

# Hydroxypropylmethylcellulose–Anionic Surfactant Interactions in Aqueous Systems \*

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## SYNOPSIS

The increase in the viscosity of an aqueous solution or gel of hydroxypropylmethylcellulose (HPMC) in the presence of an anionic surfactant is attributed to a two-step process: (a) the surfactant undergoes ion–dipole interaction with the ethereal oxygen in HPMC, in the absence or presence of water, and (b) hydrocarbon moieties in the now pendant surfactant molecules undergo hydrophobic bonding, in the presence of water, resulting in an apparent increase in the molecular weight of the HPMC. DSC of dry blends and dried gels or films confirmed HPMC–sodium lauryl sulfate interaction. Work-to-break measurements on films cast from aqueous solutions of HPMC, in the absence or presence of anionic surfactants, indicated an apparent increase in the molecular weight of HPMC in the presence of surfactants.

## INTRODUCTION

Nonionic water-soluble polymers containing long-chain hydrocarbon substituents yield higher viscosity aqueous solutions as compared with the unsubstituted polymers. This is attributed to intermolecular association of the hydrocarbon moieties, i.e., hydrophobic bonding, and the formation of aggregates that act as higher molecular weight species. The preparation and properties of such “associative thickeners” have become of significant scientific and commercial interest in recent years.<sup>1</sup>

The addition of an anionic surfactant to a dilute aqueous solution of a nonionic water-soluble cellulose ether, e.g., hydroxypropylmethylcellulose (HPMC), results in an increase in the viscosity of the solution.<sup>2</sup> The presence of an anionic surfactant in a drug tablet containing HPMC as binder results in a prolonged time of drug release in an aqueous medium, apparently due to an increase in the viscosity of the HPMC gel layer.<sup>3–5</sup>

The present investigation was undertaken to determine the nature of the interaction, if any, between the anionic surfactant and the nonionic cellulose ether, as a result of which the mixture behaves in an aqueous environment in the same manner as a hydrophobically substituted nonionic water-soluble polymer per se.

## EXPERIMENTAL

### Materials

Hydroxypropylmethylcellulose (HPMC), Dow Chemical Co. Methocel K4M, with a 2% aqueous solution viscosity of 4000 cps and a specification indicating a methoxyl content of 19–24 wt %, a hydroxypropoxyl content of 4–12 wt %, and a number average molecular weight of 93,000, was used as received. The moisture content of the HPMC was 2.5–3.0%. Sodium lauryl sulfate (SLS) (Aldrich Chemical Co.), 98% pure, and sodium 1-hexadecanesulfonate (SHDS) (Aldrich Chemical Co.), 99% pure, were used as received.

### Test Procedures

DSC analyses were carried out on 7- to 10-mg samples on a Mettler Instrument Co. Model FP 800 in-

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strument with 10°C/min programmed heating and recorded on a Kipp and Zonen chart recorder with a chart speed of 10 mm/min.

The specimens for DSC analysis were prepared by (a) dry blending HPMC and SLS and grinding by hand in a mortar with a pestle; (b) wet granulation wherein water was added to a ground blend to form a wet paste, which was passed through a fine hand screen and dried at 50°C under 20 in. Hg pressure for 24 h; (c) compressing a 400-mg HPMC-SLS mixture at 1000 psi pressure in a Carver Laboratory Press to form a 13/32 in. ID tablet that was placed in a perforated basket and rotated at 50 rpm while immersed in 900 mL distilled water at 37°C for 1 h; and (d) casting of films from a 1% aqueous solution after refrigerating the solution to eliminate air bubble entrapment, following by pouring the solution into a petri dish and drying at 50°C under 15 in. Hg pressure for 72 h.

The tensile strength, modulus of elasticity, and work-to-break of films cast from aqueous solutions were measured on an MTS tensile tester with a 500 Newton transducer load cell. The mechanical properties were measured on a 1-cm-wide film strip having a thickness of about 0.1 mm with a 5 cm length of the strip between the clamps and a crosshead speed of 5 mm/min ( $0.083 \times 10^{-3}$  m/s).

Tensile strength (MPa)

$$= \frac{\text{load at failure (N)}}{\text{film thickness (m)} \times \text{width (m)}}$$

Modulus of elasticity (MPa) =  $\frac{\text{stress (N/m}^2\text{)}}{\text{strain}}$

$$= \frac{\text{slope (N/s)} \times 60,000 \text{ (s/m)}}{\text{film thickness (m)}}$$

Work-to-break (kJ/m<sup>2</sup>)

