# Poly(Dimethylsiloxane) Coatings for Controlled Drug Release. III. Drug Release Profiles and Swelling Properties of the Free-Standing Films

**Zongming Gao,[1] Julia Schulze Nahrup,[2] James E. Mark,[1] Adel Sakr[2]**

[1]*Department of Chemistry and the Polymer Research Center, University of Cincinnati, Cincinnati, OH 45221*
[2]*Industrial Pharmacy Program, College of Pharmacy, University of Cincinnati, Cincinnati, OH 45267*

Received 3 May 2004; accepted 26 July 2004
DOI 10.1002/app.21469
Published online in Wiley InterScience (www.interscience.wiley.com).

**ABSTRACT:** Previous reports in this series have described the preparation of stable poly(dimethylsiloxane) (PDMS) latices suitable for spray-coating of drug tablets, as well as the mechanism of associated crosslinking reactions in PDMS emulsions. In the present investigation, *in vitro* evaluations were performed to study the effects of the amount of channeling agents, the addition of colloidal silica, and the pH of the dissolution media used. The study involved hydrochlorothiazide (as a marker drug) released from compressed tablets, which had been spray coated using PDMS latices with various polyethylene glycol (PEG) loadings as channeling agents. The dissolution results showed that coated tablets containing up to 25% (w/w dps) PEG could have constant release rates. Higher amounts of PEG resulted in nonlinear release patterns. The addition of colloidal silica decreased the rates of drug release. The pH of dissolution media affected the structures of the exposed PDMS films. Swelling tests were carried out to determine water uptake. Scanning electron microscopy and density measurements showed that the films obtained after soaking in higher-pH media were more condensed, with corresponding changes in drug-release rates. © 2005 Wiley Periodicals, Inc. J Appl Polym Sci 96: 494–501, 2005

**Key words:** silicones; latices; drug release; swelling

## INTRODUCTION

Studies of polysiloxane ("silicone") elastomers for biomedical applications have been carried out for many years now.[1] Such elastomers have been extensively used in the fabrication of prostheses, artificial organs, dental materials, and surgical devices, largely because of their biostability, noncarcinogenicity, nontoxicity, and biocompatibility.[2,3]

With regard specifically to tablet film coatings for controlled drug release, the first report was by Tan et al., who used coating solutions based on an organic solvent.[4] Subsequently, the formulation of aqueous-based silicone elastomers for this purpose was patented by Dow Corning.[5,6] In related work, water-based silicone coating systems were used to prepare tablet coatings for drug release by Li and Peck as well as Dahl and Sue.[7–11] They used a specific formulation of crosslinked, hydroxyl-terminated poly(dimethylsiloxane) (PDMS) with the addition of colloidal silica and different molecular weight polyethylene glycols (PEG) as channeling agents to control drug release from pharmaceutical solid oral dosage forms. Drug-release mechanisms were proposed as well. Because of the poor mechanical strength of PDMS free film obtained, it was necessary to add a large amount of colloidal silica to the polymer dispersion before the coating process. This increased the solid content in the dispersion, complicated the spray coating procedure, and decreased the stability of the coating dispersion.

Our previous reports described a new method for preparing an aqueous-based PDMS latex, and proposed a crosslinking mechanism for the polymer.[12,13] Some modifications of PDMS coating materials were also performed, and their effects on drug release were described.[14,15] In the present report, the effect of varying amounts of PEG (weight-average molecular weight $M_w$ of 8000 g/mol) in those PDMS latices was studied as it was used to control drug release from pharmaceutical solid oral dosage forms. *In vitro* evaluations were performed under various pH media to obtain drug release profiles, with documentation of the effects of addition of colloidal silica to the latices. Finally, free-standing PDMS films were characterized with regard to their swelling properties, density changes, and microstructures, and the results related to drug-delivery profiles.

