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The Influence of Different Plasticizers and Polymers on the Mechanical and Thermal Properties, Porosity and Drug Permeability of Free Shellac Films

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ABSTRACT The effect of triethyl citrate (TEC) and different molecular weights and concentrations of polyethylene glycol (PEG), in addition to the effect of different water-soluble polymers and dispersions at different levels, hydroxypropyl methylcellulose (HPMC), methylcellulose (MC), carbomer 940, polyvinyl alcohol (PVA), ethyl cellulose (EC), on the mechanical and thermal properties, drug permeability, and porosity of free shellac films were investigated. Shellac films were cast from aqueous solutions, and their mechanical properties were studied by tensile test. Thermal analyses were performed using differential scanning calorimetry (DSC).

The results showed that the addition of plasticizer caused a decrease in both elastic modulus and glass transition temperature (T_g) and an increase in elongation at break of free shellac films. This effect was related to the concentrations of plasticizers. Different molecular weights of PEGs have different plasticization mechanisms.

Moreover, the incorporation of different amounts of HPMC, MC, or carbomer in free shellac films caused an increase in the flexibility, decrease in T_g, and a marked increase in drug permeability of free shellac films, whereas the addition of PVA caused a decrease in flexibility and drug permeability and an increase in T_g. Addition of EC resulted in a slight decrease of the elasticity and a small decrease in drug permeability. However it does not show a considerable effect on the T_g. In addition, it was found that the drug permeability is directly related to the mechanical properties and T_g of shellac films.

KEYWORDS Shellac, Polyethylene glycol, Plasticizer, Water soluble polymers, Glass transition temperature, Mechanical properties, Drug permeability

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INTRODUCTION

Various film polymers have been widely used to develop sustained release or site-specific release dosage forms of drugs by numerous approaches which

more or less consist of forming matrices with drugs or a coating of the drug containing core tablets or beads. Polymers that are used in pharmaceutical coating are primarily based on cellulosic and acrylic polymers as both have good film-forming properties that enable the production of protective coatings. However, despite extensive research with such coatings, problems may still arise when they are sprayed on the tablet surface. For example, tackiness of the polymeric films may cause unwanted agglomeration during the coating process, the wrong coating composition may import a cracking tendency to the dried coating, or the coating may interact with the drug in tablet core. The incorporation of plasticizer is necessary to obtain an effective coating without defects. Plasticizers are also added to polymeric solutions and dispersions to increase the flexibility of the polymeric material. Incorporation of plasticizer in film formulations mainly alters their mechanical properties, e.g., elongation, modulus, and stress (Heinämäki et al., 1994; Ewart et al., 2002; Pillai et al., 1988).

Shellac is one of the thermosetting resins of animal origin secreted by the lac insect Kerriar Lacca. It considered as a complex ester of polyhydroxypolybasic acids. Various hydroxy acids such as aleuritic acid, shelloic acid, kerrolic acid, butolic acid, and jalaric acid have been isolated by chemical degradation of the hard resin portion of shellac. Among them, aleuritic acid and the shelloic acid are the most important (Wang et al., 1999). Shellac has been used in a number of applications which have been extended to the coating of pharmaceutical products in a form for oral administration such as a modified release coating and a seal coat for tablet cores prior to sugar coating (Maiti & Rahman, 1986). Shellac has a relatively high pK_a value (6.9–7.5) which results in a slow drug release in intestinal fluids (Cole et al., 1995).

Moreover, the provision of enteric coating on solid pharmaceutical dosage forms, such as tablets, pellets, capsules, and the like, has been carried out by a method comprising coating the dosage forms with various enteric coating materials dissolved in an organic solvent with the addition, if necessary, of plasticizers and coloring agents. This method is disadvantageous from both the economical and safety viewpoints due to the use of a large amount of expensive solvents for the preparation of the coating solutions and the risk of fires or explosions during the coating operation. A further disadvantage of the method is that air pollution caused by the vapors of the organic solvent which are discharged during the coating operation, most of which are released into the atmosphere (Kamakura et al., 1977).

It is therefore the objective of this study to investigate the providing of water coating formulations from shellac for the purpose characterized by the absence of organic solvents. Moreover, in a recent publication, we have investigated the improvement of the drug release from shellac coated pellets caused by the addition of some water soluble polymers and the influence of these polymers on the mechanism of drug release (Qussi & Suess, 2005). In order to clarify the results and for nearer investigation with more details, it was very important to study the interaction between different polymers and shellac and to investigate its influence on the thermal and mechanical properties, permeability, and porosity of the films. Furthermore, it was very important to study the plasticization efficiency of various plasticizers and determine the effective plasticizer for shellac. Therefore, the influence of triethyl citrate (TEC) and different molecular weights of polyethylene glycol (PEG) at different levels on the properties of shellac films were studied.

