

# Evaluation and Comparison of Physicomechanical Characteristics of Gelatin and Hypromellose Capsules

**S. Missaghi and R. Fassihi**

Temple University, School of  
Pharmacy, Philadelphia, PA,  
USA

**ABSTRACT** The aim of this study is evaluation and comparison of physical and mechanical properties of hypromellose and gelatin capsules. For this purpose, the empty and filled capsules of hypromellose and gelatin (size 4) were examined in regard with their physical and mechanical characteristics, employing textural analysis, and disintegration properties in various immersion fluids, utilizing a USP 28 disintegration apparatus. The results demonstrated that owing to their greater water permeability, gelatin capsules disintegrate much faster than hypromellose shells in all tested media. However, hypromellose capsules showed a more uniform pattern of dispersion in the disintegration fluids. As for mechanical properties, at ambient conditions, gelatin capsules appeared to be harder and stronger with less elasticity as compared with hypromellose shells. On the contrary, at an elevated temperature, gelatin capsules demonstrated lower resilience. This study shows that hypromellose capsules have excellent properties and are promising as far as regulatory, manufacturing, religious, and dietary issues are concerned.

**KEYWORDS** Hypromellose capsules, Gelatin capsules, HPMC, Disintegration properties, Mechanical properties

## INTRODUCTION

Gelatin has a widespread use in pharmacy and has been used as a material of choice for hard capsules, mainly due to its relative ease of manufacturing. A solution of gelatin is able to form a gel just above ambient temperature conditions, and it further results in rapid formation of a homogeneous film which is an essential factor in the manufacturing process of capsules. However, gelatin presents certain problems and disadvantages. Gelatin is obtained through denaturation of collagen (Podczek & Jones, 2004). As an amphoteric substance, gelatin reacts with both acids and bases. Moreover, as a protein, gelatin exhibits chemical properties which are characteristic of such materials, for instance, gelatin may easily be hydrolyzed by most proteolytic systems to yield amino acid components. In addition, gelatin reacts with aldehydes and aldehydic sugars, anionic and cationic polymers, metal ions, electrolytes, plasticizers, and preservatives (Rowe et al., 2003). Moreover, the properties of gelatin change when

Address Correspondence to R. Fassihi,  
Ph.D. Temple University School of  
Pharmacy, 3307 North Broad Street,  
Philadelphia, PA 19140-0000, USA; Tel.:  
+1-215-707-7670; Fax: +1-215-707-  
3678; E-mail: reza.fassihi@temple.edu

subjected to  $\gamma$ -radiation (Fassihi & Parker, 1988). Upon exposure to severe storing conditions (40°C/ 75 %RH) for about 6 months, gelatin capsules undergo a cross-linking reaction which further reduces the solubility of the capsule shells and the dissolution rate of the active drug within them (Digenis et al., 1994; Podczec & Jones, 2004). In addition, the use of animal gelatin especially in the recent past has been associated with a number of technical, regulatory, commercial, and consumer concerns (Bowtle, 2002).

Thus, several new materials have been examined as possible substitutes for gelatin in manufacturing hard capsules, among which hypromellose, formerly regarded as hydroxypropyl methylcellulose (HPMC), has gained popularity and is commercially available worldwide from various capsule shell manufacturers, including Shionogi Qualicaps Co., Ltd. (Quali-V<sup>®</sup> Capsules), Capsugel Division of Pfizer Inc. (Vcaps<sup>®</sup> Capsules), and Natural Capsules Ltd. (Cellulose Capsules).

In oral products, hypromellose has been employed as a tablet binder in either wet or dry granulation processes. It also possesses film coating properties and has been utilized in various coating applications either from organic or aqueous compositions. Hypromellose can also be used in fabrication of hydrophilic matrix systems in order to prolong the drug release from tablets or capsules (Pillay and Fassihi, 2001; Rowe et al., 2003; Li et al., 2005).

As a raw material for capsule shells, hypromellose is chemically stable and compatible with most active drugs and a variety of solid, semi-solid, and liquid excipients. The only known incompatibility for hypromellose is the interaction with some oxidizing agents (Rowe et al., 2003). Under identical storing conditions, the moisture content of hypromellose capsules, 2–5%, is much lower than gelatin capsules, 13–15%, which makes them more suitable for water-sensitive drugs (Nagata, 2002; Quali-V<sup>®</sup> HPMC capsules, Technical Manual, 2004). Moreover, hypromellose shells maintain their mechanical integrity and remain elastic even under very low moisture conditions (Ogura et al., 1998). Additionally, since hypromellose is derived from non-animal sources and is non-toxic, it eliminates the issues pertaining to regulatory, religious, and vegetarian dietary restrictions.

In terms of biopharmaceutical properties of gelatin and hypromellose capsules, studies have been conducted to evaluate whether these capsules can be considered interchangeable. The overall conclusion was that, hypromellose could be regarded as a noteworthy alternative to gelatin (Ogura et al., 1998; Honkanen, 2004).

The objective of this study is twofold: (i) evaluation and comparison of physical and mechanical properties of hypromellose and gelatin capsules; (ii) investigation of inter-variability between the capsules for each type, since capsule shell morphology plays a critical role in the manufacture of reproducible products with desired attributes.

## EXPERIMENTAL

### Materials and Methods

The empty capsule shells of hypromellose (Quali-V, Shionogi Qualicaps Co., Ltd., Whitsett, NC) and gelatin (Coni-Snap, Capsugel Division of Pfizer Inc., Morris Plains, NJ) were obtained from the respective manufacturers. Both capsules were of size 4 and possessed a white color.