*Correspondence to:* J. E. Mark (markje@email.uc.edu).
Contract grant sponsor: National Science Foundation; contract grant number: Grant DMR-0314760 (Polymers Program, Division of Materials Research)

**TABLE I**
**Composition of Uncoated Tablet Cores**

| Ingredient | Weight (mg/tablet) |
|---|---|
| Hydrochlorothiazide | 10.00 |
| Lactose | 118.75 |
| Microcrystalline cellulose | 118.75 |
| Silicone dioxide | 1.25 |
| Magnesium stearate | 1.25 |
| Total | 250.00 |

## EXPERIMENTAL

The coating material was the PDMS emulsion from the same source as used previously, and the same procedures were employed.[12] Tetraethylorthosilicate (TEOS, from Aldrich, St. Louis, MO) and 3-(2,3-epoxypropoxy)propyl-trimethoxysilane (SIG-5840, from Gelest Inc., Tullytown, PA) were used (as received) for crosslinking in a 1 : 1 ratio. Polyethylene glycol (PEG, $M_w$ 8000, from Aldrich, St. Louis, MO) was used as a channeling agent, and was dissolved in the PDMS latex directly prior to coating procedures.

The marker drug in the compressed tablet was hydrochlorothiazide (Changzhou Benchi Pharmaceutical Co. Ltd., Changzhou, China). The manufacture of the tablet core, the characterizations of the core tablet, and the coating process have been described elsewhere.[14] The composition of the tablet core and coating formulations and parameters are listed in Tables I and II, and the final coating weight was kept at 5% (w/w) of the core tablet.

Drug release analyses of the coated tablets were performed using a USP XXVI-dissolution apparatus 2 (paddle type) at 50 rpm. Standard vessels were filled with heated media at 37°C. The tablets were tested for 2 h in 750 mL 0.1*N* HCl (pH 1.2), followed by 22 h in USP-phosphate pH 6.8 buffer. The basic media was prepared by addition of 250 mL 0.2 M tribasic sodium phosphate solution to the acidic media, as described in USP XXVI. To study the effect of dissolution media pH on drug release, analyses were performed for 24 h in 1000 mL of 0.1*N* HCl and phosphate buffer, respectively. Samples of 10 mL each were taken at 1, 2, 3, 4, 6, 8, 12, and 24 h, or until drug release was complete (100%). Replacement with 10 mL of media was performed at each sample point. Drug release of the filtered samples was determined by UV measurements at 271 nm. Standards for each media, representing 100% drug release, were read before and after the sample readings for system suitability and drug release calculations. Dissolution profiles were based on analyses of an average of 6 tablets.

For the swelling tests, cast PDMS films were cut to make samples with rectangle shapes and weights of around 0.1 g. The samples were weighed and then immersed in water, and the swelling kinetics followed at constant temperature by removing the samples from the water at certain times, blotting them with general filter paper, and weighing them. The amount of water uptake ($U_A$) and speed of water uptake ($U_S$) by the samples were calculated from following equations.

$$U_A = \frac{w_t - w_0}{w_0} \quad (1)$$

$$U_S = \frac{w_t - w_0}{t} \quad (2)$$

Here, $w_t$ and $w_0$ represent the weights of the sample at swelling times t and 0 during the measurements.

Film morphologies before and after swelling were determined by scanning electron microscopy (SEM), using a Philips XL30 ESEM microscope. Density determinations were performed using standard equipment (Micromeritics AccuPyc 1330, Norcross, GA) with compressed helium at an outlet pressure of 20 psi.

## RESULTS AND DISCUSSION

### In vitro evaluation for 2 h at pH 1.2 followed by 22 h in pH 6.8 buffer

Figure 1 shows the drug release profiles in 0.1*N* HCl for 2 h followed by pH 6.8 buffer for 22 h. The core tablet (without PDMS film coating) showed 100% release in 7 h. However, there was no drug release in 24 h if only PDMS was used as film coating without the addition of channeling agents. Since the PDMS film was highly hydrophobic, it would prevent water absorption if there were no channeling agents present. This explains why there was no drug release from core tablets coated only with PDMS.

The addition of PEG, however, showed significant effects on drug release, as is also shown in Figure 1.