EXPERIMENTAL METHODS

Materials

Shellac powder 010, orange, dewaxed, and decolorized was donated by Marchand & Cie, Germany. Hydroxypropyl methylcellulose (HPMC-Metholose 65 SH 4000) was purchased from Shin-Etsu Co. Ltd, Tokyo, Japan. Polyvinyl alcohol (POLYVIOL G 28/10) was purchased from Wacker-Chemie GmbH, München, Germany. Carbomer (carbopol 940) was purchased from Caesar & Loretz GmbH Hilden, Germany. Methylcellulose (Tylose MH 1000) was purchased from Fluka AG. Chemische Fabrik and ethylcellulose (Ethylcellulose Aqueous Dispersion, NF, Aquacoat® ECD 30) was purchased from FMC Corporation, Philadelphia, USA. Theophylline (theophylline anhydrous) was donated by Arzneimittelwerk Dresden GmbH, Germany. Polyethylene glycols PEG 600, PEG 4000, PEG 35000 were purchased from Merck-Schuchardt, Germany; polyethylene glycols PEG 1500, PEG 6000 were purchased from LABORAT, GmbH, Berlin, Germany.

Methods

Preparation and Characterization of Free Shellac Films

Shellac, like other polymers with carboxyl groups, is not soluble in water. However, it is possible to prepare aqueous shellac solutions of alkali salts. The selection of the base and the method for dissolving will influence the properties of the film. A volatile alkali is preferable (Penning, 1996). Therefore ammonium hydrogen carbonate was chosen as the base.

The aqueous solutions were prepared by dissolving shellac in purified water with ammonium hydrogen carbonate under stirring and heating. At temperatures between 55–60°C the forming of CO_2 and NH_3 occurred; both compounds are volatile. Therefore excessive ammonium hydrogen carbonate which was not used for the ammonium salt formation of shellac evaporated from the solution. The pH of the clear shellac solution was 7.5–8.

For preparing polyvinyl alcohol (PVA) solutions, water was heated to 80°C and PVA was added gradually under stirring of the solution for 2–3 h. After cooling the solution, it was added slowly to the aqueous shellac/plasticizer solution under stirring for 8 h.

Hydroxypropyl methylcellulose (HPMC) and methylcellulose (MC) solutions were prepared at room temperature by adding very slowly to the water under stirring. Then HPMC or MC solutions were mixed with shellac/plasticizer solution under stirring for 4 h.

Ethyl cellulose (EC) dispersion was added directly to shellac solution under stirring for 4 h.

Carbomer solutions were prepared at room temperature with water and then they were mixed with shellac/plasticizer solution under stirring for 6 h.

Isolated films were prepared by a process named "casting and evaporation." The aqueous shellac solutions were mixed with different amounts (10, 15, 20, and 30% w/w) of different plasticizers (PEG 600, PEG 1500, PEG 4000, PEG 6000, PEG 35 000, and triethyl citrate) and also with different amounts (10, 15, 20, and 25% w/w based on the mass of shellac) of polymeric aqueous solutions or dispersions (HPMC, MC, EC, and PVA) under stirring at a temperature of 55°C for approximately 8 to 10 h. Carbomer 940 was incorporated in free shellac films at concentrations of 0.5, 1, 2, and 2.5% w/w based on the mass of shellac.

Approximately 12–15 mL of each one of all formulations were casting into Teflon molds and subsequent solvent evaporation was carried out at temperatures of 55–65°C for 5–6 h.

After complete drying the films were removed from the plate without any damage and cut using a sharp scalpel.

The films were stored in a desiccator at room temperature with 22–25% relative humidity for at least two days before testing.

The thickness of the polymer films was determined using a micrometer (Erichsen GmbH & Co KG, Hemer, Germany). From each film five samples at different points were taken. The average thickness of the films were calculated; they ranged between 95–140 μm with relatively small coefficients of variations (2–5%) for each individual membrane.

Determination of T_g of Free Shellac Films

Glass transition temperature (T_g) of free shellac films was determined using differential scanning calorimeter (PL-DSC, Polymer Laboratories Ltd, Amherst, MA, USA).

Approximately 10 mg of dried sample were loaded into non-hermetically sealed aluminum pans and tested under a N_2 atmosphere. The sample was heated from −50 to 200°C at a rate of 20°C/min.

The T_g for each film type was determined from the midpoint of a small endothermic rise of the pre- and post-transition baseline using at least three parallel thermograms.

