

Comparison of Swelling, Erosion, and Gel Strength of Polyethylene Oxide and Hypromellose

Paula Garcia Todd,¹ Jennifer L'Hote-Gaston,¹ Matthew Sheick²

¹Dow Wolff Cellulosics R&D, The Dow Chemical Company, Larkin Laboratory, Midland, MI 48674

²Kelly Services, Inc., Midland, MI 48640

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Abstract

The objective of this study was to compare swelling, erosion, and gel strength of commonly used hydrophilic polymers for controlled release. The study found that high molecular weight polyethylene oxide swelled faster and to a greater extent while hypromellose provided better gel strength in pure polymer compacts. Swelling, erosion, and gel strength of these polymers are interdependent and should be considered when formulating a hydrophilic matrix system.

Introduction

Polyethylene oxide (PEO) and hypromellose (hydroxypropyl methylcellulose, HPMC) are hydrophilic polymers commonly used for controlled-release drug delivery in oral solid-dosage forms. The influence of swelling, erosion, and gel strength properties of these two polymers is particularly important in drug formulation development with respect to the mechanism of drug release, i.e., diffusion- or erosion-based drug delivery. In fact, there have been numerous studies regarding swelling and erosion for matrices containing either HPMC (1-5) or PEO (6-9). Gel strength, defined as the strength of the hydrated gel in a pure polymer or matrix, has been previously studied for one or both polymers relative to swelling and/or erosion using a texture analyzer (10-13). The purpose of this study was to evaluate the pure polymer characteristics of swelling, erosion, and gel strength in PEO and HPMC compacts. This will provide additional insight into polymer hydration and gel formation of PEO and HPMC as a function of polymer chemistry and molecular weight.

Experimental

Materials

Table 1 lists the materials used in this study. All materials were supplied by The Dow Chemical Company.

Methods

Tablet Preparation. Compacts of pure polymer weighing 450 mg were pressed on a Carver laboratory tablet press. Tooling used was 13/32 flat-faced bevel edge, with a compression force of 4000 lb, and a dwell time of 3 s.

Swelling and Erosion. Swelling of pure polymer compacts was carried out in a Distek Dissolution System (USP 1 Apparatus) using 40-mesh baskets at 50

rpm in degassed water. Hydrated compacts were removed at predetermined times over a 24-h period to measure swelling by water uptake.

$$\text{weight gain (\%)} = \frac{\text{wet weight} - \text{original weight}}{\text{original weight}} \times 100$$

Erosion was measured using the same compacts dried in a vacuum oven at 45°C until constant mass was achieved to determine mass loss.

$$\text{mass loss (\%)} = \frac{\text{original weight} - \text{remaining dry weight}}{\text{original weight}} \times 100$$

Table 1. Materials, chemistry, and molecular weight.

Product	Chemistry	Molecular Weight
POLYOX™		
N-12K	polyethylene oxide	1,000,000
301	polyethylene oxide	4,000,000
303	polyethylene oxide	7,000,000
METHOCEL™		
E4M	hypromellose 2910	4,000
K4M	hypromellose 2208	4,000
K100M	hypromellose 2208	100,000

Gel Strength. Gel strength was measured using a TA.XTPlus texture analyzer with a 5-kg load cell. Hydrated compacts were removed from the basket at predetermined times over a 24-h period and placed directly on the platform. A 2-mm flat-tipped probe was used to penetrate the swollen compact using a test speed of 0.1 mm/s until a trigger force of 0.005 N was detected. Resistance to penetration was measured until a maximum force of 40 N was achieved. Data were collected as force-displacement profiles. Gel strength was determined as the work of penetration integrated

to the first peak normalized by the tablet thickness to the first peak (distance traveled by the probe).

$$\text{normalized work of penetration} = \frac{W_{FP}}{\text{thickness}_{FP}} = \frac{\int FdD}{\text{mm}}$$

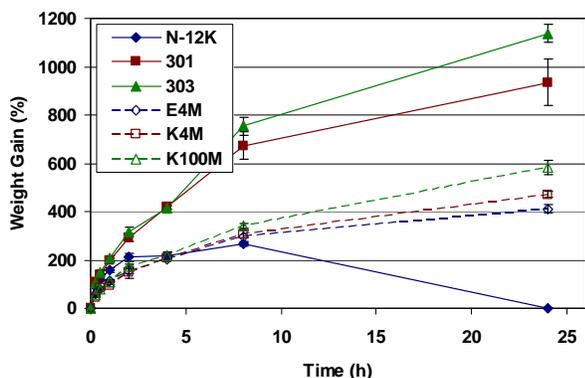
Results and Discussion

Swelling and Erosion

Swelling in pure polymer compacts of PEO and HPMC occurs upon immediate hydration of the polymer. As the dry polymer becomes hydrated, the mobility of the polymer chains increase, thereby increasing the hydrodynamic volume of the polymer compact, which allows the compact to swell (2). As polymer chains become more hydrated and the gel becomes more dilute, the disentanglement concentration may be reached, i.e., the critical polymer concentration below which the polymer chains disentangle and detach from a gelled matrix. These events result in simultaneous swelling, dissolution, and erosion (3).