**TABLE II**
**Coating Formulations and Parameters**

| Substance | Weight (g) |
|---|---|
| PDMS-dispersion (30.0% PDMS) | 30.0 |
| Water, deionized | 15.0/17.8/22.3 |
| Colloidal silica | 0.0/0.9/2.3 |
| **Coating parameter** | **Value** |
| Batch size | 50 g |
| Solid content, coating formulation | 23% |
| Tablet bed temperature | 50 °C |
| Atomizing air pressure | 2.5 kgf/cm$^2$ |
| Pan speed | 20 rpm |
| Preheating of cores | 5 min |
| Spray rate (2 s duration every 15 s) | 0.33 g/min |

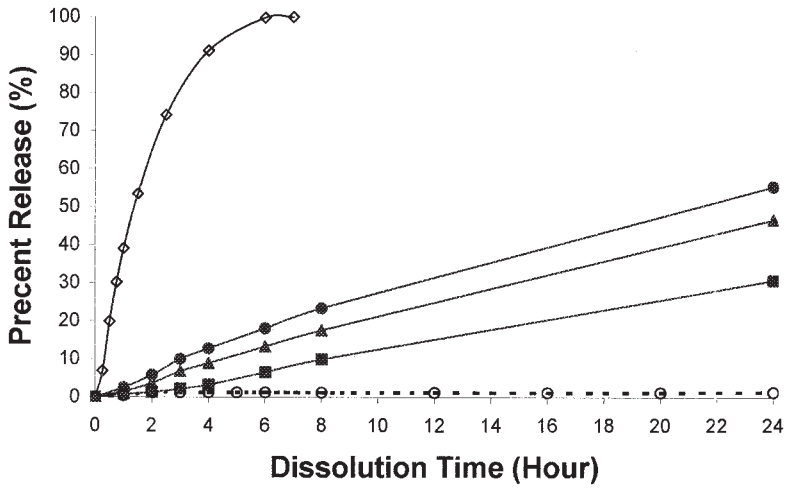


**Figure 1** Effect of PEG amount on drug release at pH 1.2 for 2 h followed by pH 6.8 for 22 h. Key: (□) core tablet; (○) coated only with PDMS; (■) 10%, (▲) 25%, and (●) 50% PEG loadings in PDMS films.

Three different PEG loadings (10, 25, and 50% w/w dps) were studied for these drug release profiles. The results clearly indicated that increasing the amount of channeling agent resulted in increasing the total amount and rate at which the drug was released. The release rates for 10 and 25% (w/w dps) PEG loadings in 24 h showed a linear relationship ($R^2 > 0.99$). The slope of the release profile represented the zero order release rate of the drug from the coated tablets at steady state conditions. Table III shows the effects of PEG loadings in the PDMS coatings on the drug release rates and amounts of drug released in 24 h. It was also indicated that the release was far below 100% in 24 h for the three PEG loadings. The 100% drug controlled release in 24 h could be achieved by modifying the structure of crosslinked PDMS coating or changing the recipe of the core tablet, which will be attempted in some of our future studies.

At 50% PEG loading, however, a nonlinear release profile was obtained, with 56% of the drug released in 24 h and 100% of the drug released in 72 h, as shown in Figure 2. The rate of release decreased gradually from 2.43%/h in the first 24 h to about 0.86%/h in the last 24 h. There may be two reasons for this rate decrease.

According to Li and Peck's study,[9] the incorporation of PEG in silicone elastomers enhanced the release of hydrophilic compounds, which was attributed to the osmotic effect developed by the uptake of water in the polymer matrix. The release of the drug was achieved by a transpore diffusion and an osmotic pumping effect. At low PEG loadings (fewer channels), the release of the drug was controlled by two mechanisms. At high PEG loading levels, the transpore diffusion became the dominant mechanism since more and larger channels were produced.

One possible explanation for the rate decrease observed in this study involves a two-step release mechanism. When a coated tablet was put into the water, channels in PDMS films were presumably produced by the leaching of the PEGs almost immediately. The dissolution of soluble compounds inside the tablet would then build up an osmotic pressure. At the same time, diffusion of the soluble drug would occur as well. The driving force for transportation of the drug would be both the effects of osmotic pressure and diffusion, which would provide a faster release. With continuous PEG leaching, more and larger channels would appear. The pressure buildup within the tablet core would be relieved by the flow of soluble compounds through the pores out of the tablet. The diffusion would become the main driving force for drug release, and the release rate would gradually decrease. In the last 24 h, the drug concentration was found to

