Drug Development and Industrial Pharmacy, 2011; 37(12): 1439–1445
© 2011 Informa Healthcare USA, Inc.
ISSN 0363-9045 print/ISSN 1520-5762 online
DOI: 10.3109/03639045.2011.584194

informa
healthcare

REVIEW ARTICLE

Novel low-molecular-weight hypromellose polymeric films for aqueous film coating applications

Hollie F. Bruce[1], Paul J. Sheskey[2], Paula Garcia-Todd[2], and Linda A. Felton[1]

[1]Health Sciences Center, College of Pharmacy, University of New Mexico, Albuquerque, NM, USA and [2]Dow Wolff Cellulosics R&D, The Dow Chemical Company, Midland, MI, USA

Abstract
The concentration of hypromellose (HPMC) is known to significantly impact the viscosity of coating solutions. The purpose of this study was to determine the viscosity of novel low-molecular-weight (LMW) HPMC products as a function of polymer concentration. The mechanical properties and water vapor permeability of free films prepared from these novel LMW HPMC polymers were also determined and the results were compared with films prepared with conventional HPMC. Solutions of LMW and conventional HPMC 2910 and 2906 containing up to 40% polyethylene glycol (PEG) 400 were prepared and the viscosities were measured using a Brookfield viscometer. Solutions were then cast onto glass plates and stored at 30°C and 50% relative humidity until films were formed. A Chatillon digital force gauge attached to a motorized test stand was used to quantify the mechanical properties of the films, whereas water vapor permeabilities were determined according to the ASTM E96 M-05 water method. As expected, the novel LMW polymer solutions exhibited significantly lower viscosities than the conventional comparators at equivalent polymer concentrations. Film strength of the LMW materials was lower than films prepared from the conventional HPMC solutions, although this effect was not as evident for the HPMC 2906 chemistry. Increasing concentrations of the plasticizer resulted in decreased tensile strength and Young's modulus and increased elongation as well as increased water vapor permeability, irrespective of polymer type. No statistical difference was found between the tensile strength to Young's modulus ratios of the F chemistry LMW and conventional HPMC polymer films.

Keywords: Hypromellose, HPMC, molecular weight, viscosity, plasticizer, mechanical strength, water vapor permeability, free film

Introduction

The coating of drug products is a process that has been carried out for many years to improve the aesthetic, protective, and functional characteristics of pharmaceuticals[1]. In addition to improving the appearance of a drug product, coatings have been used to protect the active ingredient from environmental factors, such as moisture, light, and oxygen[2]. Taste masking of bitter drugs and concealing odorous compounds are additional ways coatings have been utilized in the pharmaceutical industry[3]. Polymeric films can enhance the overall mechanical strength of a substrate[4]. Sustained, delayed, and pulsatile drug release profiles have also been achieved through the application of polymeric film coatings[5–7].

The film coating process involves the application of a thin polymer film onto the surface of a solid dosage form. Polymers are generally dispersed or dissolved in a solvent and then atomized into fine droplets that impinge onto the substrate surface during the coating process. Subsequent evaporation of the solvent causes polymer coalescence and film formation. High-viscosity solutions require high atomization air pressures to ensure accurate and consistent droplet size distribution[8]. Most polymers used to achieve sustained and delayed drug release are formulated as aqueous-based dispersions[9–11] and thus viscosity is not significantly influenced by polymer concentration. For water-soluble polymers prepared as aqueous solutions, such as hypromellose (HPMC),

Address for Correspondence: Linda A. Felton, 2705 Frontier NE, University of New Mexico, College of Pharmacy, Albuquerque, NM 87131, USA. Tel: 1-505-272-2615. Fax 1-505-272-0704. E-mail: lfelton@unm.edu

(Received 17 February 2011; revised 15 April 2011; accepted 20 April 2011)

however, viscosity limits the polymer concentrations that can be used in coating applications.

HPMC is a commonly used water-soluble polymer and is commercially available in several different grades that vary by the degree of methoxyl and hydroxypropoxyl substitution as well as by viscosity. Currently, the lowest viscosity HPMC polymers used in aqueous film coating are the 3 and 6 cP grades, with maximum recommended polymer concentrations of 15% and 10% w/w, respectively[12]. Recently, The Dow Chemical Company (Midland, MI) developed two novel lower-molecular-weight (LMW) products, based on HPMC 2910 (E chemistry) and HPMC 2906 (F chemistry), to allow higher polymer concentrations to be used for aqueous coating applications. In the current study, the viscosities of these novel LMW HPMC products were determined as a function of polymer concentration. Films were then cast and the mechanical and water vapor permeability properties were determined and compared with conventional HPMC films. The influence of plasticizer concentration in the polymeric film on mechanical strength and water vapor permeability was also investigated.

