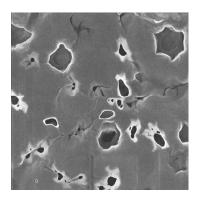# Effects of Polyethylene Glycol
on Morphology, Thermomechanical Properties, and Water Vapor Permeability of Cellulose Acetate–Free Films

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The authors determined the effects of solvent systems, polyethylene glycol (PEG) molecular weights, and various concentrations of cellulose acetate (CA) to PEG **on the thermomechanical properties and permeability of CA-free films.**

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Cellulose acetate (CA) is a polymeric excipient commonly used in formulating pharmaceutical dosage forms. CA can be used in direct compression or powder granulation for making tablets (1). It is well known that CA is used for forming the semipermeable membrane in an osmotic delivery system (2–4).

When designing a membrane-controlled drug delivery system, it is desirable to know the relationship between film composition and characteristics. The study of free films, which are prepared by casting or spray coating techniques, provides useful insights for tailoring film permeability and mechanical properties. Chowdary and Naidu reported that casting acetone solutions of CA and ethyl cellulose on a mercury surface could yield thin, uniform, flexible films (5). They found that CA films were more permeable to water vapor, salicylic acid, and diclofenac sodium compared with ethyl cellulose films. CA films were stronger and tougher than ethyl cellulose films and appeared better suited as rate-controlling membranes (6). Bengt et al. also reported that CA exhibited higher water vapor permeability than ethyl cellulose films (7).

A plasticizer is commonly used in conjunction with CA to improve film-forming characteristics and to modify the film's physical properties (8). The choice of plasticizer and its concentration can affect a film's permeability and mechanical properties (9–12). Shah and Zatz studied the interaction of CA and cellulose acetate butyrate with several plasticizers and correlated the plasticizers' efficiency with the polymer's intrinsic viscosity (13). Rao and Diwan compared the permeability of CA-free films plasticized with dibutyl phthalate, polyethylene glycol (PEG) 600, and propylene gly-

col at 40% of the polymer weight. The results showed that the film permeability decreased on the order of PEG 600 > propylene glycol > dibutyl phthalate. However, the films plasticized with dibutyl phthalate were tougher than those plasticized with the other two compounds (14). Liu et al. reported that PEG increased the drug release rate from a monolithic osmotic tablet system, whereas triacetin decreased the rate. At a plasticizer level <5% of the polymer (CA) weight, the tensile strength and the elastic modulus increased as the level of plasticizer increased. No significant difference between the films using the two plasticizers was determined. However, when the plasticizer was at 5–40% of the CA weight, the mechanical strength decreased as the plasticizer level increased. At a given level of plasticizer, the films containing triacetin were stronger than the films containing PEG (15). By investigating the effects of plasticizer on water permeability and mechanical properties of CA films, Guo observed the antiplasticization effect, i.e., as the level of plasticizer increased, the water permeability of CA initially decreased until it reached a minimum and then increased to higher values (16–18).

Although the use of PEG as a plasticizer to modify the permeability of CA films was reported, the interaction of CA and PEG requires additional elucidation. In addition, the solvent systems used in casting films could significantly affect CA–PEG interaction, film morphology, and, consequently, film properties. The objective of our study was to determine the effects of solvent systems, PEG molecular weights, and CA–PEG ratios on thermomechanical properties and permeability of CA-free films.

Materials and methods

Materials. Cellulose acetate 398-10 NF containing 39.8% acetyl groups (Eastman Chemical Company, Kingsport, TN) was used to prepare the free films. The plasticizers used were PEG 400, 1000, and 3350 (Aldrich Chemical, Milwaukee, WI). Spectral-grade acetone (AlliedSignal, Muskegon, MI) and deionized water (NANOpure water system, Barnstead, Van Nuys, CA) were used. All materials were used as received.

Preparation of free films. The films were prepared by casting polymer solutions on glass plates, then allowing the solvent to evaporate. Two solvent systems, acetone and acetone–water (94:6 by weight), were used to dissolve the CA and PEG. The total solid content was 15% by weight. The CA–PEG ratios were 10:0, 9:1, 8:2, and 7:3, or PEG was 0, 11.1, 25.0, and 42.9% of the CA weight, respectively. Two CA films without PEG were prepared for comparison purposes. After all the components were dissolved in the solvent system and the solution was allowed to stand until all trapped air bubbles were removed, the solutions were poured on preleveled glass plates and cast by use of a Gardner knife. To prevent uneven solvent evaporation from the plate surface, an aluminum pan was used to cover the glass plate. The films were dried at room temperature and 50% relative humidity (RH) for at least 24 h, and then peeled from the plates. At least 10 films were prepared for each composition. We measured film thickness with a micrometer and determined it by averaging five data points. In general, the thickness ranged from 0.04 to 0.07 mm. Table I lists solvents, types of PEG, and PEG levels used in preparing the films.