**TABLE III**
**Colloidal Silica Effects on Drug Release**

| | Without colloidal silica | | | With colloidal silica | | |
|---|---|---|---|---|---|---|
| PEG (%) | 24 hr release (%) | Release rate (%/hr) | Linearity $R^2$ | 24 hr release (%) | Release rate (%/hr) | Linearity $R^2$ |
| 10 | 30.7 | 1.24 | 0.99 | 20.6 | 0.84 | 0.99 |
| 25 | 46.6 | 1.99 | 0.99 | 27.5 | 1.12 | 0.99 |
| 50 | 55.3 | 2.43 | 0.98 | 43.7 | 1.84 | 0.99 |

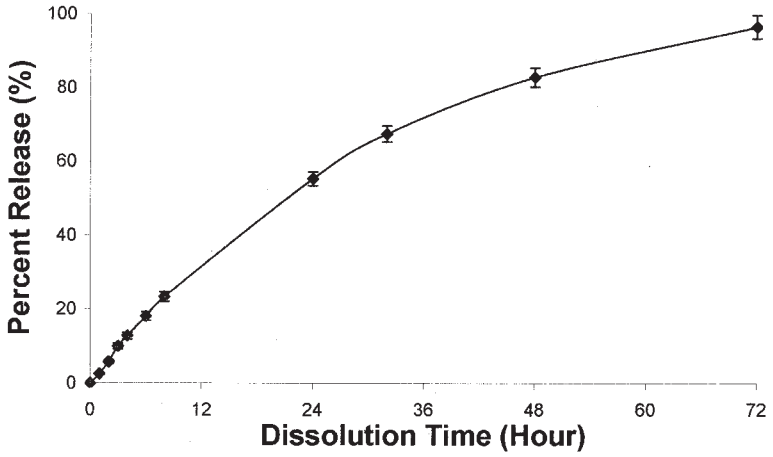


**Figure 2** Sustained drug release by PDMS film coating with 50% PEG loading at pH 1.2 for 2 h followed by pH 6.8 for 70 h.

be about 20% of the original concentration, and the average release rate was about one third of the one in the first 24 h.

A second reason for the reduced drug release was probably the effect of the pH media that the PDMS coating was exposed to. A more condensed film structure would be obtained in the pH 6.8 buffer, which would reduce drug release. The pH effects on film structure are described in the following section.

### pH effects on drug release

To study the effects of pH on controlled drug release, dissolution tests were performed in acid (pH 1.2) and phosphate buffer (pH 6.8) separately, with the results shown in Figure 3. Coated tablets with PEG loadings of 10% (open squares) and 25% (open triangles) were studied. When dissolution tests were in the pH 6.8 buffer, the drug releases after 24 h were about 4 and 19% for 10 and 25% PEG loaded samples, respectively (dotted lines in Fig. 3). The same tests in pH 1.2 media, after 24 h, however, gave about 36 and 52% drug release from coated tablets with 10 and 25% PEG loadings, respectively (dashed and dotted lines in Fig. 3). The results showed that there was a faster release rate and a larger amount of drug released if the coated tablets were exposed to acidic conditions.

For comparison, the results of dissolution tests for 2 h at pH 1.2 solution followed by 22 h at pH 6.8 buffer are also shown (solid lines) in Figure 3. If compared with dissolution tests only under acidic conditions, it is clear that there were similar release profiles until about 8 h, although the tablet samples were under acidic conditions for only 2 h, then the release rates decreased.[15] Compared with dissolution tests only at pH 6.8, the tests at pH 1.2 for 2 h followed by pH 6.8 for 22 h showed higher release rates and maximum amounts of the drug released, even though the samples were at pH 6.8 for 22 h. This indicated that the drug release could be accelerated under acidic conditions.