Materials and methods

Materials

Hypromellose 2906 (conventional METHOCEL™ F4 Premium LV and the LMW METHOCEL™ Premium VLV) and hypromellose 2910 (conventional METHOCEL™ E3 Premium LV and an investigational LMW polymer) were provided by The Dow Chemical Company. Polyethylene glycol 400 (PEG 400, Carbowax™ 400; The Dow Chemical Company) was used as the plasticizer for these HPMC materials.

Preparation of solutions

HPMC polymer solutions were prepared according to the manufacturer's recommendations. Distilled water was heated to 80–90°C and the HPMC powder was dispersed using a standard variable speed propeller-type mixer. The solutions were removed from the heat and mixed for 1 h. The appropriate amount of plasticizer was added and mixing was continued for 10 min. Solutions were covered and stored in the refrigerator overnight to allow the polymer to fully hydrate. Solutions were brought to room temperature (22°C) prior to subsequent testing or processing.

Viscosity measurements

The polymer solutions were maintained at 25°C in a heated water bath. After placing the LV-2 spindle attachment into the solutions, the Brookfield LVDV-E viscometer (Middleboro, MA) was stabilized for 10 min prior to determining the viscosities of each solution ($n=4$ per formulation).

Mechanical properties

Polymer solutions were manually cast onto glass plates using a casting knife (Paul N. Gardner, Pompano Beach, FL) and dried for 24 to 48 h at 30°C and 50% relative humidity (RH) until clear films were formed. Films ($n=6$) were cut into 101.6 mm × 12.7 mm strips and film thickness was measured with a digital micrometer. The film strips were placed between the grips of a Chatillon universal tension/compression tester (model TCD-200 MS) with a DFGS digital force gauge (Largo, FL) to evaluate the mechanical properties of the cast films. Tests were conducted according to the ASTM D882-02[13] with a gauge length of 50.8 mm and a cross-head speed of 5 mm/min. Force and deflection values were recorded for each sample and used to plot stress–strain curves. Tensile strength (σ) at break was calculated by dividing the maximum force (F) at break by the original cross-sectional area of the film (A_0), as shown in Equation 1.

$$\sigma = \frac{F}{A_0} \tag{1}$$

Percent elongation (ε) was calculated by dividing the change in deflection (ΔL) by the initial gauge length (L_0) and multiplying by 100 (Equation 2).

$$\epsilon = \frac{\Delta L}{L_0} \times 100 \tag{2}$$

Young's modulus was determined from the slope of the linear portion of the stress–strain curves.

Water vapor permeability

Films were prepared as previously described and cut to fit the permeability cups. The exposed surface area was ~38 cm². Film thickness was measured with a digital micrometer at multiple sites ($n=4$ perimeter, $n=4$ middle) and the average thickness of each film was determined. The water vapor permeability tests were conducted according to the ASTM E96 M-05[14] water method ($n=3$ films per formulation). A saturated sodium chloride solution was placed in the interior of the permeability cups to produce a 75% relative humidity environment[15]. The films were secured onto the cups using three screw clamps and the cups were then placed in a temperature and humidity controlled environment (22°C with anhydrous calcium sulfate to create 0% RH). After an equilibration period of ~24 h, the weight of the permeability cups was recorded every 24 h for 5 days. The average cumulative weight change (G) of the permeability cups was plotted against time (t). The water vapor transmission rate (WVT) was determined by dividing the slope of the graph by the area (A) of film exposed, as shown in Equation 3.

$$\mathrm{WVT} = \frac{G/t}{A} \tag{3}$$

The water vapor permeability (P_{erm}) was then calculated using Equation 4, where S is the saturated vapor pressure, R_1 and R_2 are the relative humidities in the dish and dessicator, respectively, and d is the average film thickness.

$$P_{\mathrm{erm}} = \frac{\mathrm{WVT}}{S(R_1 - R_2)} \times d \tag{4}$$

Statistical analysis

A one-way analysis of variance (ANOVA) and Holms-Sidak multiple comparison test were performed using SigmaStat, version 3.0 for Windows (SPSS Inc., Chicago, IL) to determine statistical differences in the data. Statistical differences were determined by a P-value <0.05.

Results and discussion

HPMC polymers swell upon dissolution in water, producing relatively viscous solutions that can be difficult to atomize for film coating processes[16]. Low polymer concentrations are typically employed in order to obtain solutions with viscosities sufficiently low enough for processing[12]. Recently, there has been a great deal of interest in developing polymers that can be mixed at higher concentrations without significantly increasing viscosity. Rogers and colleagues[17] showed that shorter processing times and increased efficiency during coating could be achieved when formulations containing higher polymer concentrations of lower viscosity were employed. In addition, the reduced water content in these more concentrated solutions allows for lower processing temperatures, reduced energy usage, and increased efficiency in novel continuous coating processing technologies[18,19]. The current study investigated two novel LMW HPMC products for potential film coating applications. Table 1 shows the molecular weights of the conventional and LMW materials used in the current study.