Characterization of the films. The film characteristics were measured, including morphology, thermal and mechanical properties, oxidative and thermal stability, wettability, and water vapor permeability, according to the following methods.

Film morphology. The morphologies of the film samples were examined by scanning electron microscopy (SEM) (LEO Electron Microscopy, Thornwood, NY). Both the film surfaces and cryogenically fractured cross sections were examined.

Glass transition temperature. The film's glass transition temperatures were determined with a differential scanning calorimeter

(DSC) and a single-sample automodulated DSC (MDSC model 2920, TA Instruments, New Castle, DE) connected to a liquid nitrogen cooling accessory. A film sample of about 10.0 mg was encapsulated in a regular aluminum pan and brought from $-125\,°C$ to $+230\,°C$ at a heating rate of 5 °C/min and subjected to a modulating amplitude of ±0.531 °C and a frequency of 40 s. The sample was cooled to -125 °C and heated to $+260$ °C for the second heating scan. Universal V2.4F software (TA Instruments) was used to analyze the data.

Oxidative and thermal stability. The oxidative and thermal stability of the films was evaluated in air and in nitrogen with a thermogravimetric analyzer (TA Instruments,

model 2950). We kept the purging gas flow rate at 40 mL/min and the heating rate at 20 °C/min. The temperature at 10% weight loss (T_{10}) was used for comparison.

Thermomechanical properties. The films were analyzed by dynamic mechanical thermal analysis using a Rheometric Solid Analyzer II (Rheometric Scientific, Piscataway, NJ) under nitrogen. A film sample of 19.28 $\times$ 6.35 mm was prepared and its thickness was measured. The sample was subjected to a small axial force of 5 g and a modulating frequency of 16 Hz and heated at a rate of 5 °C/min until the length of the sample was stretched by 0.5 mm. The temperature at which the film reached 0.5 mm in length was recorded as the rejuvenated temperature.
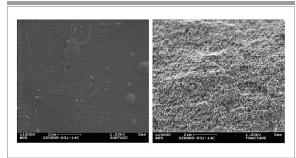
Table I: CA films used in the investigations.

Sample	Plasticizer	CA–PEG Ratio	Solvent	Appearance
1	CA only	10 : 0	acetone	clear
2	CA only	10 : 0	acetone–water	hazy
3	PEG 400	9 : 1	acetone	clear
4	PEG 400	8 : 2	acetone	clear
5	PEG 400	7 : 3	acetone	clear
6	PEG 400	9 : 1	acetone–water	opaque
7	PEG 400	8 : 2	acetone–water	opaque
8	PEG 400	7 : 3	acetone–water	opaque
9	PEG 1000	9 : 1	acetone–water	opaque
10	PEG 1000	8 : 2	acetone–water	opaque
11	PEG 1000	7 : 3	acetone–water	opaque
12	PEG 3350	9 : 1	acetone–water	opaque
13	PEG 3350	8 : 2	acetone–water	opaque
14	PEG 3350	7 : 3	acetone–water	opaque

Table II: Glass transition and rejuvenated temperature of CA films.

Sample	Plasticizer	CA–PEG Ratio	Solvent System	Glass Transition Temp. (°C)	Rejuvenated Temp. (°C)
1	CA only	10 : 0	acetone	192	206
2	CA only	10 : 0	acetone–water	192	212
3	PEG 400	9 : 1	acetone	147	162
4	PEG 400	8 : 2	acetone	−43, 165	127
5	PEG 400	7 : 3	acetone	−52, 157	99
6	PEG 400	9 : 1	acetone–water	145	187
7	PEG 400	8 : 2	acetone–water	−42, 164	177
8	PEG 400	7 : 3	acetone–water	−32, 175	153
9	PEG 1000	9 : 1	acetone–water	166	203
10	PEG 1000	8 : 2	acetone–water	175	199
11	PEG 1000	7 : 3	acetone–water	−57, 172	194
12	PEG 3350	9 : 1	acetone–water	176	207
13	PEG 3350	8 : 2	acetone–water	187	204
14	PEG 3350	7 : 3	acetone–water	173	206