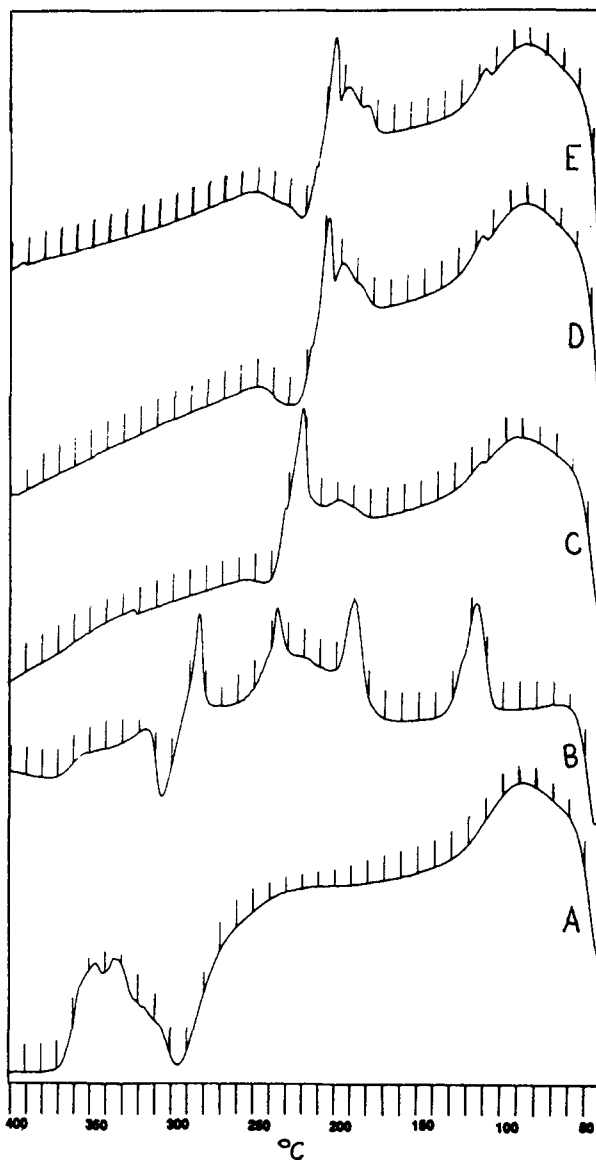
$$= \frac{\text{area under curve (N-s)} \times 0.083 \times 10^{-3} \text{ (m/s)} \times 100}{\text{film thickness (m)} \times \text{width (m)}}$$

The films for the determination of mechanical properties were prepared by casting refrigerated 2% aqueous solutions of HPMC or HPMC-surfactant mixtures, prepared at room temperature or hot water into a plastic tray and drying at 50°C under 15–20 in. Hg pressure for 72 h. The dried films had a thickness of  $0.1 \pm 0.02$  mm and a water content of 3.2–6.8%, as determined by drying at 105°C for 4 h.

## RESULTS

### DSC Thermograms of HPMC-Sodium Lauryl Sulfate Compositions

The DSC thermograms of HPMC and sodium lauryl sulfate (SLS) as well as dry blends of HPMC-SLS at 95/5, 90/10, and 85/15 (w/w) ratios are shown in Figure 1. The thermograms of the compositions containing HPMC show a broad endothermic peak at about 50–140°C while the thermogram of SLS shows a narrow peak at about 100–140°C. The lower temperature portion of the thermogram of the



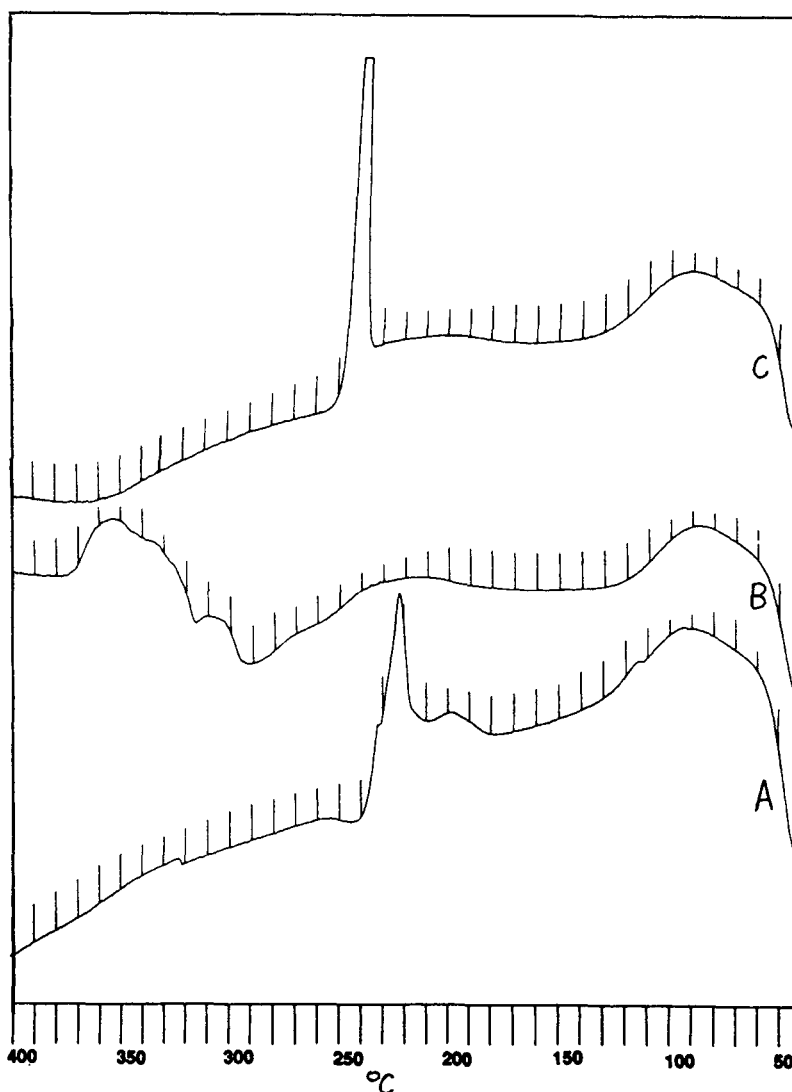
**Figure 1** DSC thermograms of HPMC-SLS dry blends. (a) 100/0, (b) 0/100, (c) 95/5, (d) 90/10, (e) 85/15.

