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RESEARCH PAPER

Influence of Plasticizers and Drugs on the Physical-Mechanical Properties of Hydroxypropylcellulose Films Prepared by Hot Melt Extrusion

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ABSTRACT

Hydroxypropylcellulose (HPC) films containing drugs or hydrophilic or hydrophobic plasticizers were prepared by a hot melt extrusion process. Polyethylene glycol 8000 (PEG 8000) 2%, triethyl citrate (TEC) 2%, acetyltributyl citrate (ATBC) 2%, and polyethylene glycol 400 (PEG 400) 1% were the plasticizing agents studied. In addition, either hydrocortisone (HC) 1% or chlorpheniramine maleate (CPM) 1% was incorporated into the films as a model drug. The physical-mechanical properties of the films that were investigated included tensile strength (TS), percentage elongation (%E), and Young's modulus (YM). Differential scanning calorimetry (DSC) was utilized to determine glass transition temperatures (T_g's). These parameters were studied as a function of time and temperature. The glass transition temperatures initially decreased with the inclusion of the drugs and plasticizers. However, after 6 months aging, films containing PEG 400 and HC showed a marked increase in T_g. The films containing PEG 400 showed physical-mechanical instability in all parameters studied. All extruded films exhibited a marked decrease in TS in contrast to a large increase in %E when testing was performed perpendicular to flow versus in the direction of flow. In addition, a consistent film of HPC in the absence of drugs or plasticizers could not be extruded due to the excessive stress on the equipment. Although the theoretical percentage of CPM on aging remained fairly constant over

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the processing temperature ranges in this study, the HC levels remaining in the extruded films during storage were a function of time and temperature.
Key Words: *Chlorpheniramine maleate; Extruded films; Hot melt; Hydrocortisone; Hydroxypropylcellulose; Physical-mechanical properties.*

INTRODUCTION

Transdermal and transmucosal drug delivery systems are frequently produced via film casting from organic or aqueous solvents. Aitken-Nichol, Zhang, and McGinity noted numerous disadvantages accompanying these techniques, including long processing times, high costs, and environmental concerns (1). In addition, Gutierrez-Rocca and McGinity showed a decrease in plasticity on aging of acrylic films cast from isopropyl alcohol (2). These researchers demonstrated that the attainment of stable mechanical properties might be as long as 2 months depending on the type and level of plasticizer and the storage conditions.

Aitken-Nichol and coworkers also reported a 25- to 35-fold increase in both tensile strength (TS) and percentage elongation (%E) in a high-density polyethylene/Eudragit E100 (50:50 polymer ratio containing 5% lidocaine HCl) extruded film when tested in the direction of orientation versus perpendicular to orientation (1). It has also been reported that alterations in cellulose film structure may affect drug transport and mechanical properties (3).

Follonier, Doelker, and Cole showed that thermally stable drugs, such as diltiazem HCl, can be hot melt extruded into pellets without significant drug degradation (4). Very little research, however, has been published on drugs concerning hot melt extruded films, including the extrusion of thermally nonstable drugs such as hydrocortisone (HC). In addition, the level and type of plasticizer, as well as processing temperature, have been demonstrated to influence the dissolution rate of drugs from films formed from aqueous dispersions (5–9). Although hot melt extrusion has recently received some attention in the pharmaceutical field, the influence of plasticizers and drugs on the relationship of the physical-mechanical properties of hot melt extruded hydrophilic films has not been investigated.

MATERIALS AND METHODS

Materials

Hydroxypropylcellulose (HPC) (MW 1,150,000), Klucel® HF, was obtained from Aqualon Company, Wilmington, DE. Plasticizers utilized included polyethylene glycol 400 NF (PEG 400) and polyethylene glycol 8000 NF (PEG 8000) (Union Carbide Corp., Danbury, CT) and triethyl citrate (TEC) and acetyltributyl citrate (ATBC) (Morflex, Inc., Greensboro, NC). The model drugs incorporated in the films were micronized HC USP, (Upjohn Co., Kalamazoo, MI) and chlorpheniramine maleate (CPM) (Sigma Chemical Co., St. Louis, MO).