Tensile Tests

The tensile tests for the films were formed using a tension/compression tester (EZ-Tester, Shimadzu, Japan) by placing the samples in non-slip grips of the machine which pulls the sample in tension at constant speed of grip separation (10 mm/min) exactly along the long axis of the sample. At least 20 replicates were performed. The stress–strain profiles were recorded and the elongation at break and elastic modulus were calculated by the following equations (Graeme et al., 1997):

$$\text{Elastic modulus (MPa)} = \frac{\text{Force at corresponding strain (N)}}{\text{Cross-sectional area (m}^2\text{)} \times \text{corresponding strain}}$$

$$\text{Elongation at break (\%/mm}^2\text{)} = \frac{\text{Increase in length (mm)} \times 100}{\text{Original length (mm)} \times \text{Cross-sectional area (mm}^2\text{)}}$$

Drug Permeability Test

Drug permeability experiments were performed using a permeation model (Fürst et al., 1990) by placing the film between two compartments: donor (20 mL) and acceptor (20 mL). As a drug model theophylline was taken. The theophylline solution was filled in the donor compartment and the acceptor compartment was charged with purified water. The permeation area of the films was 22.18 cm^2. The temperature was 37°C ± 0.5.

At timed intervals an appropriate aliquot was withdrawn from the acceptor cell and replaced with an equal volume of water. The theophylline concentrations of the samples were determined by using UV/VIS spectrophotometer (Perkin Elmer Lambda 11, Ueberlingen, Germany) at a wavelength of 271 nm.

Based on the diffusion profile, the permeability (P) was calculated according to the equation:

$$P = \frac{(S \times T \times V)}{(A \times C_1)}$$

where P is the permeability constant ($m^2\ s^{-1}$), S is the slop of plot concentration versus time (mg $m^{-3}\ s^{-1}$), T is the thickness of the film (m), V is the volume of acceptor phase (m^3), C_1 is the concentration of drug in donor compartment (mg m^{-3}), and A is the surface area of film (m^2) (Bommel et al., 1989).

Measurement of Film Porosity

The films were cut into small replicates and the weight of these replicates was exactly measured and the density and specific volume were determined using helium pycnometer (Multi Volume Pycnometer 1305, Micromeritics GmbH, Neuss, Germany).

Porosity and the pore size distribution in the shellac cast films were measured by mercury intrusion porosimetry, employing a mercury porosimeter (Quanta Chrome Corp, PoreMaster 60, Fairfield, NJ, USA).

Porosity is defined as the percentage of void space in a solid. Total porosity ($\in$) is often evaluated from mercury density (ρ_{Hg}) and helium density (P_{He}) values (Mattsson & Nyström, 2001). Each test was repeated four times and the mean was calculated.

Scanning Acoustic Microscopy

The morphology of the surfaces of free films was examined by scanning acoustic microscopy with vector contrast (PSAM). The coupling fluid for the acoustic measurements was water. The frequency used was 1.2 GHz.

RESULTS AND DISCUSSION

The Influence of Plasticizers

Typical stress–strain profiles for each individual film formulation were obtained and the elongations at break percentage and elastic modulus were calculated. Results from the physical–mechanical studies with the shellac polymer demonstrated that the addition of the plasticizers resulted in a decrease in Young's modulus of free shellac films, whereas the elongation at break was increased. The decrease in Young's modulus and the increase in elongation at break are caused by the plasticization effect on the T_g and interaction with the polymer molecules (Honary & Orfai, 2002). In all cases, the addition of the plasticizers had a significant effect on the mechanical and thermal properties of shellac films. That effect had a direct relationship between increasing amounts of plasticizer concentration and T_g depression and elongation increasing with all film formulations. This is in agreement with the findings of Pearnchob et al. (2003) who suggested that increasing plasticizer content into shellac films led to a reduction in tensile strength.

Table 1 shows the effect of different levels of plasticizers on the tensile strength of shellac films. A plasticizer concentration of 10% based on the mass of shellac might be a critical concentration, since below this concentration no significant plasticizing effect could be obtained (Pearnchob et al., 2003; Gutiérrez & McGinity, 1994).

PEG 600 has a small molecular volume and relatively high amount of hydroxyl groups. Therefore, it can diffuse into and interact with shellac chains and show thermodynamical activity (Honary & Orfai, 2002). This effect was presented by increasing the elongation at break percentage and decreasing the T_g and Young's modulus. The incorporation of 10% PEG 600 shows about 3% elongation, 308.8 MPa Young's

TABLE 1 **The Influence of Different Plasticizers on the Thermal and Mechanical Properties of Shellac Films[a]**