The viscosities of unplasticized LMW and conventional HPMC solutions were determined as a function of polymer concentration and these data are presented in Figure 1. The viscosity of the solutions increased with increasing polymer concentrations for all HPMC solutions investigated. The LMW polymers demonstrated significantly lower viscosities than the corresponding conventional polymers at equivalent polymer concentrations ($P<0.05$). These findings were attributed to the LMWs of the novel HPMC polymers. The shorter polymer chains decreased the number of entanglements that occur within the solution thereby reducing the resistance to flow or viscosity. The conventional F chemistry HPMC polymer demonstrated significantly higher viscosities than the E chemistry conventional material, most likely due to the more hydrophilic nature of the E polymer structure. In contrast, no statistically significant differences in viscosities were found between the novel E and F chemistry LMW polymer solutions at all polymer concentrations investigated.

Linear regression from the log of viscosity versus polymer concentration plot (Figure 1, $r^2 \geq 0.997$) was used to calculate the polymer concentrations at which the conventional HPMC solutions exhibited viscosities equivalent to the LMW versions. These data, presented in Table 2, demonstrate that higher concentrations of the novel LMW polymers produce viscosities equivalent to lower concentrations of the conventional systems. The maximum desirable viscosity for a coating solution has been reported as 400 cP[16]. Analysis of Figure 1 shows conventional HPMC solutions mixed at 20% w/w exhibit viscosities that exceed these recommendations and thus are not used in normal coating operations. In contrast, the LMW HPMC polymers exhibited sufficiently low viscosities at higher polymer concentrations, which may allow increased productivity in coating processes.

The viscosities of the polymer solutions as a function of plasticizer concentration were also determined and these data are presented in Figure 2. Plasticizers reduce intermolecular attractions between polymer chains causing an increase in chain mobility. The incorporation of plasticizers into coating formulations is generally necessary to improve flexibility and decrease brittleness of the resulting polymeric films[1]. PEG, a water-soluble plasticizer with a solubility parameter (23.0 $\mathrm{MPa}^{1/2}$) similar to that of HPMC 2910 (27.8 $\mathrm{MPa}^{1/2}$) and HPMC 2906 (28.2 $\mathrm{MPa}^{1/2}$), was used in this study. Selection of a plasticizer that exhibits similar intermolecular forces to the polymer is necessary to ensure compatibility and thus a good-quality film[20]. In the current study, it was found that increasing the plasticizer concentration did not significantly affect the viscosities of any of the HPMC polymer solutions investigated.

Table 1. Weight average molecular weight (MW) of low-molecular-weight (LMW) and conventional hypromellose (HPMC) polymers (values provided by The Dow Chemical Company, Midland, MI).

HPMC 2910 MW (kDa ± SD)		HPMC 2906 MW (kDa ± SD)	
d	20.5 ± 0.014	F4 LV	23.4 ± 0.072
E LMW	14.8 ± 0.014	F LMW	12.8 ± 0.156

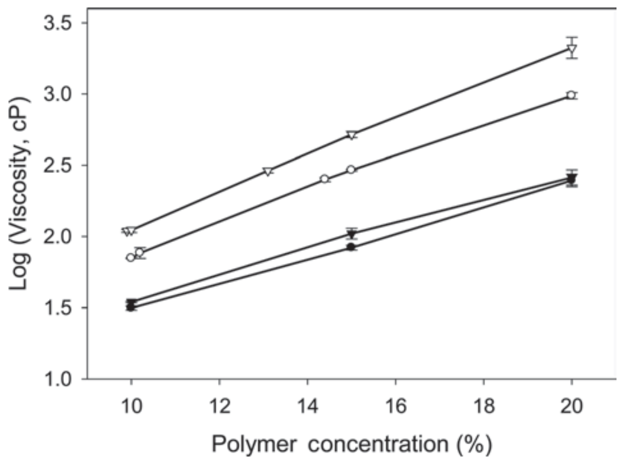

Figure 1. Viscosities of low-molecular-weight (LMW) and conventional hypromellose (HPMC) solutions as a function of polymer concentration. (●) E LMW; (▼) F LMW; (○) E3 LV; (△) F4 LV.