Processing Methods

The HPC was dried at 50°C for 24 hr prior to the incorporation of the plasticizers and drugs. TEC, ATBC, and PEG 400 were incorporated slowly into a Liquid-Solids Blender® (Paterson-Kelley Co., East Stroudsburg, PA) containing the HPC. PEG 8000, HC, and CPM were blended directly with the HPC. All additives were blended for 30 min.

A Killion extruder (model KLB-125; Killian Extruder, Inc., Cedar Grove, NJ) was heated to 170°C melt temperature (a schematic of a single-screw extruder is illustrated in Fig. 1). Polyethylene pellets were placed in the hopper and passed through the extruder for 5 min (this procedure was repeated for each batch). The blend of HPC and plasticizer or drug was placed in the hopper and extruded to obtain a homogenous film with thickness from 8 mil to 13 mil (1 mil = 25.4 μm or 0.001 inch). The temperature settings of 180°C, 190°C, and 200°C were sequentially

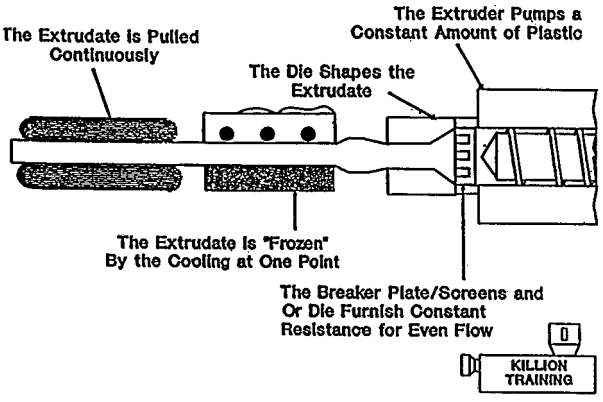

Figure 1. Schematic of the processing method for forming hot melt extruded films.

set, and film was extruded as described above. The film was collected in rolls, labeled, and sealed in 5-mil polyethylene bags. Initial testing began after 7 days of storage.

Analytical Methods

The physical-mechanical properties of the films were distinguished utilizing an Instron 4201 testing apparatus with a head speed of 10 mm/min. The method used for evaluating the mechanical properties was based on guidelines of the American Society for Testing Materials, method D 882-95a (10). Six samples from each formulation were tested. The initial grip separation was 100 mm.

A differential scanning calorimeter (TA Instruments, DSC 2920 Modulated DSC) was used to measure glass transition temperatures (T_g's) (ramp 10°C/min). Glass transition temperatures are reported using the midpoint method.

Sample analysis of HC and CPM was conducted on a Waters HPLC system with a 486 UV detector, together with a Waters pump (model 501) utilizing an Altech Nucleosil C-18 (5 μm), 250 mm × 4.6 mm column. For HC, the mobile phase was 65/35 methanol/water, flow rate 1 ml/min, injection volume 50 μl, and detection wavelength 242 nm. Analysis of CPM was performed using 30% acetonitrile with 70% pH 2.0 buffer solution (50 mM phosphate monobasic), flow rate 1 ml/min, 50 μl injection volume, and detection wavelength of 261 nm. Retention times for HC and CPM were 6.7 and 3.2 min, respectively.

Loss on drying of the films was performed on a moisture analyzer (Sartorius MA 50). Five samples of each film of weight 3 to 4 g were investigated.

Calculations were performed in the following manner:

$$\text{Tensile Strength } (\sigma) = \text{Force or Load } (F)/MA$$

where F is the maximum load, and MA is the minimum cross-sectional area of the film specimen. Results were converted to megapascal units (MPa).

$$\text{Strain } (\varepsilon) = (L_o - L)/L_o = \Delta L/L_o$$

$$\text{Elongation Percentage} = \varepsilon \times 100$$

$$\text{Young's Modulus } (E) = \Delta\sigma/\Delta\varepsilon$$

L_o refers to the initial length of the film sample, and L is the elongation at the moment of rupture. Young's modulus (YM) was calculated by extending the linear portion of the stress-strain curve and dividing the difference in stress ($\Delta\sigma$) by the difference in strain ($\Delta\varepsilon$).