In order to investigate the characteristics of the capsules, both empty and filled capsule shells were examined. For this purpose, the capsule shells were manually filled with powdered cellulose (Arbocel P290, JRS Pharma LP, Patterson, NY), lubricated with 0.5% magnesium stearate. Arbocel P290 has an average particle size of 70  $\mu\text{m}$  and a bulk density of approximately 0.30 g/mL (Arbocel<sup>®</sup>, JRS Pharma website). Both empty and filled capsules were evaluated for physical characteristics, disintegration, and mechanical properties.

### Physical Characteristics

Hypromellose and gelatin capsules were tested as received with regard to weight variation and capsule dimensions. For each capsule type, 20 samples of empty and filled capsules were randomly selected and examined for weight variation, using an analytical balance (A&D Company, Ltd. Tokyo, Japan). The dimensions of these capsules (length, width, and body wall thickness) were also measured and recorded using a texture analyzer (TA.XT2i, Texture Technologies Corp, Scarsdale, NY/Stable MicroSystems, Godalming, Surrey, UK) which has accuracy and distance resolution of 2.5  $\mu\text{m}$ .

### Disintegration Properties

The filled capsules of hypromellose and gelatin were evaluated and compared in regard with the time required for capsule disintegration. As described in the

USP (USP, 2005), a disintegration apparatus (Erweka G.m.b.H., Heusenstamm, Germany) was utilized, with the basket-rack assembly, oscillating at a frequency rate of 30 cycles per minute. The capsules were tested in immersion fluids of different compositions at 37°C. The selected media were deionized water, hydrochloric acid solution (pH = 1.5), USP alkaline borate buffer (pH = 10.0), and two phosphate buffer systems (PBS) at pH = 6.8, potassium phosphate monobasic buffer (USP, 2005) and sodium phosphate monobasic buffer, which will be herein referred to as K-PBS and Na-PBS, respectively. As per the USP, the disintegration time is recorded as the time that “all of the capsules have disintegrated except for fragments from the capsule shell” (USP, 2005). The disintegration properties of at least six capsules were examined in this study.

## Mechanical Characterization of Capsules

In order to determine the mechanical properties of the empty and filled capsules, a texture analyzer, TA.XT2i, equipped with Texture Expert Exceed software (version 2.56) and a 5-kg load cell was employed. For this study, two flat-ended probes with the respective diameters of 2 and 10 mm were utilized. The probes were individually attached to the upper arm of the instrument. The individual capsule was placed on the lower stationary platform and positioned centrally under the probe (Fig. 1). The texture analyzer was programmed to measure force in the compression mode.

The probe was then advanced onto the capsule at the rate of 1 mm/s at various compressive strain values (%). The probe retraction rate was also set at 1 mm/s. The computer-generated force-displacement profiles for each capsule were used in obtaining various compressive properties as described in Appendix 1 and illustrated in Fig. 2. An average of at least six measurements was taken for each capsule. This study simulates the situation which may take place during the packaging and handling of capsules.

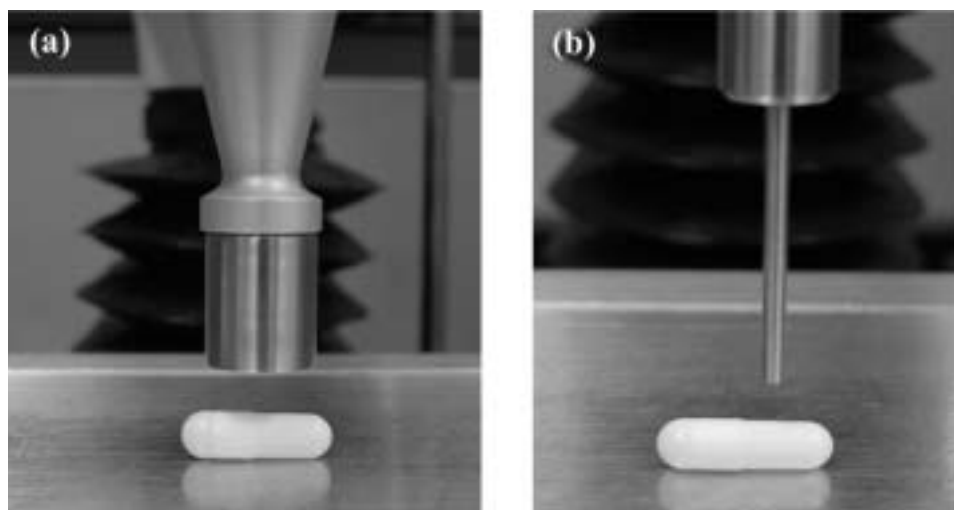
### *The Effect of Temperature on Mechanical Properties*

The empty shells of hypromellose and gelatin capsules were placed in an oven (Lab-Line/CS&E Imperial II, Chicago, IL) at 45°C for various periods of time. The capsules were removed from the oven at predetermined time intervals, 1, 24, and 72 hs and the effect of temperature on their mechanical properties was investigated using a 2-mm flat-ended probe. In addition, an average of 20 capsules were tested for a corresponding weight loss upon exposure to the elevated temperature of 45°C at each time point.