Plasticizer concentration (w/w)	Elastic modulus [MPa] (n = 20)	Elongation at break [%] (n = 20)	Glass transition temperature T_g [°C] (n = 4)
none	——	——	55.60 ± 1.00
PEG 600 10%	308.8 ± 12.0	3.0 ± 1.0	54.30 ± 1.20
PEG 600 15%	170.2 ± 13.2	13.6 ± 2.6	44.59 ± 1.00
PEG 600 20%	70.3 ± 5.90	50.2 ± 1.3	37.30 ± 0.50
PEG 600 30%	40.1 ± 1.30	85.0 ± 1.8	32.42 ± 2.00
PEG 1500 10%	338.4 ± 12.00	3.1 ± 0.5	45.64 ± 2.00
PEG 1500 15%	186.6 ± 10.0	12.9 ± 1.4	44.21 ± 1.00
PEG 1500 20%	76.7 ± 3.90	46.9 ± 11.2	35.40 ± 0.60
PEG 1500 30%	37.9 ± 1.3	117.3 ± 7.0	29.59 ± 1.00
PEG 4000 10%	443.7 ± 15.2	2.9 ± 1.1	45.60 ± 1.40
PEG 4000 15%	283.2 ± 9.1	5.7 ± 1.9	36.09 ± 1.00
PEG 4000 20%	189.4 ± 2.4	33.2 ± 2.0	30.90 ± 2.00
PEG 4000 30%	25.7 ± 1.1	153.2 ± 2.7	20.64 ± 1.00
PEG 6000 10%	495.0 ± 13.0	2.95 ± 1.0	44.00 ± 1.00
PEG 6000 15%	324.4 ± 11.4	2.9 ± 0.8	36.80 ± 0.40
PEG 6000 20%	173.7 ± 5.09	36.5 ± 1.2	31.10 ± 1.30
PEG 6000 30%	24.5 ± 1.76	160.8 ± 6.8	19.78 ± 1.00
PEG 35 000 10%	398.1 ± 9.8	3.1 ± 1.1	46.50 ± 0.80
PEG 35 000 15%	228.0 ± 11.6	4.9 ± 1.2	41.49 ± 2.00
PEG 35 000 20%	52.2 ± 4.4	104.0 ± 6.0	34.89 ± 1.00
PEG 35 000 30%	14.6 ± 1.7	179.2 ± 5.4	15.68 ± 2.00
TEC 10%	291.0 ± 7.2	3.1 ± 1	43.43 ± 1.00
TEC 15%	253.9 ± 4.8	5.4 ± 1.0	36.70 ± 0.60
TEC 20%	194.6 ± 3.8	9.5 ± 2.3	34.80 ± 1.20
TEC 30%	108.6 ± 2.0	22.35 ± 2.0	29.14 ± 1.00

[a]Mean ± SD.

Modulus, and T_g of 55.6°C. Addition of 30% PEG 600 resulted in a decrease of Young's modulus to about 108.6 and a decrease in T_g to 32.35°C.

Increasing the molecular weight is associated with increasing the molecular volume and decreasing the number of hydroxyl groups that leads to a decrease in the accessibility to diffuse into and interact with the chains of shellac. This leads to reduction of the thermodyamical activity of plasticizers. However, plasticizers with higher molecular weights showed unpredictably strong plasticization efficiency at concentrations above 20%. That could be explained by their different plasticization mechanisms, PEGs with high molecular weights have a great number of segments, then the chains become too long and will tangle the chains of polymer which also impede the interaction between the molecules of polymer themselves (Jiang et al., 2002).

PEG 1500 has a larger molecular volume and smaller number of hydroxyl groups; therefore it shows a reduction in thermodynamical effect on shellac. Increasing the molecular volume of PEG 1500 has small meaning at concentration between 10 and 15% when compared with PEG 600. The incorporation of 15% PEG 1500 increases the elongation percentage of free shellac film to about 12.95% from the initial length and decreases Young's modulus to 186.6 MPa and T_g to about 44.21°C. First, at concentrations above 20%, PEG 1500 showed obviously another plasticization mechanism. The elongation of the shellac films containing 30% w/w PEG 1500 was found to increase by nearly 117.3% from the initial length and the T_g decreased to about 29.6°C.

Strengthening of the above mentioned mechanism of plasticizers with higher molecular weight was observed with increasing its molecular weights. PEGs 4000, 6000, and 35,000 at concentration of 30% w/w increased the flexibility of the films extremely. PEG 35,000 at concentration of 30% caused an increase in elongation percentage of the films to about 179.2% followed by PEG 6000 (160.78%) and PEG 4000 (153.21%). On the other hand, the Young's modulus

of that film was decreased. Addition of 30% of PEG 4000 decreased Young's modulus to 25.67 followed PEG 6000 which decreased the modulus to 24.5 and PEG 35,000 at the same level to 14.6.

Triethyl citrate (TEC) has a small molecular volume and it can diffuse into and interact with shellac chains (thermodynamical activity); on the other hand it has a compact structure and bulkier ethyl group which reduces the accessibility of the carbonyl oxygen to interact (Landry et al., 2001). Therefore, concentrations above 20% w/w TEC were needed to improve the flexibility of shellac films. The addition of 30% TEC increased the elongation of the films to about 32.35% and decreased Young's modulus by 108.6 and T_g by 29.14°C.