RESULTS AND DISCUSSION

The HPC was extruded into opaque, flexible films with differing mechanical properties dependent on the particular plasticizer/drug present in the extruded film. These properties are seen in Table 1. Without the use of a plasticizer or drug, HPC could not be processed on the extruder due to the excessive stress it placed on the equipment. Therefore, the plasticizers and drugs utilized in this study were necessary to extrude a film successfully.

Processing studies demonstrated that a narrow concentration range of PEG 400 could be used to extrude HPC film. This ''window'' was in the range 0.75% to 1.5%. Below the lower limit, a film could not be extruded due to excessive stress on the extruder, thus indicating inadequate plasticization. Above the 1.5% threshold, the polymer powder agglomerated, producing inconsistent flow from the hopper. In addition, propylene glycol (PG) could not be used as an acceptable plasticizer with the HPC at any percentage level. The PG was not an adequate plasticizer for HPC, possibly due to its low molecular weight and high volatility at the processing temperatures utilized in this study.

Initially, as shown in Table 1, all components studied appeared to be suitable plasticizers and produced a ductile film. The elongation varied between 4.49% for hydrocortisone and 6.62% for PEG 400 (in the direction of flow). In addition to exhibiting the highest percentage elongation initially, the film containing PEG 400 had the lowest Young's modulus in addition to the lowest initial T_g. However, the 2% TEC and the 2% ATBC plasticized films had T_g's in a similar range (46.7°C for TEC and 44.2°C for ATBC vs. 41°C for the film containing 1% PEG 400). The incorporation of plasticizers or drugs, however, for all the films lowered the glass transition temperature of the HPC alone.

The results in Table 1 also illustrate that changes in percentage elongation in the direction of flow occurred with certain additives over time. However, the only change that was statistically significant was the lowering of the percentage elongation with the PEG 400 plasticized film after 6 months of storage. Initially, the PEG 400 film had the highest percentage elongation (6.6% ± 0.6%). In contrast, the PEG 8000 film had a percentage elongation of 5% ± 0.4% initially. The percentage elongation at all data points was actually lower for the PEG 8000 than the PEG 400. This could be explained by its lower molecular weight compared to the film containing PEG 8000. This finding is consistent with that of Heinamaki and coworkers (8). They found that ductility (percentage elongation) was mainly attributed to the molecu-

Table 1

Influence of Plasticizers and Drugs on Tensile Strength (TS), Percentage Elongation (%E), and Young's Modulus (YM) of HPC Extruded Films (n = 6) Stored at 25°C

	TS, Initial	TS, 3 Months	TS, 6 Months
PEG 8000 2%	13.7 (1.1)	13.2 (1.3)	12.2 (0.7)
TEC 2%	17.2 (1.7)	18.9 (1.1)	20.8 (0.7)
ATBC 2%	26.1 (2.6)	19.2 (1.5)	19.6 (1.4)
PEG 400 1%	37.6 (3.5)	29.9 (2.7)	27.9 (2.1)
HC 1%	26.7 (2.7)	33.0 (2.7)	34.1 (3.8)
CPM 1%	32.7 (3.4)	32.9 (3.1)	30.8 (1.8)
	%E, Initial	%E, 3 Months	%E, 6 Months
PEG 8000 2%	5.01 (0.4)	4.45 (0.6)	4.39 (0.7)
TEC 2%	5.29 (0.4)	5.37 (0.4)	5.08 (0.6)
ATBC 2%	6.02 (0.6)	6.13 (0.5)	6.40 (0.7)
PEG 400 1%	6.62 (0.6)	5.25 (0.6)	5.05 (0.5)
HC 1%	5.40 (0.4)	4.82 (0.4)	4.55 (0.4)
CPM 1%	5.26 (0.4)	5.03 (0.7)	4.87 (0.7)
	YM, Initial	YM, 3 Months	YM, 6 Months
PEG 8000 2%	4.25 (0.2)	4.31 (0.6)	4.21 (0.4)
TEC 2%	4.43 (0.3)	4.11 (0.4)	4.09 (0.4)
ATBC 2%	4.75 (0.6)	3.09 (0.5)	3.19 (0.4)
PEG 400 1%	4.05 (0.3)	7.13 (0.3)	6.15 (0.6)
HC 1%	6.57 (0.3)	7.98 (0.3)	8.60 (0.3)
CPM 1%	5.38 (0.3)	4.44 (0.4)	4.64 (0.3)