Figure 1: SEM images of CA film cast with acetone; (a) surface of the film, (b) cross section of the film.
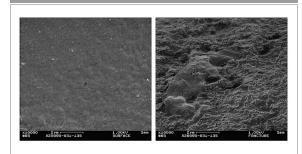

Figure 2: SEM images of CA film cast with acetone and water; (a) surface of the film, (b) cross section of the film.
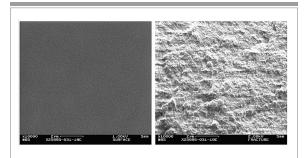

Figure 3: SEM images of PEG 400 plasticized CA film cast with acetone (CA–PEG ratio: 8:2); (a) surface of the film, (b) cross section of the film.
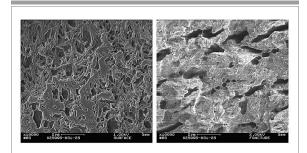

Figure 4: SEM images of PEG 400 plasticized CA film cast with acetone and water (CA–PEG ratio: 8:2); (a) surface of the film, (b) cross section of the film.

Mechanical properties. The mechanical properties of the films were measured with a SINTECH 20 (MTS Corp., Eden Prairie, MN) according to ASTM D882. A film sample of 0.5 × 3 in. was prepared, and its thickness was measured. The gauge crosshead spacing was 2 in. apart, and the speeds were 0.2 in./min for the Young's modulus in the elastic region and 2.0 in./min in the nonelastic region. The means of five specimens were reported.

Wettability. The films' wettability was examined by measuring the contact angles of water droplets on the films with a video contact angle system (VCA2000, Advanced Surface Technology, Billerica, MA) at five different locations on the film.

Water vapor permeability. The water vapor transmission rates (WVTRs) were determined according to ASTM E96. A film sample of 2.69 in. in diameter was prepared and the thickness was averaged from measurements taken at five locations. We filled a 4-oz glass jelly jar (Ball & Ball, TMs Ball Corporation/Alltrista, Muncie, IN) with 20 mL of water. The film was locked between the jar and the lid, which has a 2.15-in.-diameter hole at the center. Then the jar was maintained in the test chamber (Thermotron Industries, Holland, MI) at 32 °C and 50% RH. Three measurements of water weight loss were performed each day. The WVTR was calculated on the basis of the slope of the water weight loss versus the elapsed time.

Results

Two solvent systems, acetone and acetone–water, were used to prepare the CA-free films. Because PEG 1000 and PEG 3350 are insoluble in pure acetone, water must be used as a cosolvent in preparing the films containing PEG 1000 and PEG 3350. The use of water as a cosolvent is a common practice when preparing CA–PEG solutions for coating operations. We prepared 14 kinds of film samples, shown in Table I. The films prepared with acetone–water as the casting solvent appeared opaque and brittle. The films prepared with acetone were transparent and more flexible.

The SEM images of the surfaces and the cross sections of CA films were examined. Figures 1 and 2 show the SEM images of CA films without plasticizer for comparison (samples 1 and 2 in Table I). Figures 3 and 4 show the images of the films prepared from two solvent systems and plasticized with PEG 400 at a CA:PEG ratio of 8:2 (samples 4 and 7). To show the effect of PEG molecular weight on film morphology, Figures 5 and 6 show the images of the films containing PEG 1000 and PEG 3350 at a CA:PEG ratio of 8:2 (samples 10 and 13).

Because of its high resolution, modulated DSC was used to determine glass transition temperatures in this study. Table II shows glass transition temperature data for all of the films subjected to the second heating run.

The stabilities of the films under air and nitrogen were examined by thermogravimetric analysis. The temperature (T_{10}) at which each film sample lost 10% of its weight is reported (see Table III).

Dynamic mechanical thermal analysis was used to determine the rejuvenated temperature of a film sample. The data in Table II reflect the flexibility of the films. The films with a higher degree of elasticity usually exhibited lower rejuvenated temperatures.

Mechanical properties of the films were measured by tensile strength and percentage of elongation. The tensile strength reflects the energy required to break the film by stretching. The percentage of elongation data reflect the extent to which the films can be stretched. Table III shows the tensile strength and percentage of elongation of the films.

The wetting behavior of the films was examined by measuring the contact angles of water droplets on the film (see Table IV). We examined the film permeability by measuring WVTRs. Table IV shows the results.