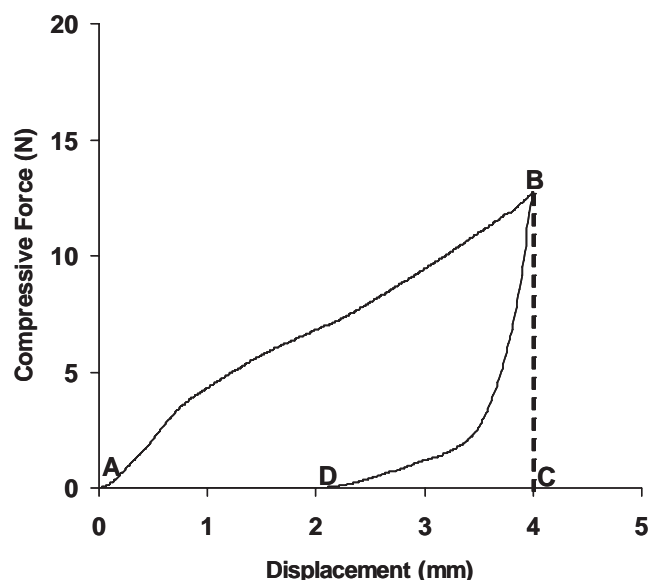
## RESULTS AND DISCUSSION

### Physical Characteristics

Table 1a outlines the physical characteristics of hypromellose and gelatin capsules. Both capsules were selected as size 4, and hence, for the most part, exhibited



**FIGURE 1** The Texture Analyzer Equipped with Flat-Ended Probes for Determining the Physicomechanical Properties of the Capsules (a) 10-mm probe; (b) 2-mm probe.



**FIGURE 2** Force-Displacement Profile of an Empty Capsule, Illustrating the Compressive Properties Which Can Be Obtained from the Curve (Area of ABC: Work of Compression; Area of BDC: Work of Recovery; Area of ABD: Net Work of Deformation; BDC/ABC: Ratio of Work of Recovery to Work of Compression; B: Maximum Force of Deformation).

comparable values. Overall, the inter-variability between gelatin and hypromellose capsules was less than 6%, when calculated for weight, length, and width of the capsules. However, the capsule body wall thickness showed an inter-variability of over 14%, which is significant (Table 1b). The importance of capsule wall thickness and its impact on various physico-mechanical properties between the two capsule types should be noted and will be discussed in a later section.

## Disintegration Properties

Table 2 demonstrates the disintegration time for the filled capsules of hypromellose and gelatin in different media. In all immersion fluids, gelatin shows a

much faster disintegration compared to hypromellose capsules. This is mainly due to the difference in water permeability of the capsules. Prior to disintegration, the capsule shells should absorb water and hydrate. In comparison to hypromellose, gelatin is more water permeable, which results in a more rapid disintegration of gelatin capsules and faster release of their contents (Nagata, 2002; Podcizek & Jones, 2004). As outlined in Table 2, pH and composition of the immersion fluids have an influence on the disintegration properties of the capsules. For instance, the disintegration time of gelatin capsules is the shortest in hydrochloric acid medium of pH = 1.5, which may be due to the greater solubility of gelatin at pH of 1.5, which is much less than its reported isoelectric point (~ 4.8) (Sheppard et al., 1942).

Hypromellose capsules, on the other hand, exhibit different disintegration properties, depending on the composition of the tested media. The longest disintegration time for hypromellose capsules was observed for K-PBS and borate buffer, which was recorded as 270.0 sec and 288.3 sec, respectively. This is due to the presence of potassium ions in these fluids that are known to enhance the gel strength of carrageenan within the hypromellose shells which will further delay capsule disruption and dissolution (Nagata & Tochio, 2002).

During the disintegration test, it was observed that hypromellose and gelatin capsules disrupt and dissolve in a different pattern. As cited, a longer lag time is associated with hypromellose capsule disruption as compared to gelatin. Following capsule disruption, all surfaces of the hypromellose shell disperse uniformly and expose its content to the medium. Gelatin capsules, however, for the most part, split along the domes of the cap and the body, forming a tube in the middle. Therefore, it takes longer for the fill material to be exposed to the immersion fluid. This may further

**TABLE 1A** Physical Properties of the Empty Shells and Filled Capsules of Hypromellose and Gelatin. Data Are Reported as Mean Value and Standard Deviation (n = 20)

|                                  | Empty capsules |               | Filled capsules |               |
|----------------------------------|----------------|---------------|-----------------|---------------|
|                                  | Hypromellose   | Gelatin       | Hypromellose    | Gelatin       |
| Weight (mg)                      | 36.38 ± 1.41   | 38.51 ± 0.78  | 147.49 ± 3.07   | 156.73 ± 3.72 |
| Length (mm)                      | 15.63 ± 0.054  | 16.19 ± 0.053 | 15.28 ± 0.23    | 16.20 ± 0.073 |
| Width (mm)                       | 5.02 ± 0.024   | 5.10 ± 0.013  | 5.07 ± 0.12     | 5.18 ± 0.093  |
| Capsule body wall thickness (mm) | 0.092 ± 0.006  | 0.107 ± 0.008 | –               | –             |

**TABLE 1B** The Inter-Variability (%) Between Gelatin and Hypromellose Capsules for Different Physical Properties

|                             | Empty capsules | Filled capsules |
|-----------------------------|----------------|-----------------|
| Weight                      | 5.53%          | 5.90%           |
| Length                      | 3.46%          | 5.68%           |
| Width                       | 1.57%          | 2.12%           |
| Capsule body wall thickness | 14.02%         | –               |