Standard deviations denoted in parentheses.

lar weight of the polymer plasticizer. Rowe found that as the molecular weight, and thus the size, of the PEG is increased, the mole fraction of available hydroxyl groups to interact with the hydroxyl groups of the HPC will decrease, and the film will become less elastic (11). However, over the 6-month study, the elongation of the film containing PEG 400 decreased from 6.6% ± 0.6% to 5.1% ± 0.5%. Since the percentage elongation was very similar for the PEG-incorporated films at 3 months and at 6 months (4.9% and 5.1%, respectively), it appears that this mechanical property stabilized at the 6-month point.

The glass transition temperatures correlated well with the results of the percentage elongation of films when measured in the direction of flow. These results are seen in Fig. 2. The PEG 400 film showed a statistical increase in T_g at 6 months versus the initial data (59.6°C to 41°C, respectively), thus explaining the significant loss in ductility. In addition, the HC film exhibited a statistical increase in T_g. Although not statistically significant, the HC-incorporated film did show a corresponding downward trend in percentage elongation. This may be explained by aggregation of the relatively hydrophobic HC particles in the HPC film, as could be seen visually. As these aggregates increase in size and number, stress points in the film are formed. Consequently, the HC-incorporated film exhibited a more brittle, less elastic texture.

The highest tensile strength values initially (in the direction of flow) were found in films containing PEG 400 and CPM, 37.6 and 32.7 MPa, respectively. The PEG 400 film, however, exhibited a significant drop in TS at the 3-month and 6-month points. Despite this loss, the film did maintain a relatively high TS at 6 months (27.9 MPa). In contrast, the CPM-incorporated film was found to be stable throughout the study. The ATBC-incorporated film showed a large drop in tensile strength following storage at 25°C for 6 months, in addition to a significant drop in YM. This could be explained due to its low miscibility with the HPC. The HC film exhibited a relatively high tensile strength, which increased during the study, but not significantly (26.7 MPa to 34.1 MPa). In addition, this