Discussion

Effects of solvent systems. The appearances of the CA–PEG 400 films clearly showed that the solvent system affected the film morphologies. The films using acetone as the casting solvent were transparent; the
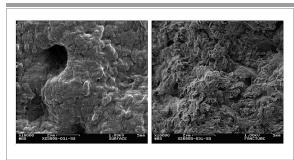
Figure 5: SEM images of PEG 1000 plasticized CA film cast with acetone and water (CA–PEG ratio: 8:2); (a) surface of the film, (b) cross section of the film.
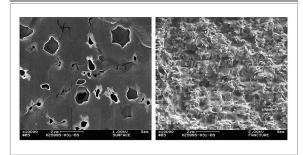

Figure 6: SEM images of PEG 3350 plasticized CA film cast with acetone and water (CA–PEG ratio: 8:2); (a) surface of the film, (b) cross section of the film.

Table III: Stabilities and mechanical properties of CA films.

Sample	Plasticizer	CA–PEG Ratio	Solvent System	T_{10} (°C) (N_2 Purge)	T_{10} (°C) (Air Purge)	Tensile Strength (MPa)	Percentage of Elongation
1	CA only	10 : 0	acetone	334.23	329.75	81.1	8.5
2	CA only	10 : 0	acetone–water	336.31	330.91	58.0	6.5
3	PEG 400	9 : 1	acetone	318.04	307.79	55.6	8.9
4	PEG 400	8 : 2	acetone	294.88	281.72	36.6	20.9
5	PEG 400	7 : 3	acetone	279.38	268.70	15.8	33.4
6	PEG 400	9 : 1	acetone–water	309.18	291.97	36.2	3.4
7	PEG 400	8 : 2	acetone–water	282.92	264.71	23.6	3.5
8	PEG 400	7 : 3	acetone–water	270.79	226.99	8.8	25.0
9	PEG 1000	9 : 1	acetone–water	330.84	298.53	38.8	2.5
10	PEG 1000	8 : 2	acetone–water	325.87	268.24	23.7	2.9
11	PEG 1000	7 : 3	acetone–water	313.91	245.21	9.8	20.1
12	PEG 3350	9 : 1	acetone–water	282.62	264.57	29.8	2.2
13	PEG 3350	8 : 2	acetone–water	320.84	211.60	23.6	3.1
14	PEG 3350	7 : 3	acetone–water	279.05	185.98	4.8	2.3

films using acetone–water were opaque. The opaqueness of the films suggests that CA is essentially immiscible with PEG. CA-free films without PEG were transparent when acetone was used as the solvent but hazy when acetone–water was used.

When comparing the SEM images of CA films in Figures 1 and 2 and the CA–PEG 400 films in Figures 3 and 4, we see that the films cast from acetone exhibited a higher degree of surface smoothness and smaller pinholes in the cross sections. These observations suggest that water in an acetone-based solvent system will affect the film morphology and miscibility of CA and PEG.

For some film compositions, we observed two distinct glass transition temperatures (see Table II). These data suggest that in these films, at least two phase domains could be detected. Comparing the glass transition temperatures of these films with those of CA and the melting temperatures of PEGs, the glass transition temperature for CA is 192 °C; the melting temperatures for PEG 400, 1000, and 3350 are

Table IV: Wettability and permeability of CA films.

Sample	Plasticizer	CA–PEG Ratio	Solvent System	Contact Angle (°)	WVTR (g mL/m²/day)
1	CA only	10 : 0	acetone	66.7	1464
2	CA only	10 : 0	acetone–water	60.0	1505
3	PEG 400	9 : 1	acetone	58.0	1508
4	PEG 400	8 : 2	acetone	49.4	1667
5	PEG 400	7 : 3	acetone	44.3	2172
6	PEG 400	9 : 1	acetone–water	52.3	1694
7	PEG 400	8 : 2	acetone–water	48.2	1983
8	PEG 400	7 : 3	acetone–water	56.1	6223
9	PEG 1000	9 : 1	acetone–water	60.1	1430
10	PEG 1000	8 : 2	acetone–water	58.0	1830
11	PEG 1000	7 : 3	acetone–water	51.9	5007
12	PEG 3350	9 : 1	acetone–water	62.4	1382
13	PEG 3350	8 : 2	acetone–water	56.8	1663
14	PEG 3350	7 : 3	acetone–water	44.6	8374*

*This point is extremely high because of the porous surface.