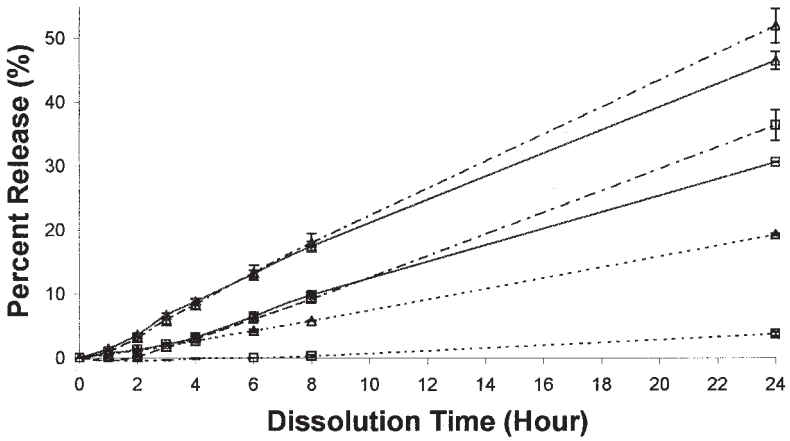


**Figure 3** Effects of various pH dissolution media (pH 1.2 and pH 6.8) on drug release. Key: (□) 10% PEG; (Δ)25% PEG; (—) at pH 1.2 for 2 h followed by pH 6.8 for 22 h; (- -) at pH 1.2 for 24 h; (· · · · · ) at pH 6.8 for 24 h.

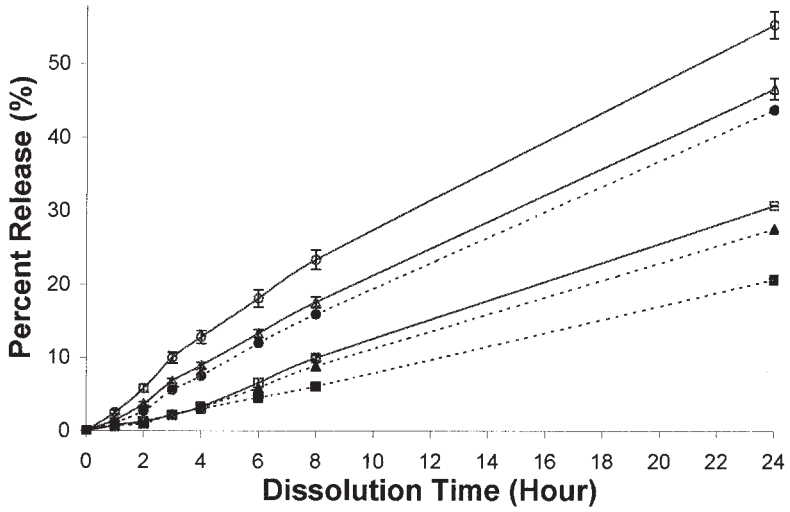


**Figure 4** Effects of colloidal silica on drug release at pH 1.2 for 2 h followed by pH 6.8 for 22 h. Key: (□) 10%, (Δ)25%, (○) 50% PEG loadings without silica; (■) 10%, (▲) 25%, (●) 50% PEG loadings with 10% silica.

Since the solubilities of the hydrochlorothiazide (pKa: 7.9 and 9.2) and lactose (component of core tablet) do not change in aqueous media between pH 1 to pH 8, the buildup of osmotic pressure and transpore diffusion are expected to have similar effects on drug release over the studied pH range. The observed differences of drug release from coated tablets in various pH media may be attributed to the effect of pH values on the structure of the PDMS coatings. This effect was analyzed using free-standing films and is discussed below.

### Colloidal silica effects on drug release

In previous studies, colloidal silica had been used to improve the mechanical properties and decrease the tackiness of the coating.[7–11] The comparison of dissolution results of coated tablets with and without colloidal silica in the PDMS film coating are shown in Figure 4. The tests were performed under 2 h in pH 1.2 followed by 22 h in the pH 6.8 buffer. Three PEG loadings (10, 25. and 50% w/w dps) were studied. The solid lines with open patterns stand for the samples without colloidal silica, and the dotted lines with solid patterns stand for the samples with 10% (w/w dps) colloidal silica in the PDMS coating.

At each PEG loading, there was a higher release rate and maximum amount of drug released after 24 h for the coated tablets without colloidal silica. The specific values are listed in Table III. The drug release at 50% PEG loading with 10% silica addition was lower than that through 25% PEG loading without silica. Similarly, the release from 25% PEG loading with 10% silica was lower than that of 10% PEG loading without silica. Since colloidal silica is expected to interact with PDMS to make the network have a higher crosslink density, the addition of colloidal silica could thus produce more condensed film structure compared with the film without silica. That is also the reason why improved mechanical properties of the PDMS coating were observed after addition of colloidal silica. Furthermore, the colloidal silica could block some channels produced by the leaching of the PEG. Even at the same PEG loading level in the film, the silica particles could make the size of channels decrease to prevent the drug from releasing. That was probably the reason why the drug release through 50% PEG loading with the silica film was even lower than that for the 25% PEG loading without silica. However, for coated tablets with or without silica alone, the more channeling agents, the faster the drug released through the film. This indicated that the channeling agent was a key factor in controlling drug release through PDMS film coatings.