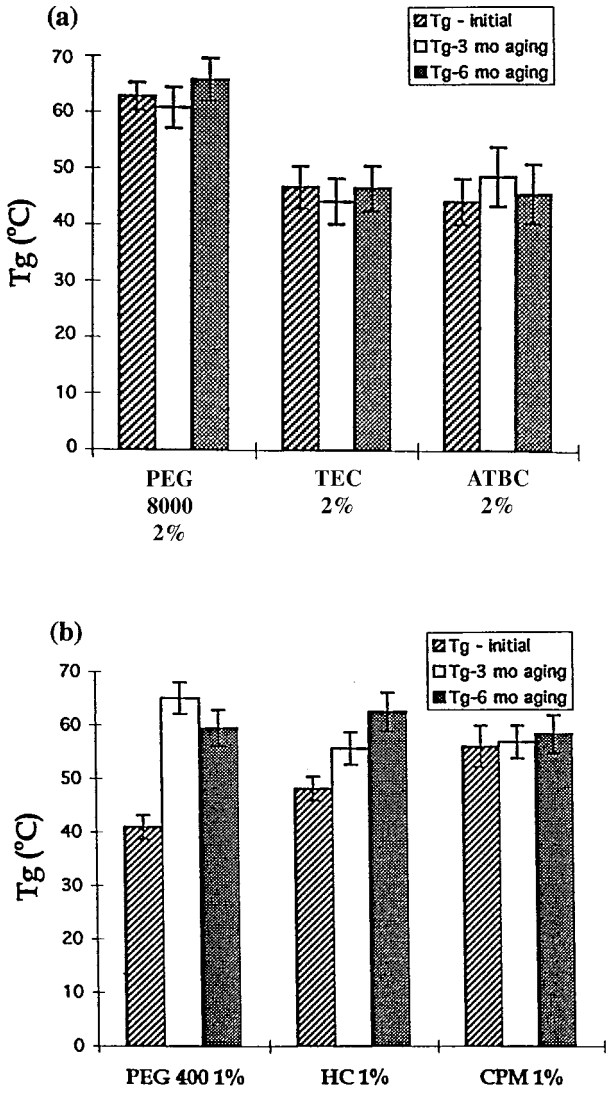

Figure 2. (a) Glass transition temperatures of HPC films containing PEG 8000 2%, TEC 2%, and ATBC 2% at 1 week, 3 months, and 6 months; (b) glass transition temperatures of HPC films containing PEG 400 1%, HC 1%, and CPM 1% at 1 week, 3 months, and 6 months.

same film exhibited a downward trend in percentage elongation on storage. Drug aggregation in the HPC film due to HC's relative hydrophobic properties or HC degradation may explain the film's mechanical property changes.

Initially, the films containing PEG 8000, TEC, ATBC, and PEG 400 had essentially the same Young's Modulus (Table 1). The HC film had the highest YM throughout the study and the lowest percentage elongation. Not surprisingly, even visually, this film appeared to be the most brittle film, exhibiting the most irregular breaks on testing. Hydrocortisone's hydrophobic properties, in contrast to the hydrophilic HPC, could likely contribute to the brittle character of the film. The other films, in contrast, showed a similar consistent breakage during the mechanical tests.

An interesting inverse relationship was discovered with tensile strength and percentage elongation when these two mechanical properties of the films were measured in the direction of flow of the film versus perpendicular to flow. As shown in Fig. 3, TS decreased a minimum of fourfold when tested perpendicular to orientation when compared to the measurement of TS of the film in the direction of orientation. Conversely, elongation percentage statistically increased with all films tested. The

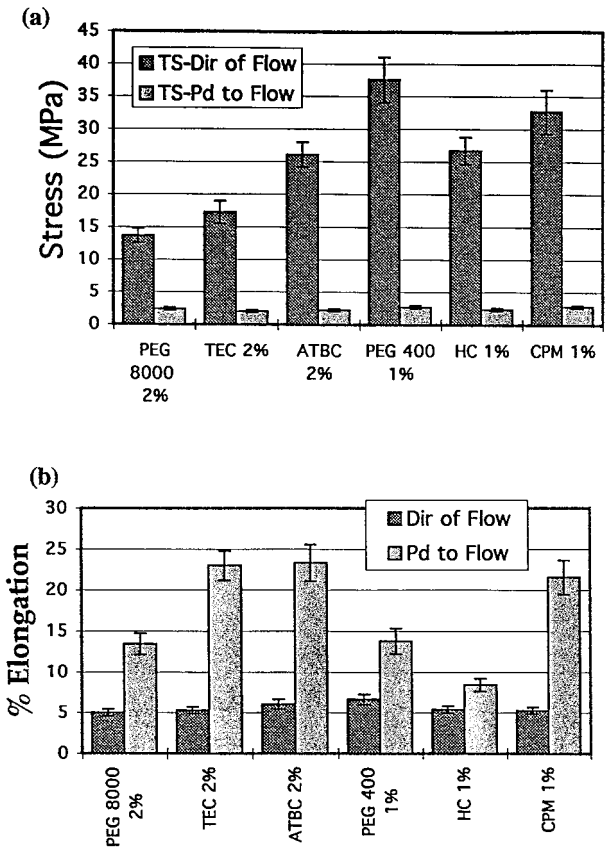

Figure 3. (a) Tensile strength of HPC films containing various plasticizers and drugs tested in direction of flow and perpendicular to flow; (b) percentage elongation of HPC films containing various plasticizers and drugs tested in direction of flow and perpendicular to flow.