The mechanical strength and water vapor permeability of the HPMC polymer films were determined as a function of plasticizer concentration to gain a better understanding of the design space with these novel LMW HPMC polymers. The LMW films without plasticizer were brittle and cracked and therefore mechanical and water vapor studies could not be performed. The data from the LMW films were compared with conventional HPMC films prepared from solutions at equivalent viscosities. Water vapor permeability was found to be dependent on the concentration of the hydrophilic plasticizer in the films, irrespective of polymer type, as shown in Figure 3, with increased permeability noted with increased plasticizer concentration. These results are in agreement with previous studies that demonstrated films with higher levels of hydrophilic plasticizers exhibited higher water vapor permeabilities[21–24].

No significant differences in water vapor permeability between the LMW and conventional films cast from solutions of equivalent viscosities at the 20% and 30% plasticizer concentrations were observed. However, at the 40% plasticizer concentration, the LMW HPMC films exhibited a statistically higher water vapor permeability compared with the films cast from the conventional polymers. Similar results were seen when the water vapor permeability of the HPMC polymer films cast from solutions at equivalent polymer concentrations (20% w/w) were compared (data not shown).

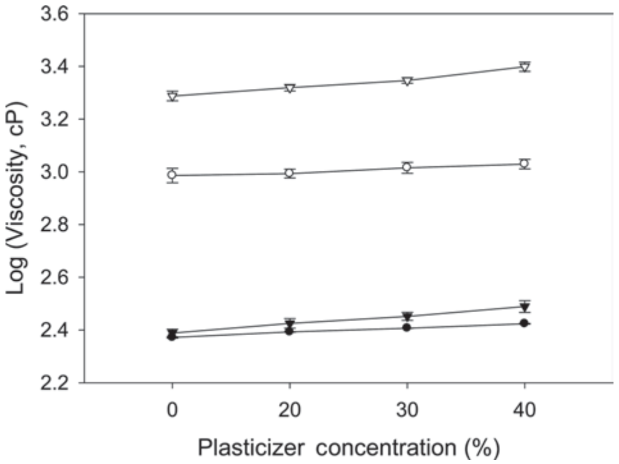

Figure 2. Viscosities of 20% low-molecular-weight (LMW) and LV hypromellose (HPMC) solutions as a function of plasticizer (PEG 400) concentration. (•) E LMW; (▾) F LMW; (○) E3 LV; (▿) F4 LV.

The mechanical properties of the HPMC films cast from solutions at equivalent viscosities were determined as a function of plasticizer concentration (Figures 4–6). As expected, tensile strength decreased with an increase in plasticizer concentration, irrespective of polymer type. These findings are in agreement with Aulton et al.[25] and are attributed to the disruption in the intermolecular interactions between polymer chains. Heinamaki et al.[26], Honary and Orafai[27], Yuan et al.[24], and Qussi and Suess[28] also reported similar findings. The LMW polymer films exhibited lower tensile strength than their respective

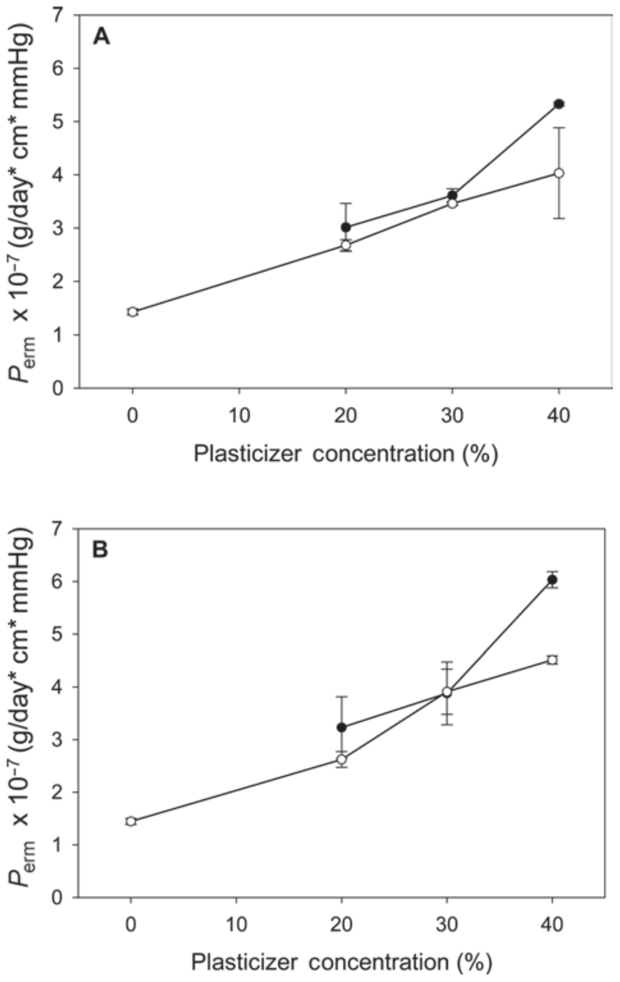

Figure 3. Effect of plasticizer concentration on the water vapor permeability of low-molecular-weight (LMW) and conventional hypromellose (HPMC) films cast from solutions at equivalent viscosities. (A) (•) 20% E LMW (○) 14.4% E3 LV; (B) (•) 20% F LMW (○) 13.1% F4 LV.