**TABLE 2** Disintegration Time (Seconds) For the Filled Capsules of Hypromellose and Gelatin in Selected Immersion Fluids. Data Are Reported as Mean Value and Standard Deviation (n = 6)

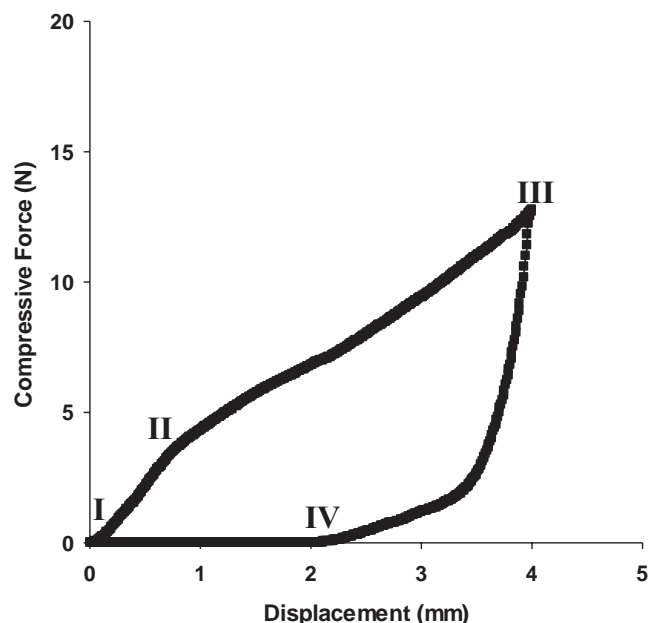
| Disintegration media        | Hypromellose capsules | Gelatin capsules |
|-----------------------------|-----------------------|------------------|
| Deionized water             | 154.0 ± 3.6           | 52.7 ± 2.5       |
| Hydrochloric acid, pH = 1.5 | 151.7 ± 16.8          | 34.0 ± 3.6       |
| K-PBS, pH = 6.8             | 270.0 ± 28.8          | 53.3 ± 6.6       |
| Na-PBS, pH = 6.8            | 179.7 ± 10.0          | 40.3 ± 4.5       |
| Borate buffer, pH = 10      | 288.3 ± 26.9          | 46.3 ± 5.0       |

lead to a faster release of the capsule content for hypromellose, as compared to gelatin, after the first capsule disruption takes places (Podczek & Jones, 2002).

## Mechanical Characterization of Capsules

In assessing the mechanical characteristics of the capsules two flat-ended probes were used. The 10-mm probe was employed to compress a larger area of the capsule, including cap, seal, and the body, while the 2-mm probe was utilized to apply the compression force only to a local point of the capsule.

Regardless of the type of the probe used in the study, the typical force-displacement profile for the capsules resembles a hysteresis loop, consisting of an initial linear portion followed by a non-linear curvature (Fig. 3). The former indicates that the deformation in this region is based on Hook's law; therefore, the applied compression force is directly proportional to the probe displacement. This portion of the profile represents the elastic deformation of the capsules, the slope of which is used in calculating the modulus of elasticity. The non-linear portion indicates that the specimen is plastically deforming under the applied compression load. Furthermore, at a lower depth of compression (up to about 20% of

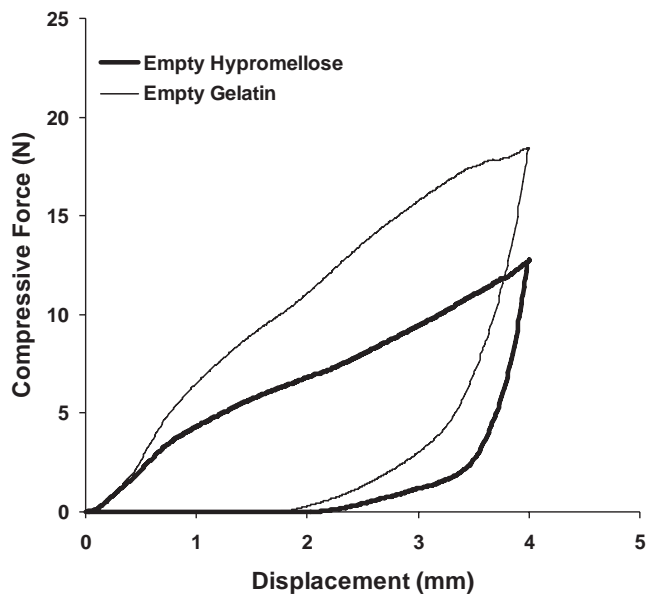


**FIGURE 3** Typical Force-Displacement Profile for an Empty Capsule of Hypromellose, Demonstrating Different Areas of Deformation When Compressed to the Depth of 4 mm (I-II: Elastic Deformation; II: Yield Point; II-III: Plastic Deformation; III-IV: Capsule Recovery).

the capsule width), the force-displacement profiles of the capsules exhibit a small hysteresis and the force values approach zero at the same time that the probe returns to its initial position. This indicates that the capsule deformation is mainly elastic and hence reversible. However, as the depth of probe penetration increases, the hysteresis becomes more intense with the unloading force values dropping to zero before the probe returns to its initial position. This is due to the contribution of plastic deformation (permanent) which starts to occur after the yield point is reached. The yield point corresponds to the maximum stress that the capsule can withstand without undergoing permanent deformation. Figure 3 demonstrates a typical hysteresis loop for a hypromellose empty capsule tested at the compression depth of 4 mm (equivalent of about 80% compressive strain).