greatest increase occurred with the TEC-containing film (from 5.3% in the direction of flow to 23% perpendicular to flow). Aitken-Nichol et al. (1) found similar results in the case of tensile strength with a hot melt extruded high-density polyethylene (HDPE)/Eudragit E-100/lidocaine HCl film. However, in percent elongation at break, these workers found a significant decrease in contrast to the present study. This can be explained by the cellulose structure itself and consequent cross-linking by the various plasticizers and drugs incorporated into the film in contrast to the HDPE/Eudragit structure. When extruded, the cellulosic material oriented in the direction of flow out of the film die. As the material flows out of the extruder, the film is pulled and wound into rolls. Thus, the more rigid covalent bonds have already been strained to some extent. In contrast, the rather linear cellulose strands would be interconnected by bonding by three reactive hydroxyl groups present on each anhydroglucose monomer unit of the cellulose chain. Although chaining out is possible by etherification, it is suggested that this cross-linking of the HPC backbone structure is by hydrogen bonding and other intermolecular forces that are not as rigid as the covalent bonds of the more linear cellulose structure (12). Thus, perpendicular to flow, there was more latitude for elongation. The tensile strength at break, however, would be decreased, as this study demonstrated.

The tensile strength and percent elongation of the extruded films were investigated for films of three different thicknesses (9 mil, 11 mil, and 13 mil) and processed at three temperatures (180°C, 190°C, and 200°C). Table 2 illustrates these comparisons. The film containing PEG 400 showed a statistical decrease in tensile strength at the greater thickness level. At the 13-mil thickness, striation and pooling of the plasticizer was evident, visually creating irregularities in the film. The ATBC film had greater tensile strengths at 11 and 13 mil, which were statistically significant when compared to the 9-mil film. The most stable films investigated in terms of tensile strength thickness differences were the film containing PEG 8000 and the TEC film.

The only difference in TS found at the three different processing temperatures was for the film containing PEG 400 (Table 2). The tensile strength fell markedly as the temperature increased. PEG 400 is a relatively low molecular weight polymer. The volatility of this plasticizer increased as a function of processing temperature, therefore less PEG 400 was incorporated into the extruded film as temperature increased. All other films investigated at different temperatures were found to be stable.

All films investigated at different thicknesses showed a statistical increase in percentage elongation from the 9-mil thickness range to the 13-mil thickness range. This finding is consistent with the finding of Park et al. that, for cast HPC films, percentage elongation increased as film thickness increased (13). The only statistical difference in percentage elongation at the three different processing temperatures was for PEG 400, which exhibited a decrease for this mechanical property as the temperature increased. Again, the increased volatility of the PEG 400 may explain this film's function of processing temperature.

Table 2

*Tensile Strength (TS) and Percentage Elongation (%*E*) as a Function of Film Thickness and Processing Temperature (*n = *6)*

	TS, 9 mil	TS, 11 mil	TS, 13 mil	TS, 180°C	TS, 190°C	TS, 200°C
PEG 8000 2%	11.3 (1.3)	13.7 (1.1)	14.4 (1.4)	13.7 (1.1)	15.8 (1.3)	14.0 (1.4)
TEC 2%	19.2 (1.5)	17.3 (1.7)	20.0 (1.8)	17.2 (1.7)	19.4 (1.4)	17.0 (1.6)
ATBC 2%	18.5 (2.3)	26.1 (1.9)	22.6 (2.2)	26.1 (1.9)	23.2 (2.0)	22.0 (2.1)
PEG 400 1%	35.0 (3.3)	37.6 (3.5)	25.6 (3.0)	37.6 (3.5)	27.3 (2.9)	18.6 (1.7)
HC 1%	23.0 (2.3)	26.7 (2.1)	28.9 (2.7)	26.7 (2.1)	24.4 (2.5)	22.1 (2.4)
CPM 1%	30.1 (3.2)	32.7 (3.4)	34.7 (3.1)	32.7 (3.4)	33.0 (3.0)	29.7 (3.2)
	%E, 9 mil	%E, 11 mil	%E, 13 mil	%E, 180°C	%E, 190°C	%E, 200°C
PEG 8000 2%	4.9 (0.5)	5.0 (0.4)	5.0 (0.4)	5.0 (0.5)	5.1 (0.5)	5.0 (0.5)
TEC 2%	5.4 (0.6)	5.3 (0.4)	5.9 (0.4)	5.3 (0.5)	5.4 (0.5)	5.4 (0.4)
ATBC 2%	5.8 (0.6)	6.0 (0.6)	6.1 (0.6)	6.0 (0.6)	6.4 (0.6)	6.1 (0.6)
PEG 400 1%	5.0 (0.6)	6.6 (0.6)	6.8 (0.7)	6.6 (0.6)	6.0 (0.6)	5.1 (0.6)
HC 1%	4.3 (0.4)	4.5 (0.4)	4.7 (0.4)	4.5 (0.4)	4.3 (0.4)	4.0 (0.5)
CPM 1%	5.3 (0.4)	5.3 (0.4)	5.8 (0.4)	5.3 (0.4)	5.4 (0.4)	5.2 (0.3)