The results showed that the T_g is a good indicator for the flexibility and elasticity of the films. The DSC studies correlated very well with results from the physical–mechanical tests, as the T_g was reduced to the greatest extent by maximal increasing of the elongation percentage and decreasing of Young's modulus. PEG 35,000 at a concentration of 30% leads to a decrease in T_g to 15.68°C, followed by PEG 6000 (19.78°C) and PEG 4000 (20.64°C). Films containing 20–30% of such plasticizers were very soft and weak due to the excessive plasticization of the polymer.

Therefore it was considered that PEG 600 and PEG 1500 are the best plasticizers for shellac followed by TEC at higher concentrations.

The Influence of Polymers

The incorporation of carbomer and HPMC and MC into shellac films resulted in an increase the percent of elongation at break and a decrease in the elastic modulus.

The results of the physical–mechanical test showed that MC at concentrations of 20–25% (w/w based on the mass of shellac) decreases the percent of elongation at break of the films from about 3 to 145%. Hydroxypropyl methylcellulose (HPMC) at a concentration of 20% (w/w) increased the elongation at break percentage to 22.2 and a concentration of 25% increased the elongation at break percentage to 47.4. The addition of only 2–2.5% carbomer could increase the elongation percentage to 31–52. Respectively, the elastic modulus values of the films were continuously decreased with increasing the concentrations of such polymers (Table 2). The addition of 25% MC to shellac reduced the modulus to 37.93, while the reduction in modulus for the same level of HPMC was 40.1. Carbomer at a concentration of 2.5% w/w caused a reduction in modulus by 60.67 MPa.

TABLE 2 **The Influence of Polymers on the Thermal and Mechanical Properties of Shellac Films**[a]

Polymer additives (w/w based on the mass of shellac)	Young's modulus [MPa] (n = 20)	Elongation at break [%] (n = 20)	Glass transition temperature T_g [°C] (n = 4)
none	338.4 ± 1.2	3.05 ± 0.6	45.64 ± 2.0
HPMC 10%	214.4 ± 4.0	13.2 ± 2.4	49.2 ± 1.0
HPMC 20%	144 ± 5.0	22.3 ± 1.3	45.72 ± 1.0
HPMC 25%	70.8 ± 3.0	43.0 ± 10.8	43.11 ± 1.2
MC 10%	317.0 ± 12.0	7.0 ± 3.8	44.2 ± 1.0
MC 20%	63.1 ± 5.0	140.3 ± 9.0	35.32 ± 0.5
MC 25%	56.9 ± 3.0	145.2 ± 20.0	35.22 ± 0.5
Carbomer 0.5%	439.8 ± 3.5	3.08 ± 1.1	41.34 ± 1.0
Carbomer 2%	110.2 ± 4.5	31.91 ± 2.9	38.47 ± 1.2
Carbomer 2.5%	60.7 ± 2.6	52.52 ± 5.3	38.43 ± 2.0
PVA 10%	335.0 ± 16.0	4.7 ± 0.5	48 ± 2.0
PVA 20%	489.0 ± 5.0	2.80 ± 1.00	67.34 ± 1.0
PVA 25%	570 ± 14.0	1.50 ± 0.80	71.98 ± 3.0
EC 10%	317.5 ± 3.4	3.3 ± 2.0	48.5 ± 1.0
EC 20%	360.1 ± 4.0	2.8 ± 2.3	48.92 ± 0.5
EC 25%	365.4 ± 5.3	2.1 ± 2.1	49.02 ± 0.5

[a]Mean ± SD.

In addition, the incorporation of PVA at different concentrations increased the elastic modulus and decreased the elongation. The results showed that PVA at a concentration of 25% (w/w based on the mass of shellac) decreased the elongation percentage to 1.5 and increased the elastic modulus of free films to 570 MPa. Ethyl cellulose (EC) demonstrated a decrease in elongation at break to 2% at a concentration of 25% (w/w).

It is well documented in the literature that the more efficient plasticization effect is greater than the lowering of T_g (Wu & McGinity, 1999). Based on this criteria, all the DSC results could be correlated again with the results obtained from the physical–mechanical tests. Methyl cellulose (MC) has the largest plasticization efficiency on shellac films. Methyl cellulose (MC) at concentrations of 20–25% decreased the T_g to about 35°C, followed by carbomer which decreased the T_g at all concentrations to 38°C, followed by HPMC which decreased the T_g to 43°C at a concentration of 25% (w/w). Polyvinyl alcohol (PVA) increased the T_g of free films. The addition of 25% (w/w based on the mass of shellac) increased the T_g to about 72. In addition, EC was shown to exert no effect on the thermal properties of the films.