Figures 4 and 5 depict the force-displacement profiles for the capsules at ambient conditions, using the 10-mm and 2-mm flat-ended probes, respectively. The 10-mm probe was employed for evaluation of the empty shells, and the 2-mm probe was used for both empty and filled capsules.

Table 3 lists various compressive properties of empty and filled capsules using the 10-mm probe.

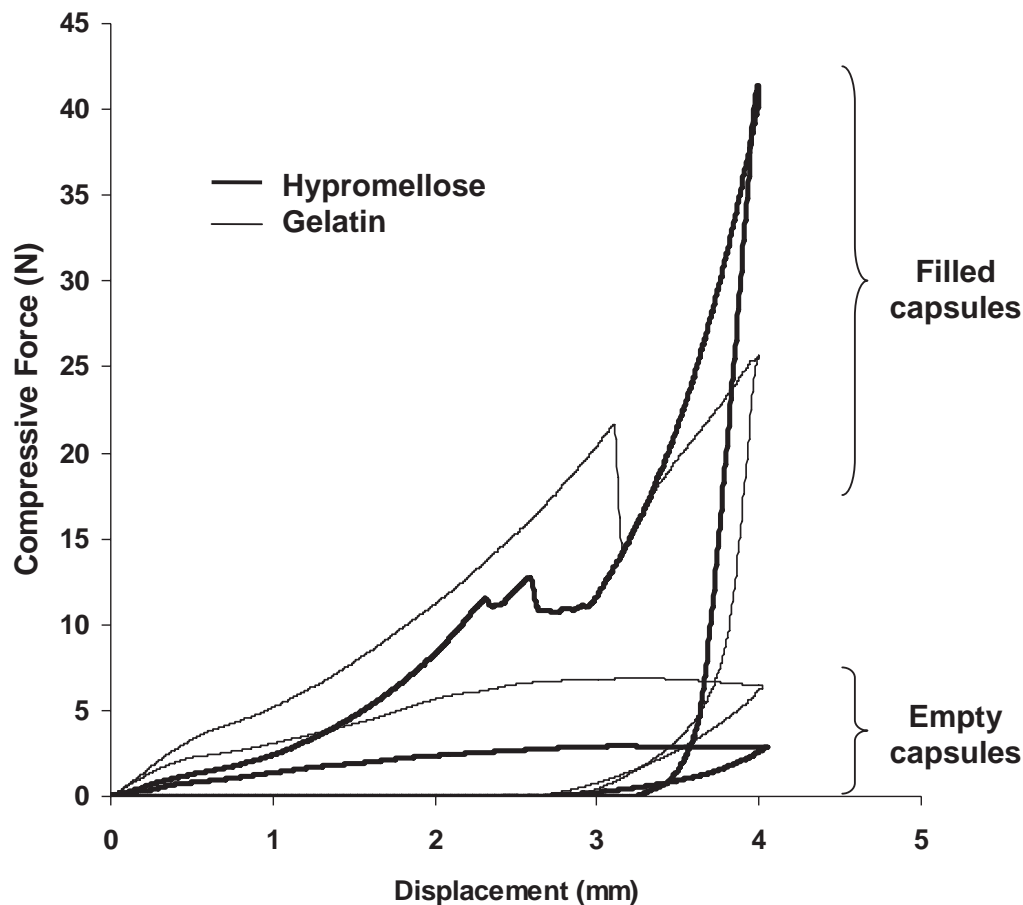


**FIGURE 4** Force-Displacement Profiles of the Capsules at Ambient Conditions Using the 10-mm probe.

Under the conditions of this study, none of the capsules (whether filled or empty) fractured while the test was performed using a 10-mm flat probe.

The compressive properties of different capsules, using a 2-mm flat-ended probe, are outlined in Table 4. The values were obtained at the same depth of compression (4 mm) for both empty and filled capsules. While the empty capsules of hypromellose fractured, the empty gelatin shells maintained their integrity under the same testing conditions. However, filled capsules of both hypromellose and gelatin fractured under the applied compression load, with gelatin exhibiting a greater extent of crack propagation to the capsule walls.

As demonstrated in Fig. 4 and 5 and Tables 3 and 4, when a larger surface of the capsule is subjected to compression, more resistance is developed against the probe advancement into the shell. Therefore, the compressive properties of greater values are obtained for the 10-mm probe as compared to the 2-mm when tested at similar compression depths and in the



**FIGURE 5** Force-Displacement Profiles of the Capsules at Ambient Conditions Using the 2-mm probe.

**TABLE 3** Comparison of Compressive Properties of Empty Capsules Using a 10-mm Flat-Ended Probe. Data Are Reported as Mean Value and Standard Deviation (n = 6) at the Compression Depth of 4 mm

| Compressive properties (10-mm probe) | Empty capsules |              |
|--------------------------------------|----------------|--------------|
|                                      | Hypromellose   | Gelatin      |
| Work of compression (N.mm)           | 26.81 ± 2.31   | 42.62 ± 1.58 |
| Work of recovery (N.mm)              | 4.77 ± 0.46    | 9.88 ± 0.23  |
| Work of recovery/Work of compression | 0.18 ± 0.002   | 0.23 ± 0.003 |
| Net work of deformation (N.mm)       | 22.04 ± 1.85   | 32.74 ± 1.35 |
| Maximum force of deformation (N)     | 12.75 ± 0.99   | 18.47 ± 0.46 |
| Elastic modulus (N/mm <sup>2</sup> ) | 4.70 ± 0.12    | 6.57 ± 0.20  |

absence of capsule fracture. Same situation applies upon comparison of empty and filled capsules, where the fill material within the capsules increases the capsule resistance and further leads to higher values of mechanical properties compared to the empty shells.