Standard deviation denoted in parentheses.

A slight yellow discoloration appeared after extrusion of the HC-containing films. However, at the lower processing temperature, the discoloration was less pronounced. The stability of the HC in the HPC film was dependent on the processing temperature (Table 3). One week after extrusion, at the higher processing temperature only 70.2% of the theoretical amount of HC remained in the film; however, at the lowest processing temperature, almost 94% of the initial drug load was retrieved. In addition, at the lower temperature, after 12 months of storage at 25°C, 91.4% of the theoretical amount still remained in the film, in contrast to 62.9% theoretical amount for films processed at the higher temperature. Aitken-Nichol et al. (1) found a similar result for diphenhydramine HCl in Eudragit E-100 hot melt extruded films and reported a yellow discoloration due to thermal instability. Initially, these authors found only 80% theoretical amount of diphenhydramine after extrusion due to processing temperature degradation.

This instability of the HC at the temperature of the extruded films utilized for mechanical testing can explain some of the mechanical instability and the increasing brittleness of the HC films at the higher temperatures. This instability as a function of temperature was most likely due to an oxidation process at the C-17 or C-21 side chains or to a transformation of HC to a D-homosteroid (14). This degradation product is evidenced by a pronounced peak in the high-performance liquid chromatography (HPLC) profiles in Fig. 4. However, as the processing temperature decreased, the percentage theoretical HC incorporated in the film increased. Therefore, by reducing the processing temperature to 170°C, over 91% of the hydrocortisone, a thermally unstable drug, was present after 12 months. In addition, a residence time of the material of less than 2 minutes in the extruder may contribute to the relatively high percentage of HC remaining in the extruded film.

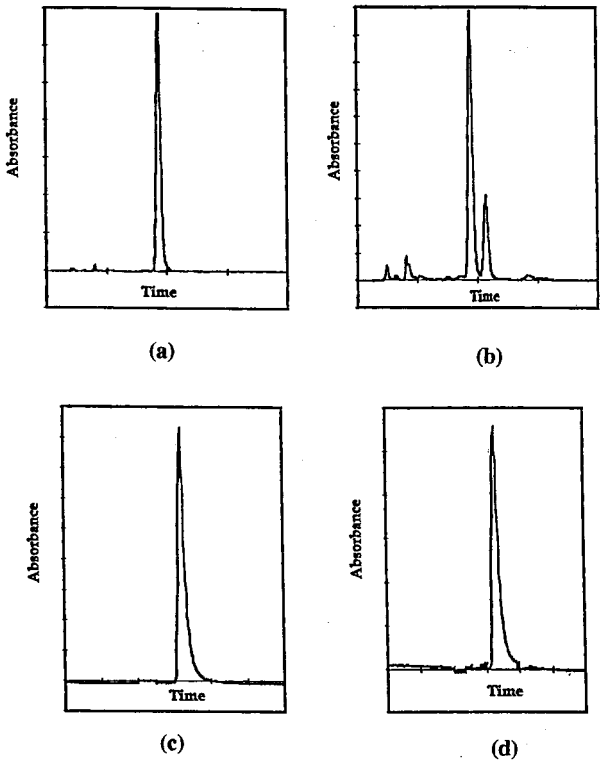

Figure 4. HPLC chromatographs: (a) hydrocortisone standard curve; (b) sample film containing 1% hydrocortisone in HPC extruded at 200°C; (c) chlorpheniramine maleate standard curve; (d) sample film containing 1% chlorpheniramine maleate in HPC extruded at 200°C (retention times for HC and CPM were 6.7 and 3.2 minutes, respectively).