As it was stated, the addition of MC, HPMC, and carbomer resulted in an increase of elongation percentage and decrease the elastic modulus as the level of such polymers added to shellac films was increased. The decrease in elastic modulus was due to a lowering of the T_g and the increase in elasticity of the polymer. Ethyl cellulose (EC) has no plasticization effect on free shellac films. The results could be explained by the miscibility between the polymers. The solubility of polymers is one parameter for the miscibility (Tarvainen et al., 2001). Methyl cellulose (MC), HPMC, and carbomer are good soluble in water and have a higher affinity to diffuse into and interact with the polymer molecules in water, thereby increasing the mobility of polymeric chains at different magnitudes. On the other hand, EC is not soluble in water. There was no reduction in the T_g and a slight increase in the elastic modulus at different concentrations due to the hydrodynamic effects of the hydrophobic additive like EC, including the orientation of filler particles, and on reinforcing effects, such as physical or chemical bonding of insoluble materials to polymer matrix (Felton & McGinity, 2002).

Glass transition temperature (T_g) is another parameter for the miscibility between two polymers; good miscibility between two polymers resulted in reduction of the T_g (the presence of MC, HPMC, and carbomer).

Furthermore, the fall of the mobility of shellac chains which associated with the increasing of the T_g by addition of PVA showed that this polymer has a strong bonding with shellac molecules and may yield a cross-linking network. In addition, PVA could form crystallite in aqueous solutions after drying (Lim & Wan, 1994; Lim, 1995). Increase of the crystallinity of the films is accompanied with an increase of the T_g of polymeric films (Sudhamani et al., 2003, Sarisuta et al., 1999).

Drug Permeability of Free Shellac Films

In this study theophylline was used as drug model and the influences of the polymers at different concentrations on the permeation properties of free shellac films were investigated. The permeability constants of the films were calculated.

The permeability of shellac films containing MC, HPMC, or carbomer was significantly larger than the permeability of films initially not containing polymer. The values obtained are listed in Table 3. The permeability of

TABLE 3 **Permeability Constants P ($m^2s^{-1}\cdot10^{-14}$) of Free Shellac Films Containing Different Concentrations of Different Polymers**

Concentration of polymer additive (% w/w based on the mass of shellac)	Permeability Constant [$m^2s^{-1}\cdot10^{-14}$]				
	0%	10%	15%	20%	25%
Shellac + PEG 1500 10%	3.58 ± 0.3	—	—	—	—
Shellac + HPMC	—	10.62 ± 0.4	22.56 ± 0.5	44.76 ± 1.0	54.20 ± 2.0
Shellac + MC	—	11.93 ± 0.3	23.86 ± 1.0	48.80 ± 0.8	59.60 ± 1.7
Shellac + EC	—	2.47 ± 0.2	2.40 ± 0.5	1.12 ± 0.5	1.08 ± 0.6
Shellac + PVA	—	2.98 ± 0.5	2.80 ± 0.4	1.80 ± 0.7	1.40 ± 0.3

shellac films containing PVA or EC was smaller than the permeability of films initially not containing polymer.

The results show also that there is a direct relationship between the drug permeability and the concentrations of HPMC, MC, and carbomer which increased the permeation properties of free shellac films, and a further increasing of the concentrations of these polymers leads to a further increase of theophylline permeability (Figs. 1, 2, and 3).

The permeability results are good correlated with the mechanical properties of free films. The plasticization effect of water soluble polymers enhances segmental mobility, leading to an increase in the number, size, and distribution of the pores and diffusion channels (the results of porosity study are shown in Table 4). Therefore it increased the hydrophilicity of the hydrophobic film and the diffusion of water. The dissolving of such polymers in the aqueous mediums and leaching out leads to creating a microporous membrane. Figure 4 shows the creation of pores after the leaching out of HPMC. This result is in agreement with results of Pearnchob N. et al. (2004) who reported recently that the addition of some water soluble additives resulted in an enhancement of the permeability of shellac films.

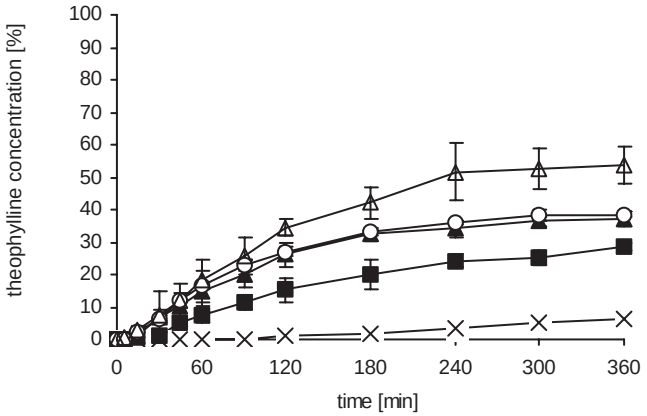

FIGURE 1 **The Effect of HPMC on Drug Permeability of Shellac Films Containing 10% w/w PEG 1500, (×) HPMC 0% w/w, (■) HPMC 10% w/w, (▲) HPMC 15% w/w, (○) HPMC 20% w/w, and (△) HPMC 25% w/w. Means ± SD, *n* = 8.**