### Swelling properties of cast PDMS films

To study the effects of PDMS films on drug release in different pH media, swelling tests of PDMS free films with 10% PEG loading in pH 1.2 and pH 6.8 were performed. Figures 5 and 6 show the water uptake and the speed of water uptake of free films in pH 1.2 and pH 6.8 media, respectively. It was clearly indicated that as a function of swelling time, the water uptake increased at the beginning for the films in both pH media. However, the amount of water uptake by films soaked in the pH 6.8 media was greater and the speed of water uptake was faster as well. The speed of water uptake reached its maximum in less than 15 min.

With PEG as channeling agents in the PDMS films, Li and Peck studied the leaching of PEG and film

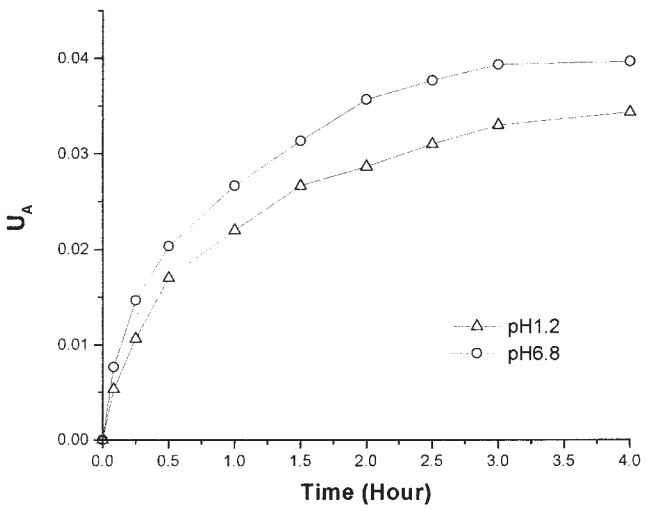


**Figure 5** The amount of water uptake of PDMS free films with 10% PEG loading swelled in various pH media.

swelling in deionized water. They pointed out that the water uptake by the free films was found to occur simultaneously with the leaching of PEGs.[7] They also reported that the leaching of PEG from the films can be considered as being a matrix-controlled diffusion process that involves the diffusion of water into the elastomer matrix, the dissolution of PEG, and the subsequent diffusion of PEG through the water-swollen silicone elastomer matrix to the water sink.

The leaching of PEG from PDMS films at various pH values would be similar and could follow the results obtained by Li and Peck. The reason why there was more water uptake and a higher speed of water uptake for the free film in pH 6.8 than that of the free film in pH 1.2 may be due to the pH effects on the structure of the PDMS free film. Many studies showed that the hydrolysis and condensation reactions of alkoxysilanes had a strong dependence on solution pH values.[16–21] The minimum at ~ pH 2 corresponds to the isoelectric point of silica, and surface silanol groups are protonated and deprotonated at lower and higher pH values, respectively. The overall condensation rate is minimized at about pH 1.5 and maximized at intermediate pH (2 to 7).

Although no colloidal silica was added to the PDMS free films, the alkoxysilane TEOS was used as a crosslinking agent in the film, and could produce silica *in situ* during the crosslinking reactions.[12] It made the films' properties depend on the swelling pH media. This case was quite similar to that for the addition of colloidal silica, as already discussed.

When the film was in the pH 6.8 solution, water can almost immediately be absorbed into the film via PEG hydration and dissolution. Then, the silica produced by the *in situ* TEOS condensation during the film formation tended to have further condensation reactions and acted as a crosslinking agent. In this case, the PDMS film became more condensed after being soaked in the pH 6.8 buffer. However, there was little or no such silica condensation if the film was swollen in the pH 1.2 solution.