In general, PEO demonstrated a faster rate of water uptake and greater swelling than HPMC (Figure 1). This is particularly evident when comparing high molecular weight PEO 301 and PEO 303 ($\geq 4,000,000$ MW) to HPMC K4M, K100M, and E4M. PEO 301 and 303 showed a faster rate of hydration than all HPMC as noted by the slope of the lines in the first 8 h. Beyond 8 h, similar hydration rates were observed for both PEO 301 and 303 and HPMC. PEO N-12K also swelled more than HPMC up to 2 h, at which time polymer hydration reached the disentanglement threshold, and polymer dissolution and erosion dominated swelling. Overall, high molecular weight PEO swelled twice as much as HPMC.

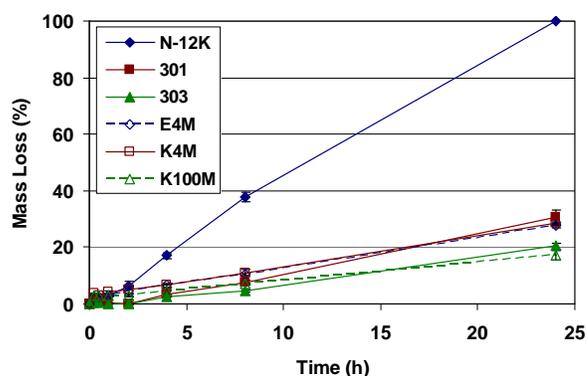
Figure 1. Swelling (% weight gain) for PEO and HPMC.



High molecular weight polymers showed significantly greater swelling and less erosion than lower molecular weight polymers for both PEO and HPMC (Figures 1 and 2), which is consistent with earlier work (4,7). With regard to PEO, both PEO 303 and PEO 301 demonstrated significantly greater swelling and less erosion overall than PEO N-12K. After 8 h, PEO 303 showed significantly greater swelling and less erosion

than PEO 301. For all PEO, the rate of hydration decreased as the disentanglement concentration was approached and polymer dissolution began to occur. This transition also coincided with notable increases in polymer erosion for lower molecular weight polymers PEO N-12K and 301 with extended hydration time. Similar observations were noted with HPMC K100M and K4M in terms of swelling and erosion. This suggests that erosion is largely dependent on molecular weight as opposed to the type of polymer (PEO or HPMC). Polymer substitution chemistry (HPMC) was also less of an influence in swelling and erosion as noted by data observed for K4M and E4M.

Figure 2. Erosion (% mass loss) for PEO and HPMC.



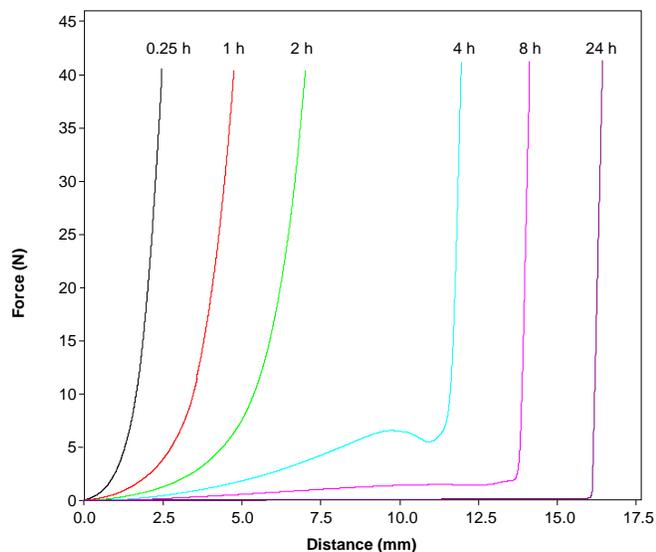
Gel Strength

Representative force-displacement profiles by texture analysis for PEO 303 and HPMC K100M are shown in Figure 3 and Figure 4. Force transition regions in a force-displacement textural profile of a swollen tablet have been previously defined (12, 14). The resistance to penetration encountered by the probe is a function of the extent of hydration and the gel strength of the swollen tablet. Initial resistance to penetration is high as noted by a sharp increase in the slope of the peak coupled with minimal distance traveled, a measure of swollen tablet thickness and an indicator of swelling. This suggests minimal formation of a gel layer in the swollen tablet at the outer edge, causing the probe to reach the maximum force without penetrating the tablet core. As hydration time progresses, a lower slope is observed, which indicates weaker gel strength in the gel layer as the probe moves through the thick gel layer towards the glassy core. Swelling is also observed by the increase in the distance traveled during the penetration test.