For further comparison both empty and filled capsules of hypromellose and gelatin were subjected to various compressive strains ranging from 10% to 90% of the capsule original (uncompressed) dimension. The test was performed at ambient conditions employing the 2-mm probe. It was, overall, concluded that an increase in the compression depth leads to an increase in the net work required for capsule deformation and a decrease in the ratio of work of recovery to work of compression prior to the point of fracture. This is mainly due to the progressive contribution of plastic deformation as the depth of compression is increased

which, in turn, leads to a lesser degree of recovery upon removal of the loading force (Figs. 6 and 7).

The point of fracture at ambient condition was recorded as about 60% compressive strain for hypromellose empty capsules, and as 50% and 60% for filled hypromellose and gelatin capsules, respectively. The empty gelatin capsules did not fracture under these conditions.

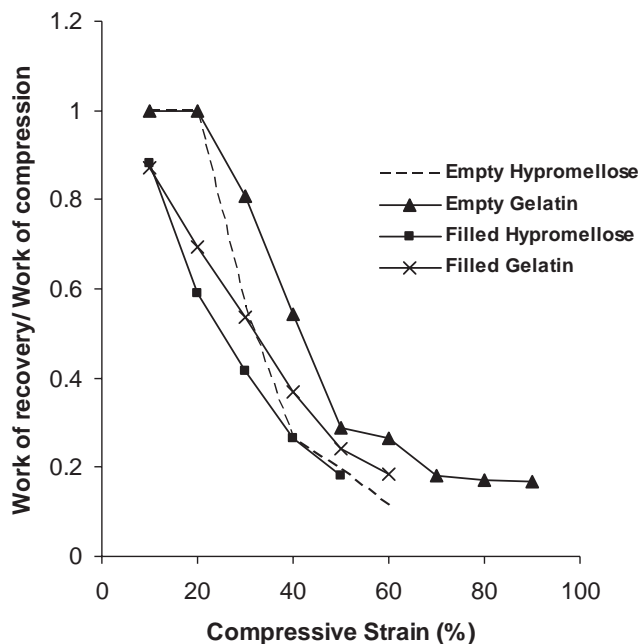
Based on the obtained results of this study, it appears that when tested at ambient conditions, the capsules of gelatin seem to be harder than those of hypromellose, owing to the higher elastic modulus of gelatin shells. Additionally, when held in hand, hypromellose capsules feel softer and more flexible as compared to gelatin shells. Upon comparison of the net work of deformation, it seems that due to their greater values, gelatin capsules can be considered tougher than those of hypromellose. Therefore, gelatin capsules are capable of absorbing more energy prior to their fracture. Furthermore, gelatin capsules are stronger than those of hypromellose, since they exhibit a greater value of compressive strength under the same testing conditions. Gelatin capsules may owe their mechanical properties to their reportedly higher water content compared to hypromellose shells which renders the capsule shells more viscoelastic. In addition, gelatin capsules possess a greater wall thickness in comparison to hypromellose (0.107 mm and 0.092 mm, respectively), which may further contribute to the observed characteristics of the capsule shells.

In order to remove the free and/or unbound water from the matrix of the capsule shells, an elevated temperature of 45°C appeared to be more effective and non-destructive to the capsules. When the empty

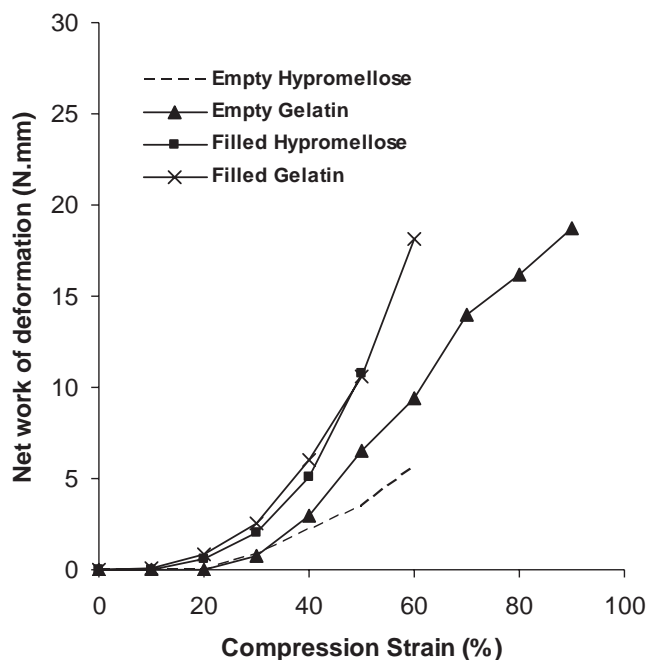
**TABLE 4** Comparison of Compressive Properties of Empty and Filled Capsules Using a 2-mm Flat-Ended Probe. Data Are Reported as Mean Value and Standard Deviation (n = 6) at the Compression Depth of 4 mm For All Capsules (– = Not Applicable Due to Capsule Fracture; § = Not Obtained Since Empty Capsules of Gelatin Did Not Fracture)