Table 3

Influence of Processing Temperature and Storage at 25°C on Percentage CPM and Percentage HC Remaining in HPC Extruded Films (n = *6)*

°C	CPM, 1 Week	CPM, 6 Months	CPM, 12 Months
170	98.6 (1.6)	98.5 (1.9)	98.4 (1.9)
180	98.5 (1.9)	98.5 (2.1)	98.1 (2.4)
190	98.1 (2.2)	97.6 (2.7)	97.3 (2.5)
200	97.9 (2.3)	97.7 (2.2)	97.6 (2.3)
°C	HC, 1 Week	HC, 6 Month	HC, 12 Months
170	93.9 (2.3)	92.4 (3.0)	91.4 (2.4)
180	87.7 (2.2)	83.1 (2.8)	79.9 (2.2)
190	75.9 (3.2)	70.7 (2.7)	71.6 (2.4)
200	70.2 (3.8)	68.8 (3.3)	62.9 (3.1)

Standard deviations denoted in parentheses.

In contrast, CPM produced a relatively clear, homogeneous film on extrusion. At all processing temperatures, over 97% of the theoretical level of drug was measured in the films 1 week after processing (Table 3). Over 97% of CPM remained in all of the films at the end of 6 months. At the lowest processing temperature, even after 12 months, 98.4% of the theoretical drug load was found in the films. The chemical stability of CPM correlates well with the mechanical properties measured in this study.

As described in the Methods section, the HPC was dried at 50°C for 24 hr to facilitate the extrusion process. Although storage of the processed films was in sealed plastic bags, a loss on drying moisture analysis was conducted on the HC and CPM films. The HC film was found

to contain 6.5% ± 1.6% moisture loss on drying. The CPM film exhibited very similar results (6.5% ± 1.4%).

As has been reported, water itself may act as a plasticizer in polymers such as polyvinylpyrrolidone, and a change in mechanical properties may be observed with the loss of water (15). It was observed that the dried HPC powder contained 1.2% (±0.3%) water. Even though these films were stored at 25°C in sealed polyethylene bags, all of the HPC films in this investigation absorbed a substantial amount of moisture. Films were analyzed for moisture content at all time points throughout the study. All films at all time points ranged in moisture content from 4.9% to 8.3%, with no statistical differences between any of the films at any time. This could be expected since, in all cases, at least 98% of the films consisted of HPC. As one may reason, temperature and humidity could be a relevant factor that affects not only the physical-mechanical properties of the films, but also other factors, such as drug diffusion and permeability.

CONCLUSIONS

Hot melt extrusion technology is a viable process to produce thin, flexible, and stable HPC films. A pure HPC film could not be produced without a plasticizer due to the high stress that was exhibited in the extruder. With the exception of PEG 400, all plasticizers investigated demonstrated adequate stability for the duration of the study. PEG 400, although initially exhibiting excellent plasticizer qualities for the HPC films, was found to be unstable in all parameters tested.

Chlorpheniramine maleate 1% was demonstrated to be an excellent plasticizer for HPC, providing a mechanically stable film for the duration of the study. In addition, CPM demonstrated chemical stability in the HPC film for up to 12 months. Hydrocortisone 1% was shown to be a good plasticizer, comparable to that of the conventional plasticizers studied. The chemical stability of HC incorporated into the HPC extruded films was demonstrated to be a function of processing temperature and residence time in the extruder. At the highest melt temperature (200°C) less than 63% of the theoretical level of HC remained in the film after 12 months. However, at 170°C, over 91% of the theoretical level was found to be present in the film for the same period.

All extruded films exhibited a marked decrease in tensile strength, in contrast to a large increase in percentage elongation, when testing was performed perpendicular to flow versus in the direction of flow.

The results of this investigation concerning the physical-mechanical stability of HPC films are relevant to our ongoing development of improved formulations for topical drug delivery and wound care.

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