**Table I Shifts in Peak Temperatures (°C) in DSC Thermograms of HPMC-SLS Dry Blends**

Peak	HPMC	SLS	HPMC-SLS
endo	50-140	—	50-140
endo	—	120	(shift) 115
endo	—	190	200
endo	—	235	(shift) 230, 225
endo	—	—	220, 210, 205
exo	—	—	240, 235, 230
endo	—	285	260
exo	295	—	—
exo	—	305	—
endo	330, 345	—	(shift)—, 325

HPMC and HPMC-SLS compositions may be due to the presence of water. However, the 100-140°C portion of the SLS and HPMC-SLS thermograms may be due to the presence of the hydrocarbon moiety in the surfactant.

Examination of Figure 1 reveals that the thermograms of the HPMC-SLS compositions are significantly different from those of either HPMC or SLS. The endothermic peak in SLS, centered at about 120°C, has become a shoulder at 115°C on the adjacent lower temperature peak in HPMC-SLS compositions. The large peak in SLS, centered at 190°C, has shifted to a small peak centered at 200°C in HPMC-SLS compositions. The large peak centered at 235°C in SLS has become a shoulder at

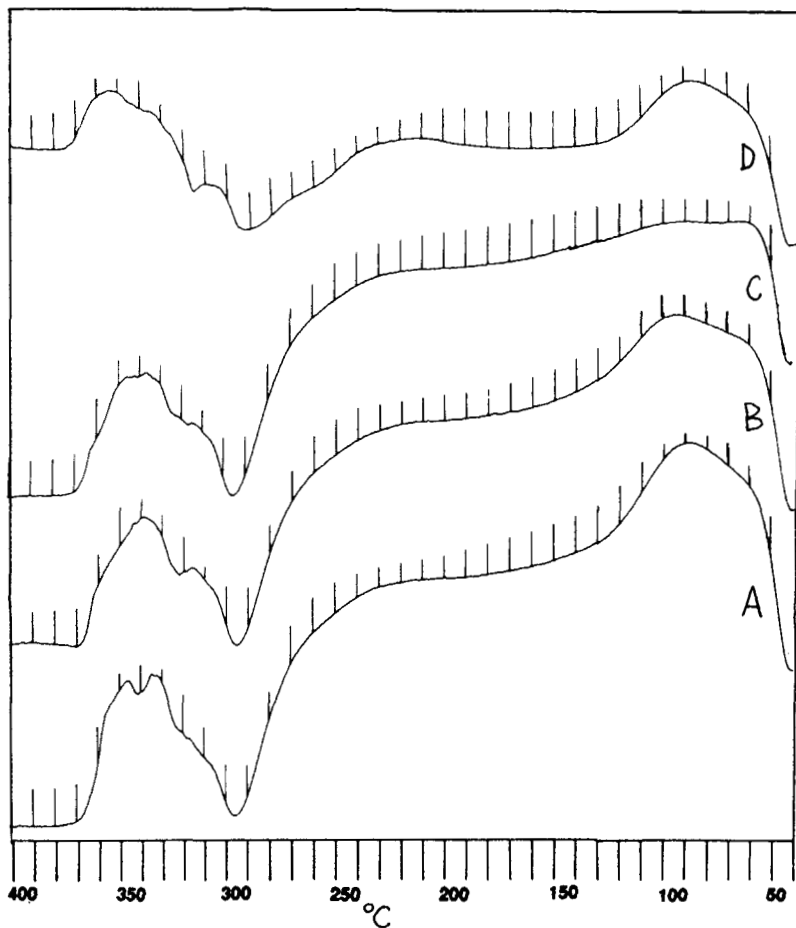


**Figure 2** DSC thermograms of HPMC-SLS blends and films. (a) 95/5 dry blend, (b) 100/0 film, (c) 95/5 film.

about 230 or 225°C in the HPMC-SLS thermograms. A new peak appears at 220, 210, or 205°C in HPMC-SLS compositions, the shift to the lower temperatures occurring as the SLS content of the HPMC-SLS composition increases from 5 to 15%. This new peak is the dominant feature in the HPMC-SLS thermograms and is accompanied by an exothermic peak centered at 240, 235, or 230°C in the HPMC-SLS thermograms. A large endothermic peak at 285°C in SLS has shifted to a small endothermic peak at 260°C in the HPMC-SLS