| Compressive properties (2-mm probe)       | Empty capsules |              | Filled capsules |              |
|---|----------------|--------------|-----------------|--------------|
|   | Hypromellose   | Gelatin      | Hypromellose    | Gelatin      |
| Work of compression (N . mm)              | –              | 19.52 ± 1.62 | –               | –            |
| Work of recovery (N . mm)                 | –              | 3.31 ± 0.40  | –               | –            |
| Work of recovery/Work of compression      | –              | 0.17 ± 0.002 | –               | –            |
| Net work of deformation (N . mm)          | –              | 16.20 ± 0.89 | –               | –            |
| Maximum force of deformation (N)          | –              | 6.87 ± 0.17  | –               | –            |
| Elastic modulus (N/mm <sup>2</sup> )      | 1.57 ± 0.14    | 4.16 ± 0.23  | 2.89 ± 0.51     | 6.04 ± 0.70  |
| Compressive Strength (N/mm <sup>2</sup> ) | 2.95 ± 0.22    | §            | 11.99 ± 0.56    | 20.14 ± 1.10 |
| Work of failure (N . mm)                  | 5.921 ± 0.18   | §            | 9.47 ± 0.28     | 27.18 ± 0.94 |



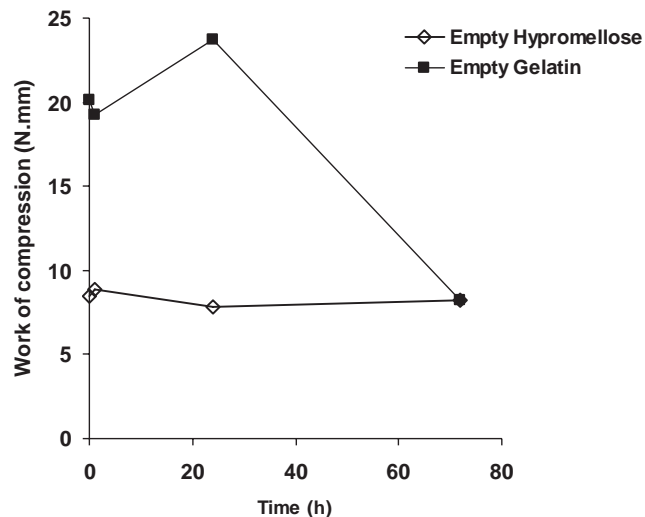


**FIGURE 6** Comparison of the Ratio of Work of Recovery to Work of Compression Against Compressive Strain for Different Capsules as Obtained Using the 2-mm Flat Probe. Each Data Point Represents an Average of Six Measurements.



**FIGURE 7** Comparison of Net Work of Deformation Against Compressive Strain for Different Capsules as Obtained Using the 2-mm Flat Probe. Each Data Point Represents an Average of Six Measurements.

capsules were exposed to this temperature, the compressive properties of gelatin capsules were affected to a greater degree compared to those of hypromellose



**FIGURE 8** Comparison of Work of Compression Versus Time for Hypromellose and Gelatin Capsules at the Compression Depth of 4 mm When Exposed to the Elevated Temperature of 45°C.

shells. As demonstrated in Fig. 8, at a high temperature, gelatin shells show a more erratic pattern for the work of compression with the passing of time. At 72 hs, when subjected to compression testing, the empty gelatin capsules fractured significantly at the compression depth of 4 mm, causing a marked decrease in the work of compression (Fig. 8). However, gelatin capsules did not exhibit any sign of fracture at earlier time points. Hypromellose shells, on the other hand, fractured at all time points consistent to their behavior at ambient conditions.

In another experiment, the weight reduction of capsule shells upon exposure to 45°C at different time points was determined and compared to their initial weight prior to placing them in the oven (Table 5). The results show that longer exposure to the elevated temperature results in the moisture loss from the capsule shells with a more marked effect on gelatin shells (21.99% versus 3.62% for gelatin and hypromellose at 72 hs, respectively). This may further reduce the plasticity of gelatin capsules and render them more brittle as compared to hypromellose shells.

Another parameter in comparison between hypromellose and gelatin capsules is resistance to crack propagation. Upon fracture at certain compression depth, gelatin capsules exhibit a greater tendency of crack propagation as compared to hypromellose capsules. This effect is more pronounced when the capsules are exposed to the elevated temperature of



**TABLE 5** Extent of Weight Reduction For Empty Shells of Hypromellose and Gelatin, Compared to Their Initial Weight, Upon Exposure to 45°C For Different Time Periods. Data Are Reported as Mean Value and Standard Deviation (n = 20)

| Exposure time to 45°C (h) | Weight reduction (%)  |                  |
|---------------------------|-----------------------|------------------|
|                           | Hypromellose capsules | Gelatin capsules |
| 1                         | 2.80 ± 0.22           | 5.92 ± 0.47      |
| 24                        | 2.97 ± 0.27           | 7.55 ± 0.85      |
| 72                        | 3.62 ± 0.32           | 21.99 ± 2.97     |

45°C which can be attributed to the brittleness of gelatin capsules at higher temperatures.

## CONCLUSIONS

Comparison of gelatin and hypromellose capsules in this work demonstrated the key differences in their disintegration and physicomechanical properties. Gelatin capsules demonstrated a faster disintegration in all tested immersion fluids, whereas hypromellose exhibited a more uniform pattern of capsule dispersion within the tested media. It is expected that the formulation of the fill material will also influence the disintegration properties of the capsules.