Table 2. Polymer concentrations of low-molecular-weight (LMW) and conventional hypromellose (HPMC) polymer solutions at comparable viscosities (unplasticized), as calculated from data in Figure 1.

Polymer type	Polymer concentration	Viscosity (cP ± SD)	Polymer type	Polymer concentration	Viscosity (cP + SD)
E LMW	10%	32 ± 1	E3 LV	7.2%	34 ± 1
	15%	84 ± 3		10.2%	77 ± 7
	20%	249 ± 26		14.4%	251 ± 8
F LMW	10%	34.7 ± 0.4	F4 LV	6.2%	34 ± 1
	15%	105 ± 10		9.9%	110 ± 3
	20%	261 ± 34		13.1%	290 ± 11

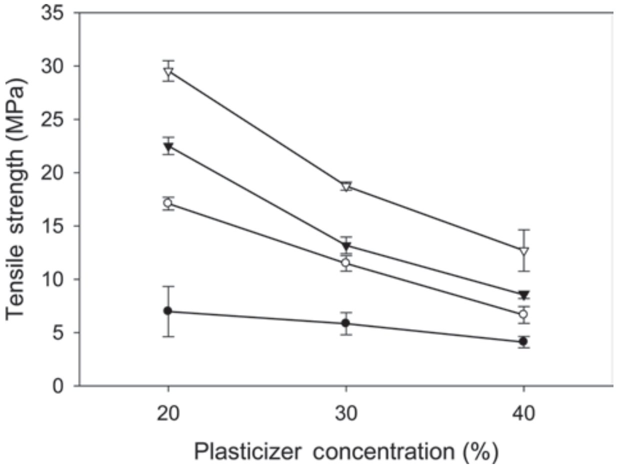

Figure 4. Tensile strength of low-molecular-weight (LMW) and conventional hypromellose (HPMC) films cast from solutions at equivalent viscosities. (•) 20% E LMW; (▾) 20% F LMW; (○) 14.4% E3 LV; (▿) 13.1% F4 LV.

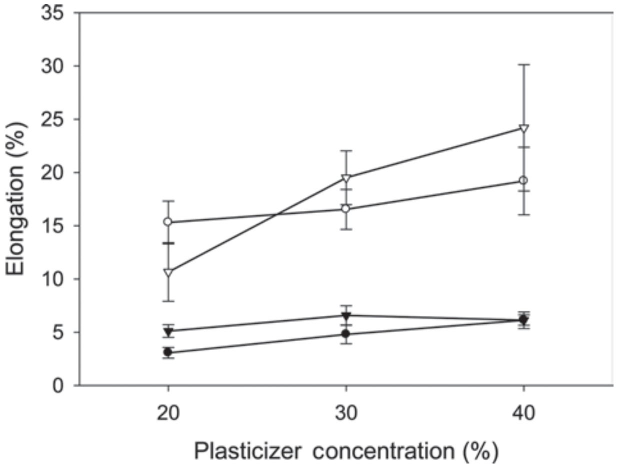

Figure 5. Percent elongation of low-molecular-weight (LMW) and conventional hypromellose (HPMC) films cast from solutions at equivalent viscosities. (•) 20% E LMW; (▾) 20% F LMW; (○) 14.4% E3 LV; (▿) 13.1% F4 LV.

conventional HPMC comparators. These results may be attributed to the decreased number of intermolecular bonds within the shorter polymer chains of the LMW polymer films and are in agreement with Rowe and Forse[29] who suggested that higher-molecular-weight polymers produce films with higher tensile strengths. Interestingly, the F LMW films exhibited higher tensile strengths than the conventional E chemistry HPMC polymer films, suggesting that these novel F chemistry polymers may have potential coating applications.

As expected, the percent elongation of the conventional HPMC films increased with increasing plasticizer concentration, as shown in Figure 5, indicating enhanced flexibility of the polymeric films. These results are again in agreement with Aulton et al.[25], Heinamaki et al.[26], Yuan et al.[24], and Qussi and Suess[24] who also found that higher plasticizer concentrations produced more flexible films. The LMW HPMC polymer films, however, exhibited significantly lower elongation values than the conventional films at each plasticizer level investigated ($P<0.05$). Moreover, increasing plasticizer concentrations in the LMW films did not significantly increase percent elongation. These data suggest that the LMW films are not as ductile as the conventional HPMC polymers, which again may be attributed to the shorter polymer chain length.