systems. A large exothermic peak at 305°C in SLS is absent in the HPMC-SLS systems. Similarly, a large exothermic peak centered at 295°C in HPMC is absent in the HPMC-SLS compositions. The large endothermic peaks centered at 330 and 345°C in HPMC have become minor shoulders or are absent in HPMC-SLS thermograms.

The various shifts in the thermograms of HPMC-SLS (Fig. 1) are summarized in Table I. The appearance of the new endothermic and exothermic peaks in the thermograms of the dry blends confirms an interaction between these materials on mixing.

The DSC thermograms of HPMC and 95/5 HPMC-SLS films, which were cast from aqueous solutions and dried, are compared with an HPMC-SLS dry blend in Figure 2. The general features of the HPMC-SLS film are similar to those of the dry blend and distinctly different from the thermograms of either dry HPMC powder, HPMC film, or SLS. The major endothermic single peak in the thermogram of the 95/5 HPMC-SLS film is centered at 235°C, which is somewhat higher than the major peak at 220°C in the thermogram of the corresponding dry blend. It is noteworthy that this major feature of the 95/5 HPMC-SLS film thermogram



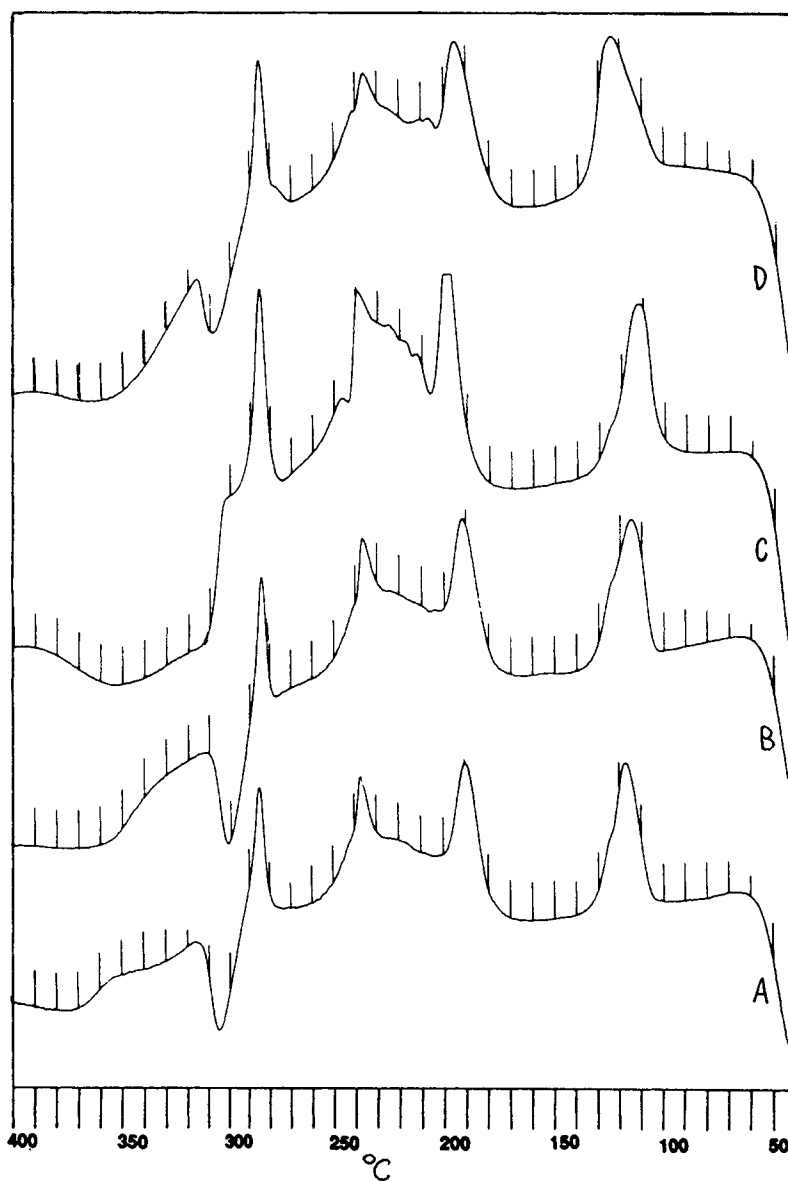
**Figure 3** DSC thermograms of HPMC. (a) Dry powder as received, (b) powder dried at 50°C at 20 in. Hg pressure for 72 h, (c) sample (b) heated to 140°C and cooled, (d) film prepared from 1% aqueous solution and dried at 50°C at 20 in. Hg pressure for 72 h.

is present despite the fact that the composition contains only 5% SLS. The endothermic peak at 200°C and the exothermic peak at 240°C in the dry blend are absent in the thermogram of the film.