2.6, 34.3, and 51.8 °C, respectively. These results suggest that the free films prepared from acetone and acetone–water systems could contain at least two phases, one CA-rich, the other PEG-rich. At low PEG lev-

els, only one glass transition temperature was detected by MDSC, but at higher PEG levels, more than two glass transition temperatures were observed. The glass transition temperatures from MDSC spectra of
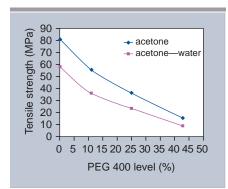
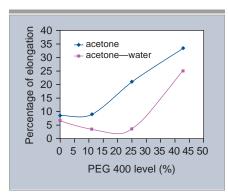**Figure 7:** Solvent system effects on tensile strength.

Figure 8: Solvent system effects on percentage of elongation.
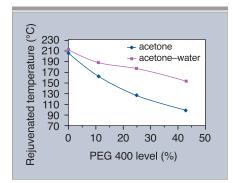

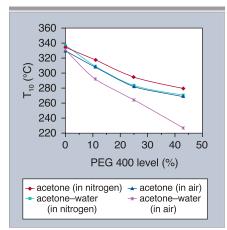**Figure 9:** Solvent system effects on rejuvenated temperature.

Figure 10: Solvent system effects on films' stabilities.

the first heating run could not be clearly defined; however, they became apparent on the second heating run, and those data are reported here. Therefore, the effect of heat treatment on CA–PEG interaction should not be discounted. The heat treatment could facilitate further phase separation of CA and PEG, especially when PEG levels were high, so that two distinct glass transition temperatures were observed.

The effects of solvent systems on film morphologies also can explain why lower WVTR values were observed on the films prepared from acetone (see Table III). However, no significant differences were observed in contact angles for the films that had the same composition but were prepared from two solvent systems (see Table IV).

Comparing the values of tensile strength, percentage of elongation, and rejuvenated temperature for the films made from acetone and acetone–water solvent systems, we concluded that films made from acetone solutions are stronger, tougher, and more flexible than the corresponding films made from acetone–water solutions. Figures 7–9 show the results. The films made from acetone solutions also exhibit a higher degree of thermal and oxidative stability (Figure 10).

Effects of PEG molecular weight and concentration. Figures 4–6 show the SEM images of the surfaces and the cross sections of CA films plasticized with PEG 400, 1000, and 3350 at a CA:PEG ratio of 8:2 and prepared using the acetone–water solution. It is apparent that the films containing higher molecular weight PEG exhibit scattered, larger, patch-like holes on a smoother surface but smaller pinholes in the cross sections. The PEG level in the film also affects the morphologies. As the PEG concentration increases, the surface smoothness decreases, and the pinholes and their size in the cross sections increase.

The data in Table II show that incorporation of PEG into CA films will decrease the glass transition temperature of CA. When the CA:PEG ratios are 9:1 and 8:2, respectively, the effectiveness of decreasing the glass transition temperature is on the order of PEG $400 > 1000 > 3350$. One should note that for a given molecular weight, the films with a 9:1
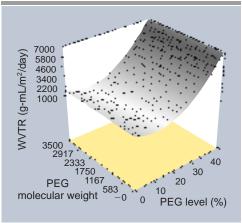

Figure 11: The level and molecular weight of PEG effects on WVTR.

CA:PEG ratio show lower glass transition temperatures than do the films with an 8:2 or 7:3 CA:PEG ratio. Thus, increasing the PEG level in the films may not necessarily decrease the film's glass transition temperature as one might anticipate. Considering molecular weight and concentration effects together, PEG 400 at 10% level gave the lowest glass transition temperature. At a 7:3 CA:PEG ratio, the glass transition temperature showed no dependence on the PEG's molecular weight. This could imply that the films were over-plasticized and that the phase separation could be further enhanced when PEG exceeded a certain level.

Figure 11 shows the effect of PEG level and molecular weight on WVTRs. The plot suggests that a minimum concentration of plasticizer is required to affect the permeability. Other authors also reported this phenomenon (19). When the plasticizer level was less than about 15% of the film composition, we detected no change in the WVTR, which increased slowly as the PEG level continued to increase. When the PEG level was greater than 20%, the WVTR increased abruptly.