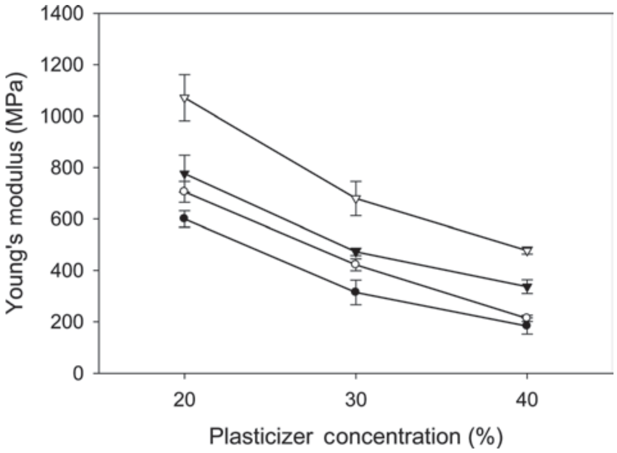

Figure 6. Young's modulus of low-molecular-weight (LMW) and conventional hypromellose (HPMC) films cast from solutions at equivalent viscosities. (•) 20% E LMW; (▾) 20% F LMW; (○) 14.4% E3 LV; (▿) 13.1% F4 LV.

Young's modulus, also referred to as elastic modulus, is defined as the ratio of applied stress and corresponding strain and is a measure of film stiffness. As with tensile strength, Young's modulus decreased as the concentration of plasticizer was increased (Figure 6). These data are in agreement with Aulton et al.[25], Heinamaki et al.[26], and Qussi and Suess[28]. Plasticizers disrupt intermolecular bonding between the polymer chains, resulting in a more flexible film. The E and F chemistry LMW polymers exhibited lower Young's modulus than the conventional polymer comparators, again likely due to the shorter polymer chains. In addition, both F chemistry films exhibited a higher Young's modulus than the conventional HPMC E chemistry polymer films, indicating that the structure of the F chemistry polymers produce more rigid films, regardless of polymer molecular weight. These findings may be related to the limited ability of the hydrophilic PEG to disrupt the intermolecular bonding of the F chemistry polymers which are slightly less hydrophilic than the E chemistry materials due to the lower proportion of hydroxypropoxyl side groups.

Mechanical properties of free films are often used to predict the performance of coatings applied to solid substrates. Defects, such as film cracking, edge splitting, and peeling result from internal stresses that develop during the coating process[29]. These internal stresses occur due to shrinkage of the film during solvent evaporation and differences in the thermal expansion between the polymer film and substrate. Changes in volume caused by substrate swelling during storage can also contribute to internal stress[30]. The total internal stress (P) within a polymer film can be calculated by using Equation 5,

$$P = \frac{E}{3(1-\nu)}\left[\frac{\Phi_s - \Phi_r}{1-\Phi_r}\right] + \Delta\alpha_{(\text{cubic})}\Delta T + \frac{\Delta V}{V} \quad (5)$$

where E is the Young's modulus of the film, ν is the Poisson's ratio of the polymer, φ_s is the volume fraction of the solvent at the solidification point, φ_r is the volume fraction of the solvent remaining in the dry film at ambient conditions, $\Delta\alpha_{(\text{cubic})}$ is the difference between the thermal expansion coefficient of the coating and the tablet substrate, ΔT is the difference between the glass transition temperature of the polymer film coating and the ambient temperature during manufacturing and storage, ΔV is the volumetric change of the tablet core, and V is the original volume of the tablet core[30,31]. Thus, the total internal stress within a film is directly proportional to the Young's modulus and factors that affect film ductility will influence the internal stress within the polymer film. Internal stresses have also been shown to affect film–tablet adhesion[32].

According to Rowe[31], film cracking or edge splitting occurs when internal stresses within the film become equivalent to or greater than its tensile strength. Thus, the tendency of a film to crack may be predicted by the ratio of tensile strength to Young's modulus (σ/E), with higher values indicative of fewer such defects. The σ/E ratios of the four HPMC polymers used in this study are plotted as a function of plasticizer concentration in Figure 7. The E LMW films exhibited an increase in σ/E with increasing plasticizer concentration, indicating a decreased cracking tendency that was attributed to a reduction in internal stresses. At the highest plasticizer level (40% w/w), the σ/E ratio of the E LMW polymer films was not statistically different from the other materials investigated, suggesting that the E LMW polymers must be sufficiently plasticized for coating applications. Interestingly, plasticizer concentration did not significantly affect the σ/E ratio for both F chemistry polymers and the conventional E chemistry material.