In order to eliminate the possibility that the absent peaks and the new peak result from the thermal processing, e.g., drying, of the HPMC-SLS compositions, DSC thermograms of thermally treated HPMC and SLS were obtained and are compared in Figures 3 and 4, respectively. The thermograms of HPMC, thermally processed in the absence of

water or after conversion to a film, are essentially similar to that of dry HPMC powder, subjected to DSC analysis as received (Fig. 3).

The thermograms of SLS, which has been thermally processed, were compared to that of dry SLS powder, subjected to DSC analysis as received (Fig. 4). When the SLS was heated to 90°C, cooled, and then subjected to DSC analysis, the exothermic peak at 305°C in the dry SLS was replaced by an endothermic shoulder at about 305°C. The 90°C treatment appears to be consistent with the loss of water



**Figure 4** DSC thermograms of SLS. (a) Dry powder as received, (b) powder dried at 50°C at 20 in. Hg pressure for 72 h, (c) sample (b) heated to 90°C and cooled, (d) recrystallized and dried at 50°C at 20 in. Hg pressure for 72 h.

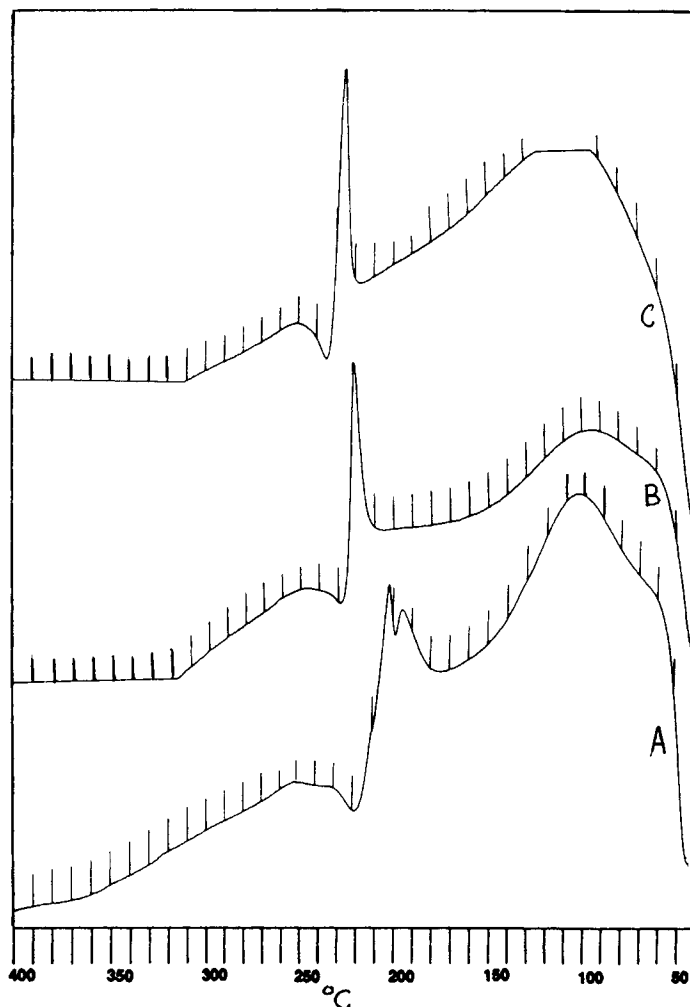
from a hydrate, if any. The change at about 305°C may indicate a change in the crystal state of the dehydrated SLS.

Notwithstanding, it is apparent that thermal processing of the individual components is not responsible for the major single peak at 220°C in the HPMC-SLS blends.

