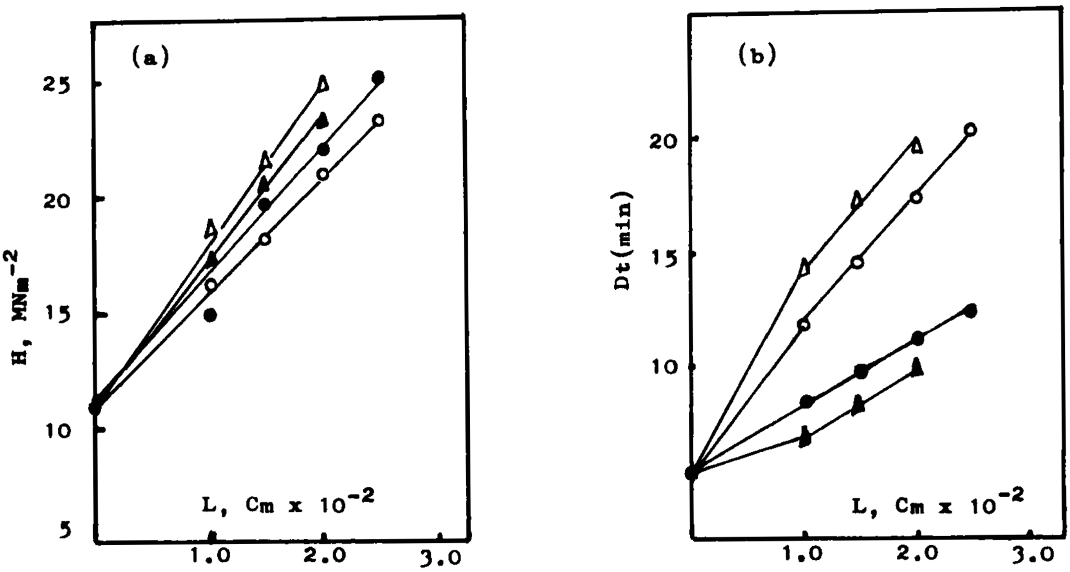


Fig. 13(a,b) Effect of Film Thickness L, of Different Eudragit Resins on Hardness H, (a) and Disintegration Time Dt, (b) of Thiamine Hydrochloride Tablets Prepared with 90.46% w/w of Celutab.

Key: △ RS_{100}, ○ L_{100}, ● E_{100} and ▲ RL_{100}.

CONCLUSION

The study of water vapour transmission offers some information on the stability of vitamin tablets coated with Eudragit resin. Film coating with this resin was seen to retard the release of the vitamin from the tablets and would hence affect bioavailability. The results show that stable thiamine hydrochloride tablets could be produced by film coating the tablets with Eudragit resins. Eudragit RS_{100} and RL_{100} were found to have low permeability to vapour. A tablet formulation which disintegrates and dissolves quickly and is therefore bioavailable can be produced provided the film thickness is effectively controlled.

FOOTNOTES

1. FMC Corporation Pennsylvania USA
2. Sheffield Union N.J. USA.
3. E. Mendell USA
4. Rhom Pharm, W. Germany.
5. Hoffman La Roch Basle Switzerland.

6 I. Gallencamp Ltd, U.K.

II. Baty dial micrometer Sussex, U.K.

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