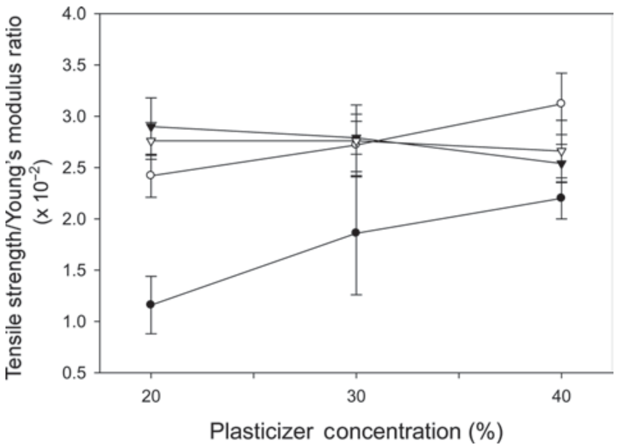

Figure 7. Ratio of tensile strength and Young's modulus of low-molecular-weight (LMW) and conventional hypromellose (HPMC) films cast from solutions at equivalent viscosities. (•) 20% E LMW; (▾) 20% F LMW; (○) 14.4% E3 LV; (▿) 13.1% F4 LV.

Previously, Rowe and Forse[29] used commercially available HPMC products (METHOCEL™ E3 up to E15) to investigate the influence of polymer molecular weight on the incidence of cracking and edge splitting. In that study, decreased defects in film coated tablets were observed with higher-molecular-weight polymers up to a nominal value. Rowe suggested that the molecular weight at which the incidence of such defects becomes negligible is the same as that at which there is no further increase in tensile strength. Rowe and Forse[29], however, did not evaluate the effects of plasticizer in that study. Plasticizers lower the internal stresses in polymeric films that are attributed to cracking and edge splitting[31] and have been shown to significantly influence the tensile strength of free films[24,25,27]. Thus, it is not surprising that the σ/E ratios of the E chemistry LMW films increased with increasing plasticizer concentration.

Conclusions

In the current study, the solutions of the LMW polymers exhibited significantly lower viscosities than the conventional HPMC materials at equivalent polymer concentrations. Mechanical testing indicated that the conventional HPMC polymer films were stronger and more ductile than the LMW films prepared from solutions at equivalent viscosities. Plasticization of the LMW HPMC was necessary to form films. Increasing concentrations of the plasticizer PEG 400 resulted in decreased tensile strength and Young's modulus and an increase in percent elongation, irrespective of polymer type. In addition, water vapor permeability increased as the plasticizer concentration was increased. Overall, the F chemistry LMW polymers exhibited similar σ/E ratios to the conventional HPMC polymers, suggesting that these materials may have potential applications in film coating.

Declaration of interest

This work was supported (in part) by The Dow Chemical Company.

References

1. Porter SC, Felton LA. (2010). Techniques to assess film coatings and evaluate film-coated products. Drug Dev Ind Pharm, 36:128–142.
2. Felton LA. (2007). Characterization of coating systems. AAPS Pharmscitech, 8:E112.
3. Li SP, Martellucci SA, Bruce RD, Kinyon AC, Hay MB, Higgins JD 3rd. (2002). Evaluation of the film-coating properties of a hydroxyethyl cellulose/hydroxypropyl methylcellulose polymer system. Drug Dev Ind Pharm, 28:389–401.
4. Fell JT, Rowe RC, Newton JM. (1979). The mechanical strength of film-coated tablets. J Pharm Pharmacol, 31:69–72.
5. Dashevsky A, Ahmed AR, Mota J, Irfan M, Kolter K, Bodmeier RA. (2010). Effect of water-soluble polymers on the physical stability of aqueous polymeric dispersions and their implications on the drug release from coated pellets. Drug Dev Ind Pharm, 36:152-160.