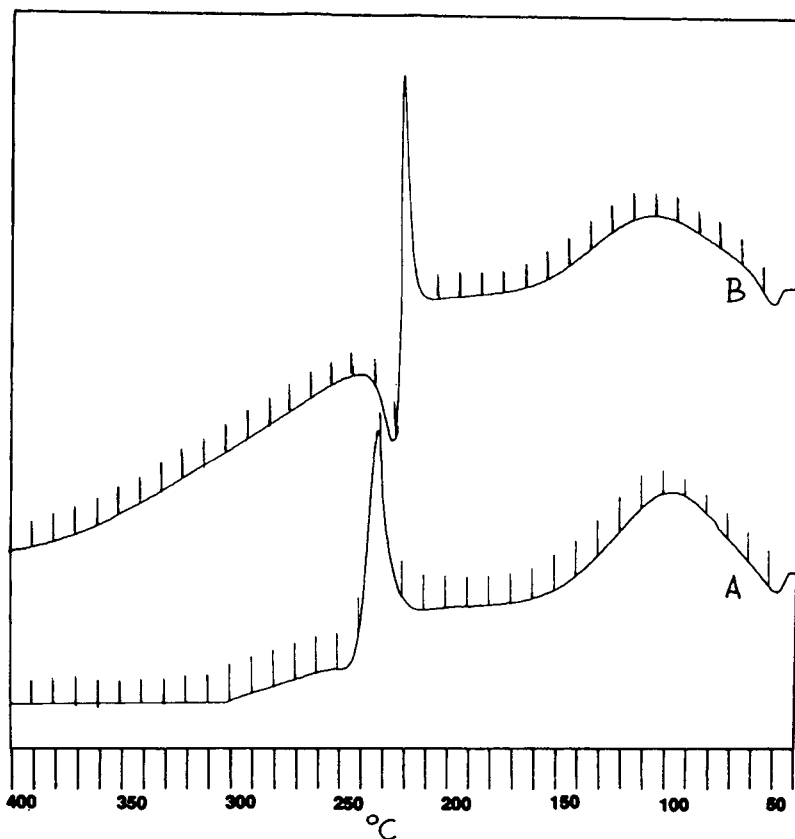
The DSC thermograms of 90/10 HPMC-SLS blends, which have been granulated with water and then dried, are essentially the same as those of the materials prepared without granulation (Fig. 5). The thermogram of the 90/10 blend granulated with 92% water is similar to that of the corresponding dry blend shown in Figure 1 and has the 195 and 205°C endothermic peaks. The dry blends may actually

contain some water due to the hygroscopic nature of the reactants. The thermogram of the 90/10 blend granulated with 190% water does not show the 195°C peak and is similar to the thermogram of the film shown in Figure 2 and has the single major peak at 215°C.

The DSC thermograms in Figure 6 of gels cut from the surfaces of HPMC-SLS tablets that have been immersed in water show peaks due to the presence of water centered at about 110°C and the endothermic peaks at 240°C (90/10 HPMC-SLS) and 215°C (85/15 HPMC-SLS). The exothermic peaks at 225 and 255°C, respectively, are also present in Figure 6. The persistence of these peaks in the DSC thermograms of dried samples prepared from gels



**Figure 5** DSC thermograms of 90/10 HPMC-SLS granules prepared by wet granulation. (a) Dry blend granulated with 92% water and dried at 50°C at 20 in. Hg pressure for 24 h, (b) dry blend granulated with 190% water and dried at 50°C at 20 in. Hg pressure for 24 h, (c) dry blend granulated with 190% water and air dried.



**Figure 6** DSC thermograms of HPMC-SLS gels obtained from surface of compressed tablet immersed in water and gel dried at room temperature for 24 h. (a) 90/10 gel, (b) 85/15 gel.

indicates that the HPMC-SLS interaction is not significantly influenced by the presence of excess water. The major peaks in the DSC thermograms of HPMC-SLS after contact with water are summarized in Table II. The absence of an endothermic peak at 195–200°C in the thermograms of all specimens that have been in contact with water is noteworthy.

#### Stress-Strain Relationships in HPMC-Surfactant Films

Films containing either HPMC or HPMC and a surfactant were cast from aqueous solutions. The polymer casting solution was prepared either with room temperature water followed by refrigeration or with hot water followed by refrigeration. The

**Table II** Major Peaks (°C) in DSC Thermograms of HPMC-SLS after Contact with Water

Figure	Sample	HPMC-SLS	endo	exo
1	Dry blend	95/5	200, 220	240
2	Film	95/5	—, 235	—
1	Dry blend	90/10	200, 210	240
5	Granules (92% water)	90/10	195, 205	230
5	Granules (190% water)	90/10	—, 215	230
6	Gel	90/10	—, 240	255
1	Dry blend	85/15	200, 205	230
6	Gel	85/15	—, 215	225

polymeric solutions contained either 1 or 2% HPMC, depending on composition. The cast films were dried in an oven at 50°C under 15–20 in. Hg pressure. The water content of these dried films ranged from 3.2 to 6.8%.

The dried films were tested on a tensile tester and the tensile strength, modulus of elasticity, and work-to-break were calculated from the load versus time plot.

The plots for films containing HPMC and a 90/10 HPMC–SLS combination are shown in Figure 7. The films were prepared by the room temperature water–refrigeration method and contained  $6.7 \pm 0.1\%$  water. The mechanical properties are summarized in Table III.

The tensile strength and modulus of elasticity of the HPMC and HPMC–SLS films are almost identical, but the area under the curve (AUC) and the work-to-break (WTB) calculated therefrom are very different. The WTB of the HPMC–SLS film is 65% higher than the WTB of the HPMC film.

Since WTB is related to molecular weight, these data suggest that the polymer in the HPMC–SLS film has an apparent molecular weight that is higher than that of the polymer in the HPMC film.