As for their mechanical properties, upon comparing hypromellose and gelatin capsules, as supplied by the manufacturers, at ambient conditions, gelatin shells are harder, stronger, and less elastic compared to hypromellose capsules. When exposed to the stress conditions, the elevated temperature of 45°C, gelatin shells lose their mechanical properties more significantly and become brittle relative to hypromellose capsules. In general, hypromellose capsules may

be considered as a promising alternative to gelatin shells, with potentials for greater acceptability by manufacturers, regulatory organizations, and consumers.

## REFERENCES

- Bolton, W. (1998). *Materials for Engineering*. Oxford: Butterworth-Heinemann.
- Digenis, G. A., Gold, T. B., & Shah, V. P. (1994). Cross-linking of gelatin capsules and its relevance to their in vitro – in vivo performance. *J. Pharm. Sci.*, 83, 915–921.
- Fassihi, A. R., & Parker, M. S. (1988). Influence of gamma radiation on the gel rigidity index and binding capability of gelatin. *J. Pharm. Sci.*, 7 (10) 876–879.
- Honkanen, O. (2004). Biopharmaceutical Evaluation of Orally and Rectally Administered Hard Hydroxypropyl Methylcellulose Capsules. Ph.D. Dissertation, University of Helsinki, Helsinki, Finland.
- Li, C. L., Martini, L. G., Ford, J. L., & Roberts, M. (2005). The use of hypromellose in oral drug delivery. *J. Pharm. Pharmacol.*, 57, 5, 533–546.
- Nagata, S. (2002). Advantages to HPMC Capsules: A New Generation. *Drug Deliv. Technol.*, 2 (2), 34–39.
- Nagata, S., & Tochio, S. (2002). The influence of the composition of the test fluids on dissolution from HPMC capsules, Poster Presentation. AAPS annual meeting and exposition.
- Ogura, T., Furuya, Y., & Matsuura, S. (1998). HPMC capsules – an alternative to gelatin. *Pharm. Technol. Eur.*, 11, 32–42.
- Pillay, V., & Fassihi, R. (2001). Probing the dynamics of matrix hydration in the presence of electrolytes. *Drug Deliv.*, 8 (2) 87–92.
- Podczek, F., & Jones, B. E. (2004). *Pharmaceutical Capsules* London: Pharmaceutical Press.
- Podczek, F., & Jones, B. E. (2002). The in vitro dissolution of theophylline from different types of hard shell capsules. *Drug. Dev. Ind. Pharm.*, 28, 1163–1169.
- Rowe, R. C., Sheskey, P. S., & Weller, P. J. (2003). *Handbook of Pharmaceutical Excipients*. London: Pharmaceutical Press.
- Sheppard, S. E., Houck, R. C., & Dittmar, C. (1942). The Sorption of Soluble Dyes by Gelatin. *J. Phys. Chem.*, 46, 158–176.
- USP 28/ NF 23. (2005). United States Pharmacopoeial Convention, Inc.: Rockville, MD.
- Online Sources available as of January 2006**
- Arbocel®, <http://www.jrspharma.com/> (2005). JRS Pharma LP.
- Bowtle, W. (2002). Options in materials for liquid-filled capsules. *Pharmaceutical Manufacturing and Packing Sourcer*, <http://www.samedanltd.com/>
- Quali-V® HPMC capsules, Technical Manual (2004). Shionogi Qualicaps, Inc. <http://www.qualicaps.com/>

## APPENDIX 1

**Work of compression** represents the extent of capsule deformation under the compression load and is obtained via calculating the area under the loading curve (loading AUC) (Fig. 2).

**Work of recovery** is the extent to which the capsule is recovering upon removal of the compression load. It is obtained through the decompression force sensed by the probe during retraction and is represented as the area under the unloading curve (unloading AUC) (Fig. 2).

**Net work of deformation** is the area of the hysteresis loop formed in the force-displacement profile of each capsule. It can be calculated via subtraction of unloading AUC from loading AUC (Fig. 2).

The ratio of **work of recovery to work of compression** is obtained via dividing the unloading AUC by the loading AUC. This ratio may assume a range of values between 0–1, with 0, meaning no recovery and 1, indicating a full recovery of the capsule (Fig. 2).

**Maximum force of deformation** represents the greatest value of compression force on the respective force-displacement profile of the capsule. This value is usually encountered at the predetermined depth of compression; however, depending on the deformation pattern of the material, it may be sensed prior to achievement of the maximum depth. This value is

particularly useful when the capsule deforms but does not fracture under the designed test conditions (Fig. 2).

**Elastic modulus** is an indication of the elasticity of capsules and can be obtained via compression stress divided by the corresponding compressive strain value (Bolton, 1998). Compression stress, in turn, is calculated by dividing the compression force by the initial cross-sectional area of the capsule under compression. The elastic modulus can also be obtained as the slope of the linear portion of the stress-strain curve for each capsule. The higher the elastic modulus, the lower is the elasticity of the capsule.

**Compressive strength** of the capsule is defined as the maximum stress that the shell wall can withstand under compression without fracturing (Bolton, 1998).

**Work of failure** is defined as the work required for the capsule to fracture and hence is an indication of capsule toughness. A greater value for work of failure indicates that the capsule is capable of absorbing more energy prior to its failure. This value is obtained from the area under the force-displacement curve to the point that the capsule fractures (Bolton, 1998).

**Compressive strain** is obtained via dividing the change in the dimension of the capsule by its original dimension when the capsule is subjected to compressive forces. Since compressive strain is a ratio, it has no units and is often expressed as a percentage (Bolton, 1998).

Copyright of Drug Development & Industrial Pharmacy is the property of Taylor & Francis Ltd and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.