6. Felton L, Haase M, Shah N, Zhang G, Infeld M, Malick A, McGinity JW. (1995). Physical and enteric properties of soft gelatin capsules coated with Eudragit L 30 D-55. Int J Pharm, 113:17–24.
7. Bussemer T, Bodmeier R. (2003). Formulation parameters affecting the performance of coated gelatin capsules with pulsatile release profiles. Int J Pharm, 267:59–68.
8. Mueller R, Kleinebudde P. (2007). Comparison of a laboratory and a production coating spray gun with respect to scale-up. AAPS Pharmscitech, 8:3.
9. Siepmann F, Siepmann J, Walther M, MacRae R, Bodmeier R. (2006). Aqueous HPMCAS coatings: effects of formulation and processing parameters on drug release and mass transport mechanisms. Eur J Pharm Biopharm, 63:262–269.
10. Siepmann F, Siepmann J, Walther M, MacRae RJ, Bodmeier R. (2008). Polymer blends for controlled release coatings. J Control Release, 125:1–15.
11. Muschert S, Siepmann F, Leclercq B, Carlin B, Siepmann J. (2010). Simulated food effects on drug release from ethylcellulose: PVA-PEG graft copolymer-coated pellets. Drug Dev Ind Pharm, 36:173–179.
12. Dow Chemical Company. (2002). Technical Literature: METHOCEL™ Cellulose Ethers.
13. American Society of Testing Materials (ASTM). (2002). ASTM D882-02: Standard Test Method for Properties of Thin Plastic Sheeting.
14. American Society for Testing Materials (ASTM). (2005). ASTM E96/E 96 M-05: Standard Test Methods for Water Vapor Transmission of Materials.
15. Bley O, Siepmann J, Bodmeier R. (2009). Characterization of moisture-protective polymer coatings using differential scanning calorimetry and dynamic vapor sorption. J Pharm Sci, 98:651–664.
16. Cunningham C. (2007). Reducing coated tablet defects from laboratory through production scale: performance of hypromellose or polyvinyl alcohol-based aqueous film coating systems. AAPS Annual Meeting, San Diego, CA.
17. Rogers T, Sheskey P, Furukawa H, Mallon C, Trampe M, Holbrook D. (2008). Investigation of a novel hypromellose polymer for high-productivity tablet coating applications. AAPS Annual Meeting, Atlanta, GA.
18. Porter S. (2010). The role of high-solids coating systems in reducing process costs. Tablets Capsules, 8:10–16.
19. Cunningham C, Hansell J, Nuneviller F 3rd, Rajabi-Siahboomi AR. (2010). Evaluation of recent advances in continuous film coating processes. Drug Dev Ind Pharm, 36:227–233.
20. Hancock B, York P, Rowe R. (1997). The use of solubility parameters in pharmaceutical dosage form design. Int J Pharm, 148:1–21.
21. Guo J-H. (1993). Effects of plasticizers on water permeation and mechanical properties of cellulose acetate: antiplasticization in slightly plasticized polymer film. Drug Dev Ind Pharm, 19:1541–1555.
22. Guo J-H. (1994). An investigation into the formation of plasticizer channels in plasticized polymer films. Drug Dev Ind Pharm, 20:1883–1893.
23. Hsu ER, Gebert MS, Becker NT, Gaertner AL. (2001). The effects of plasticizers and titanium dioxide on the properties of poly(vinyl alcohol) coatings. Pharm Dev Technol, 6:277–284.
24. Yuan J, Shang P, Wu S. (2001). Effects of polyethylene glycol on morphology, thermomechanical properties, and water vapor permeability of cellulose acetate-free films. Pharm Tech, 62–74.
25. Aulton M, Abdul-Razzak, M, Hogan J. (1981). The mechanical properties of hydroxypropylmethylcellulose films derived from aqueous systems part I: the influence of plasticizers. Drug Dev Ind Pharm, 7:649–668.
26. Heinamaki J, Lehtola V, Nikupaavo P, Yliruusi J. (1994). The mechanical and moisture permeability properties of aqueous-based hydroxypropyl methylcellulose coating systems plasticized with polyethylene glycol. Int J Pharm, 112:191–196.
27. Honary S, Orafai H. (2002). The effect of different plasticizer molecular weights and concentrations on mechanical and thermomechanical properties of free films. Drug Dev Ind Pharm, 28:711–715.
28. Qussi B, Suess WG. (2006). The influence of different plasticizers and polymers on the mechanical and thermal properties, porosity and drug permeability of free shellac films. Drug Dev Ind Pharm, 32:403–412.
29. Rowe RC, Forse SF. (1980). The effect of polymer molecular weight on the incidence of film cracking and splitting on film coated tablets. j Pharm Pharmacol, 32:583–584.
30. Okutgen E, Hogan J, Aulton M. (1995). Quantitative estimation of internal stress development in aqueous HPMC tablet film coats. Int J Pharm, 119:193–202.
31. Rowe RC. (1983). A reappraisal of the equations used to predict the internal stresses in film coatings applied to tablet substrates. J Pharm Pharmacol, 35:112–113.
32. Felton L, McGinity J. (1997). Influence of plasticizers on the adhesive properties of an acrylic resin copolymer to hydrophilic and hydrophobic tablet compacts. Int J Pharm, 154:167–178.