The load versus time plots for films containing

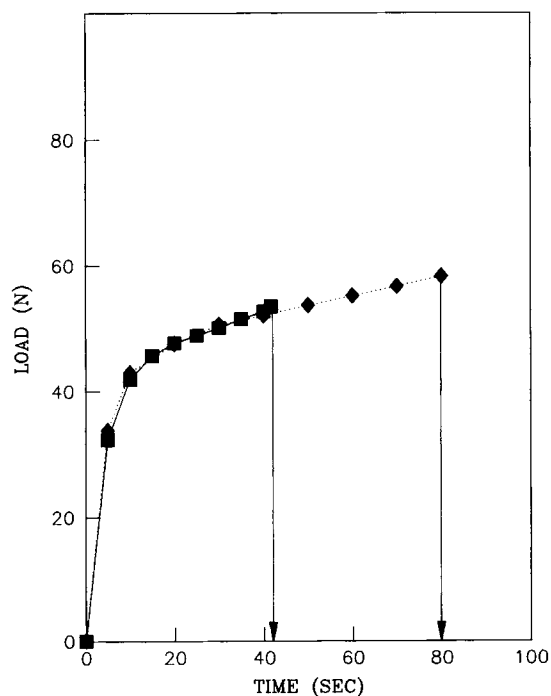
**Table III Mechanical Properties of HPMC–SLS Films<sup>a</sup>**

HPMC–SLS weight ratio	100/0	90/10
Tensile strength, MPa	58	58
Modulus of elasticity, MPa	1878	1882
Area under the curve, N-s	2430	4011
Work-to-break, kJ/m <sup>2</sup>	202	333
Water content, wt %	6.8	6.6

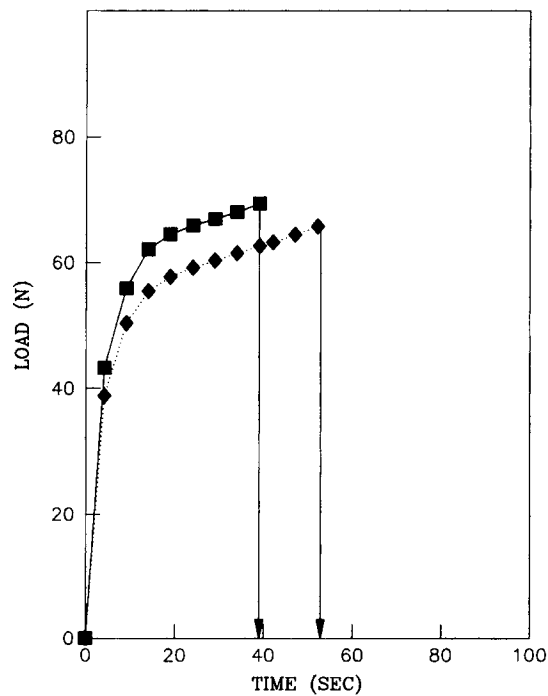
<sup>a</sup> Films cast from aqueous solution prepared with room temperature water followed by refrigeration.

HPMC and 85/15 HPMC–surfactant combinations are shown in Figures 8 and 9. The surfactants were SLS (Fig. 8) and sodium 1-hexadecanesulfonate (SHDS) (Fig. 9). The films were prepared by the hot water–refrigeration method and contained  $3.8 \pm 0.3\%$  water. The mechanical properties are summarized in Table IV.

The tensile strength and modulus of elasticity of the SLS- and SHDS-containing films are only 4 and 6% lower, respectively, than the corresponding values for the surfactant-free HPMC film. However, the AUC and the WTB are 36 and 33% higher for the HPMC–SLS and HPMC–SHDS films, respectively, than the WTB for the HPMC film.

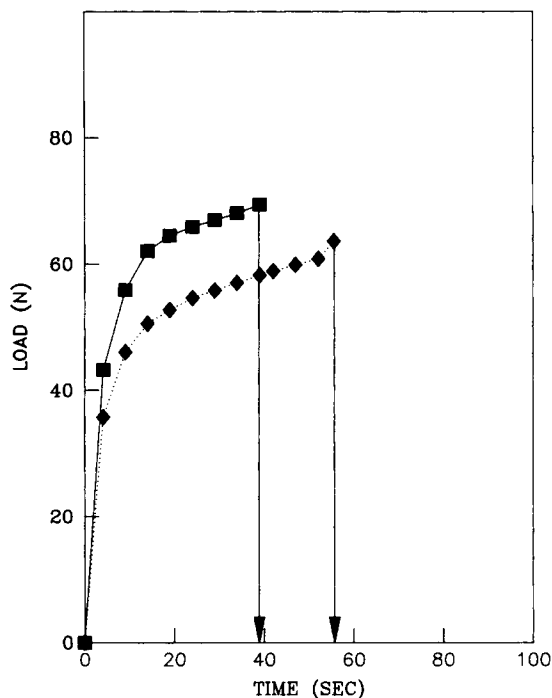


**Figure 7** Load vs. time plot for HPMC–SLS films prepared by room temperature water–refrigeration procedure. (■) 100/0, (◆) 90/10.