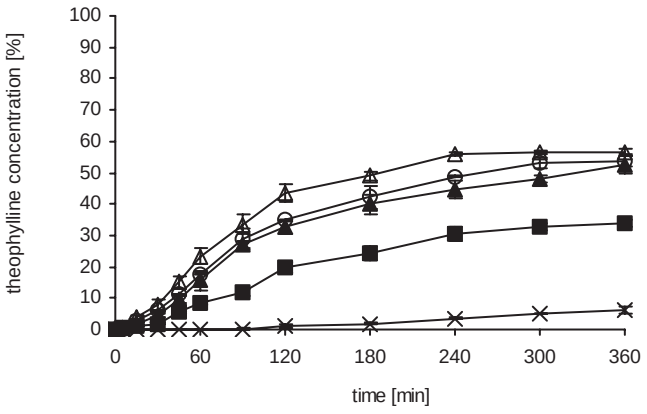

FIGURE 2 **The Effect of MC on Drug Permeability of Shellac Films Containing 10% w/w PEG 1500, (×) MC 0% w/w, (■) MC 10% w/w, (▲) MC 15% w/w, (○) MC 20% w/w, and (△) MC 25% w/w. Means ± SD, *n* = 8.**

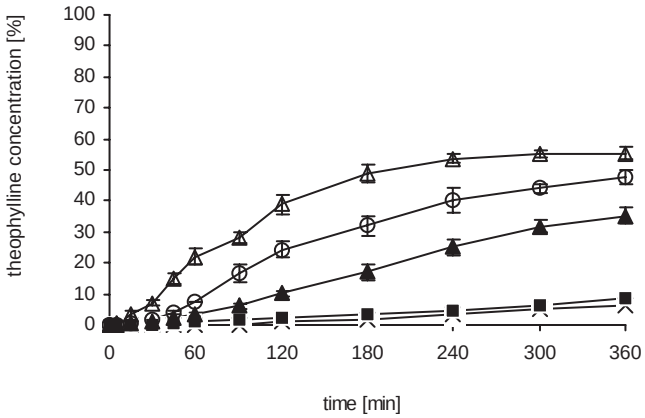

FIGURE 3 **The Effect of Carbomer 940 on Drug Permeability of Shellac Films Containing 10% w/w PEG 1500, (×) carbomer 0% w/w, (■) carbomer 0.5% w/w, (▲) carbomer 1% w/w, (○) carbomer 2% w/w, and (△) carbomer 2.5% w/w. Means ± SD, *n* = 8.**

In addition, carbomer increases the viscosity of alkaline solutions due to hydration of the carboxyl groups in its structure resulting in increasing the swelling of coating material (Muramatsu et al., 2000). Thus, much higher drug permeability can be expected in these coatings.

Furthermore, the incorporation of PVA or EC in free shellac films lowered the theophylline permeation (Figs. 5 and 6) due to the low solubility of such polymers in water (PVA is poor soluble in water and EC is insoluble in water). In addition, the presence of poor soluble or insoluble additives (PVA and EC) leads to increasing of the crystallinity and cross-linking in the film in addition to the reinforcing effects of insoluble polymer (EC), which hinders polymer chain mobility with a corresponding fall in the size and number of pore, diffusion pathways, and diffusivity (Okhamafe & York, 1987).

Hydrophilic polymers or other inserted substances could increase the permeability of films in several ways:

TABLE 4 **The Porosity of Free Shellac Films Containing Different Amounts of Different Polymers[a]**

Concentration of polymer additive (% w/w based on the mass of shellac)	Porosity [%]				
	0%	10%	15%	20%	25%
Shellac + PEG 1500 10%	1.05 ± 0.0	—	—	—	—
Shellac + HPMC	—	1.40 ± 0.1	2.87 ± 0.1	4.33 ± 0.1	5.12 ± 0.1
Shellac + MC	—	1.40 ± 0.1	3.21 ± 0.2	4.71 ± 0.3	5.89 ± 0.5
Shellac + EC	—	1.00 ± 0.0	0.87 ± 0.0	0.75 ± 0.0	0.55 ± 0.0
Shellac + PVA	—	1.02 ± 0.0	0.80 ± 0.0	0.76 ± 0.0	0.60 ± 0.0

[a]Means ± SD, $n = 4$.