In the case of PEO 303, the transition from the glassy core to a fully hydrated rubbery phase began to occur at around 4 h (Figure 3). This is denoted by the peak in the force-displacement profile, which indicates a significantly thick gel

layer has formed around the glassy core of the compact and a softening of the core has occurred due to water penetration. The peak is a result of the probe hitting the glassy core, fracturing the core as the force increases, followed by a drop in the resistance before the probe travels completely through the compact. Beyond 4 h, full hydration of the tablet is noted by the very weak gel strength and the swollen tablet thickness.

Figure 3. Representative force-displacement profile for POLYOX™ 303.



For HPMC K100M, the transition from the glassy core to a fully hydrated rubbery phase began to occur at around 8 h (Figure 4). After 24 h, the compact showed very weak gel strength and a maximum swollen tablet thickness that was less than that of PEO 303 at the same time point.

Gel strength was quantitatively defined by the work of penetration normalized by the swollen tablet thickness at the specified time point (Figure 5). In general, the normalized work of penetration was found to decrease with extended hydration time, consistent with earlier studies using textural analysis (10-12). HPMC (K4M and K100M) was found to exhibit higher gel strength as compared to PEO up to 8 h. This is due to a slower hydration of the compacts and a lower rate of water uptake for HPMC, as noted in the previous swelling data (Figure 1). Beyond 8 h, both PEO and HPMC are fully hydrated gel compacts that have very low gel strength regardless of polymer chemistry or molecular weight.

For PEO, gel strength was found to be a function of molecular weight. This holds true for all time points except for 2 h, where PEO N-12K showed significantly higher gel strength than PEO 301. This is primarily due to minimal swelling and increased erosion of the PEO N-12K compact at this time, which yields a thin gel layer around a fully hydrated core.

The higher resistance to penetration detected is a result of the probe hitting the core without encountering a substantial gel layer. In contrast, PEO 301 compacts at 2 h consist of a thick gel layer surrounding a partially hydrated core which continues to show significant swelling capacity and minimal erosion. The probe travels through this thick gel layer to the core, detecting a lower resistance to penetration. This is consistent with visual observations of swelling and erosion for PEO N-12K and PEO 301 compacts at this time point.

Figure 4. Representative force-displacement profile for METHOCEL™ K100M.

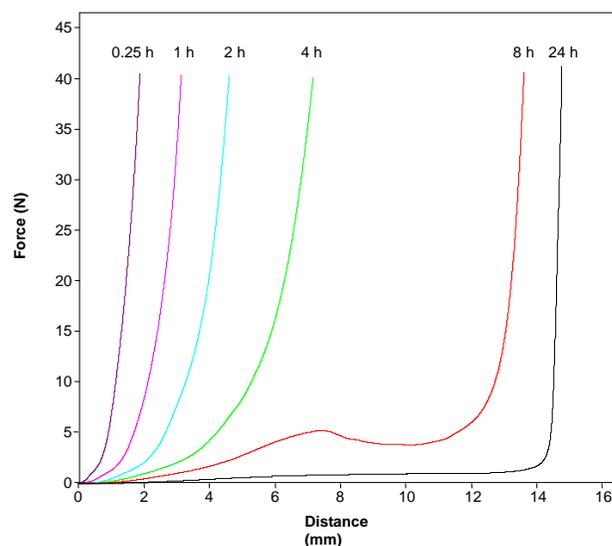
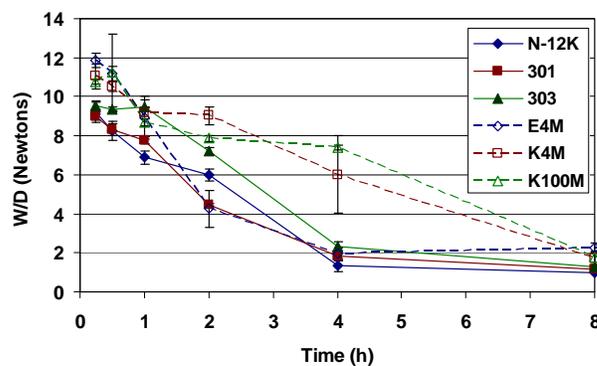


Figure 5. Gel strength for PEO and HPMC, as normalized by swollen tablet thickness.



For HPMC, gel strength was largely dependent on polymer substitution chemistry. Both K100M and K4M showed higher gel strength as compared to E4M. However, gel strength of K-chemistry HPMC was found to be less dependent on molecular weight. Neither K100M nor K4M showed a predominately high gel strength versus the other polymer up to 8 h. This is not surprising given the similar swelling and erosion results observed for both polymers in Figures 1 and 2.

Conclusions

This study found that high molecular weight PEO had a higher rate of hydration and swelled twice as much as HPMC. Swelling was determined to be dependent on both the type of polymer as well as molecular weight, whereas erosion was mainly dependent on molecular weight. HPMC (K-chemistry) provided stronger gel strength than PEO in the pure polymer compacts. Gel strength was found to be largely dependent on the polymer type, and the influence of molecular weight on gel strength was more evident for PEO than HPMC. Overall, the swelling, erosion, and gel strength properties of hydrophilic polymers should all be considered when formulating a matrix system for controlled release.

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