**Figure 8** Load vs. time plot for HPMC–SLS films prepared by hot water–refrigeration procedure. (■) 100/0, (◆) 85/15.





**Figure 9** Load vs. time plot for HPMC-SHDS films prepared by hot water-refrigeration procedure. (■) 100/0, (◆) 85/15.

## DISCUSSION

The DSC thermograms of dry blends of HPMC and SLS are significantly different from those of either of the components. As shown in Figure 1 and summarized in Table I, the thermograms of dry blends containing 5–15% anionic surfactant show new endothermic and exothermic peaks and peaks found in the thermograms of the components either shifted or are absent in the thermograms of the blends.

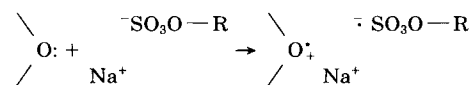
DSC thermograms of wetted HPMC-SLS mixtures in the form of films cast from aqueous solution (Fig. 2), granulated mixtures, i.e. blends contacted with water (Fig. 5), and gels removed from the surface of compressed tablets immersed in water (Fig. 6), all dried before DSC analysis, are similar to those of the dry blends (Table II) and different from those of the nonionic cellulose ether and the anionic surfactant.

The appearance of a new peak in the DSC is indicative of the presence of a new entity, presumably formed by the interaction of the cellulose ether and the surfactant. This new entity is formed in the dry state as well as in the presence of water. The drying of mixtures after contact with water does not appear to be responsible for the changes in the thermograms

since thermal treatment of HPMC (Fig. 3) as well as SLS (Fig. 4) do not result in changes.

Noncovalent interactions between molecules include hydrogen bonding, cation-anion, donor-acceptor, dipole-dipole, and ion-dipole. Ion-dipole interactions are well known in small molecule-small molecule,<sup>6,7</sup> polymer-small molecule,<sup>8-10</sup> and polymer-polymer<sup>11-14</sup> systems.

It is proposed that the HPMC-anionic surfactant interaction is an ion-dipole interaction between the ethereal oxygen in the nonionic cellulose ether and the cation in the surfactant. However, since the cation is closely associated with the anion in the surfactant, the electron from the oxygen probably resides in the vicinity of the ion pair. This may be represented as follows:



It should be noted that a search of the literature has failed to unearth a representation of an ion-dipole interaction. The preceding is admittedly an oversimplification but is worthy of consideration.

The area under the curve in a plot of load versus time is used in the calculation of work-to-break. It is primarily characteristic of the polymeric material and secondarily of the fine structure, e.g., orientation and crystallinity of the specimen,<sup>15</sup> and is related to the molecular weight.

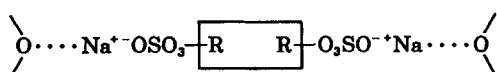
The increased work-to-break values for the HPMC films containing SLS (Figs. 7 and 8) and SHDS (Fig. 9), as summarized in Tables III and IV, indicate that the polymer in the film containing the surfactant has an apparent molecular weight that is higher than that of HPMC in the absence of surfactant.

**Table IV** Mechanical Properties of HPMC-Surfactant Films<sup>a</sup>

Surfactant	None	SLS	SHDS
HPMC-surfactant weight ratio	100/0	85/15	85/15
Tensile strength, MPa	69	66	62
Modulus of elasticity, MPa	2906	2720	2724
Area under the curve, N. sec	2322	3167	3078
Work-to-break, kJ/m <sup>2</sup>	193	263	255
Water content, wt %	4.1	3.5	4.1

<sup>a</sup> Films cast from aqueous solution prepared with hot water followed by refrigeration.

Ion-dipole interaction between the surfactant and HPMC results in the generation of a polymeric structure containing pendant hydrocarbon chains. In the presence of water, these hydrocarbon moieties undergo hydrophobic bonding resulting in noncovalent chain extension of the cellulose ether molecules. The apparent higher molecular weight of the cellulose ether in the presence of surfactant results in a higher viscosity solution and gel. This may be represented as follows:



The hydrophobic bonding is not restricted to two surfactant molecules but may involve multiple surfactant molecules associated with multiple polymer chains.

In brief, the mechanism proposed for the increase in viscosity noted on the addition of an anionic surfactant to an aqueous solution or gel containing a nonionic cellulose ether such as HPMC, involves two steps, i.e., an ion-dipole interaction between the polymer and the surfactant, in the absence or presence of water, followed by hydrophobic bonding between pendant hydrocarbon moieties in the surfactants associated with different polymer chains, in the presence of water.

As noted earlier, DSC indicates the disappearance of an endothermic peak at 195–200°C in the thermograms of all HPMC-SLS compositions that have been in contact with water, prior to drying (Table II). It may be speculated that this is related to some phenomenon that occurs when the composition is contacted with water, but it cannot be stated unequivocally that this is related to hydrophobic bonding.

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