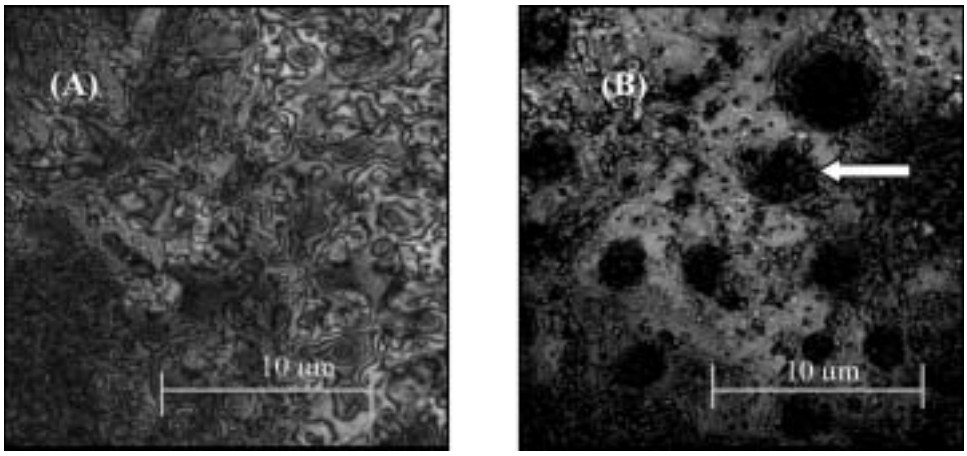

FIGURE 4 **Scanning Acoustic Microscope Images Showing (A) Shellac Film Containing 25% HPMC After 5 min in Water; (B) Shellac Film Containing 25% HPMC After 1 h in Water.**

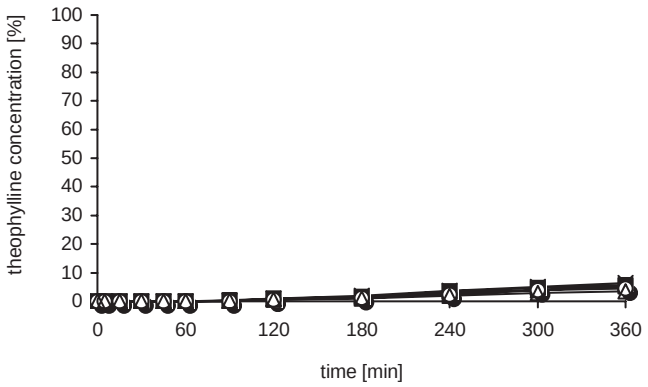

FIGURE 5 **The Effect of PVA on Drug Permeability of Shellac Films Containing 10% w/w PEG 1500, (×) PVA 0% w/w, (■) PVA 10% w/w, (▲) PVA 15% w/w, (○) PVA 20% w/w, and (△) PVA 25% w/w. Means ± SD, $n = 8$.**

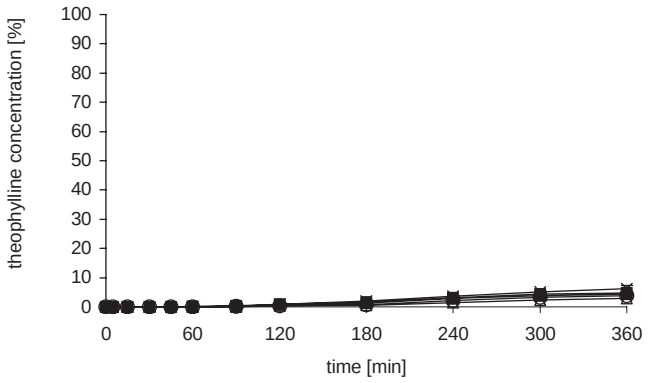

FIGURE 6 **The Effect of EC on Drug Permeability of Shellac Films Containing 10% w/w PEG 1500, (×) EC 0% w/w, (■) EC 10% w/w, (▲) EC 15% w/w, (○) EC 20% w/w, and (△) EC 25% w/w. Means ± SD, $n = 8$.**

1. Changing the properties of the film matrix by altering the polymer configuration, changing the properties of the crystalline and amorphous regions and increasing directly the hydrophilicity of the film. Such films would appear to be homogeneous or at least sub micro-heterogeneous;
2. Introducing increased porosity into the films by forming capillaries and a hydrated network giving direct connection between the two sides of the film;

3. Acting as the carriers of penetrates by forming complexes having increased membrane solubility or diffusion coefficient.

These effects need not necessarily occur independently (Danbrow & Friedman, 1975).

CONCLUSION

All plasticizers which were used in this study have a good plasticization efficiency on free shellac films; the incorporation of these plasticizers into shellac films caused a significant reduction in the T_g of the films and a marked decrease in Young's modulus and an increase in elongation at break. The plasticization efficiency was related to the concentrations and molecular weights of the plasticizers. Moreover, plasticizers with high molecular weights have another plasticization mechanism.

Free shellac films containing different amounts of HPMC, MC, EC, PVA, and carbomer 940 were prepared. The addition of HPMC, MC, and carbomer enhanced the plasticization effect of plasticizer, which is advantageous with regard to the mechanical stability of shellac films and further processing. On the other hand, the addition of PVA and EC resulted in more brittle films. In addition, the drug permeability of shellac films was improved by the presence of water soluble polymers such as HPMC, MC, and carbomer.

Poor water soluble and insoluble polymers such PVA and EC enhanced the reduction of drug permeability.

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