Table IV shows that for a given level of PEG, the WVTR decreased as the PEG molecular weight increased. The films that have higher plasticizer levels and lower molecular weights of PEG tended to have higher WVTRs. This trend is consistent with the SEM images that indicated large pinholes.

In general, PEG-plasticized films exhibited lower contact angles than CA-free films without a plasticizer (see Table IV). Apparently, PEG increases the wettability of the films. This is not surprising because
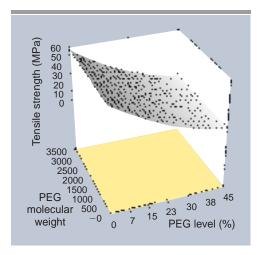
Figure 12. The level and molecular weight of PEG effects on tensile strength.
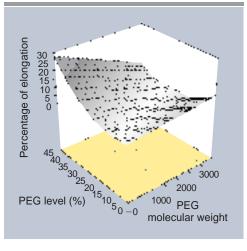

Figure 13. The level and molecular weight of PEG effects on percentage of elongation.
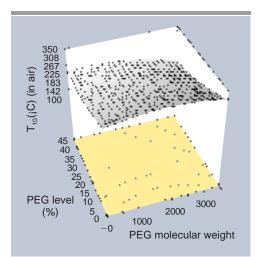

Figure 14. The level and molecular weight of PEG effects on oxidative stability.
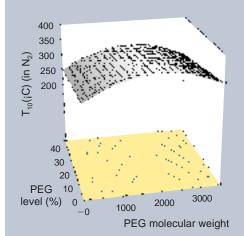

Figure 15. The level and molecular weight of PEG effects on thermal stability.

PEG increases the hydrophilicity of the film. However, no dependence of film wettability on PEG molecular weight was observed at the levels used in the experiments.

Figures 12 and 13 show the effects of PEG level and molecular weight on a film's mechanical properties. At a given PEG level, PEG molecular weight had no significant effect on tensile strength. However, the strength decreased as the level of PEG increased.

The changes in percentage of elongation depended on the level of PEG. Below the 25% of PEG level, the level and molecular weight of PEG had no effect on percentage of elongation. Above the 25% PEG level, the percentage of elongation increased with an increase in PEG level. The slope decreases with PEG molecular

weight. However, there was no difference in the percentage of elongation for PEG 3350 plasticized films at all levels studied. These results suggest that PEG 400 is a more effective plasticizer than PEG 1000 and 3350 for films' mechanical properties.

The flexibility of films indicated by percentage of elongation was consistent with the rejuvenated temperature determined by dynamic mechanical thermal analysis (see Table II). The higher the level and the lower the molecular weight of PEG, the more flexible the film was.

Figures 14 and 15 show the effect of PEG level and molecular weight on the stabilities of the films. For a given PEG, the film stability decreased as the PEG level increased. The effect of PEG molecular

weight on thermal stability is more complex. PEG 1000 seemed to provide a higher degree of stability in the range of our investigation.

Statistical analysis. For films prepared from the same solvent, PEG molecular weight and level are the two factors influencing properties. To compare the degree of influence and the interactive effect, we performed statistical analyses on the results, as shown in Figures 11–15. The bottom contour figures in the three-dimensional plots show whether PEG level and molecular weight affect film properties. The corresponding three-dimensional plots show the degrees of influence graphically. It is evident that PEG level is the dominating factor influencing films' mechanical properties. Its influence is much higher than that of PEG molecular weight, which significantly affects thermal stability and percentage of elongation. Its effect on thermal stability is most evident.

The results of statistical analysis provide a clear picture of how film properties are influenced by changes in PEG level and molecular weight. For a given film property in the range of investigation, the three-dimensional schematic representations can be used to predict the required PEG level and PEG type by its molecular weight.

Conclusion

This study attempted to provide a systematic evaluation of the effects of solvent system, PEG molecular weight, and concentration in the films on thermomechanical properties and permeability of CA-free films. The results and the trends suggested by the statistical analysis provide a useful guideline for formulators to design a CA–PEG coating system for controlled drug delivery applications. The results strongly suggest that water in the solvent system for film casting can influence the morphology and ultimately the properties of the films. Although the films prepared from acetone were transparent, flexible,

stronger, tougher, and less permeable to water vapor, water must be added in acetone to dissolve PEG 1000 and 3350 in solution. The influence of PEG molecular weight and concentration in the films were analyzed statistically so that schematic models could be provided to help formulators anticipate the thermomechanical properties and permeability of a coating system made of CA and PEG.

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