It could be concluded that the film structure was more condensed when soaked in the pH 6.8 media than when soaked in the pH 1.2. Since there was the same PEG loading in the free film, the pore size would be smaller in the condensed film. And the smaller the pore radii, the larger the capillary pressures when immersed in water. This could explain the reason that there was higher speed of water uptake in the pH 6.8 media. On the other hand, since it was more condensed, it could have a more integrated structure, which could help to hold more water in the film during the swelling process.

Figures 7 and 8 are SEM images of the cross section of a PDMS free film after being soaked in two pH media. Microscopy studies clearly indicated that the more condensed film was obtained after swelling in pH 6.8. Additionally, density studies of the PDMS free film with 0 and 10% PEG loading, before and after swelling in two pH media, gave the results listed in Table IV. After swelling, the densities were higher for the free films soaked in pH 6.8 no matter how much PEG was contained. This indicated that a condensed film structure was obtained after being soaked in the higher pH media.

This could also explain the difference in dissolution results in the different pH media. Since a more condensed film structure was formed in the pH 6.8 media, it should have a less amount and slower rate of drug release compared with that in the pH 1.2 media. Furthermore, even when the dissolutions were performed at pH 1.2 for 2 h followed by 22 h in pH 6.8 buffer, the

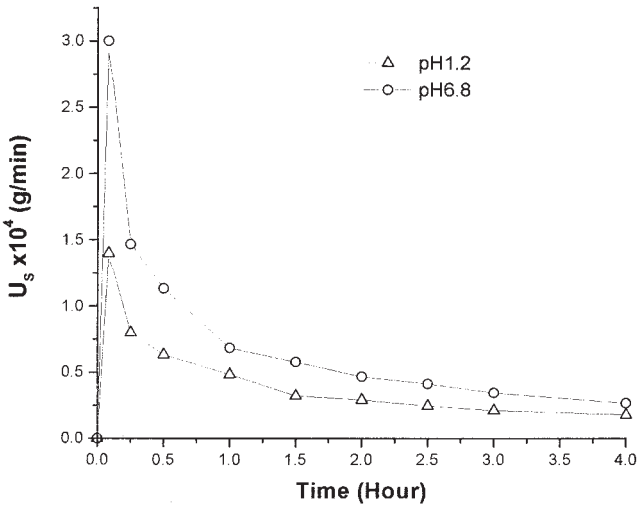


**Figure 6** The speed of water uptake of PDMS free films with 10% PEG loading swelled in various pH media.

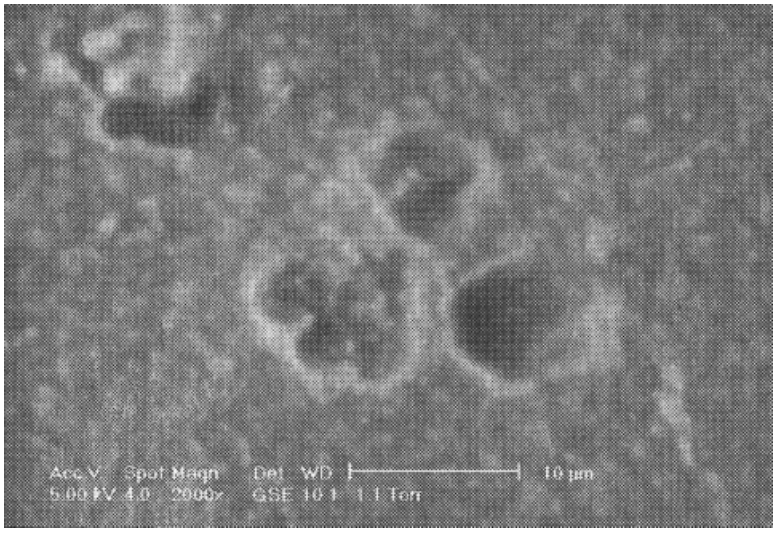


**Figure 7** The cross section of a PDMS free film after swelling in pH 1.2 media.

drug release amounts and rates were much higher than that observed only in pH 6.8. However, interestingly, it had a similar release profile compared with that in only pH 1.2 until around 8 h. Then, the release rate and amount tended to decrease gradually. This indicated that the 2 h soaked in pH 1.2 media made the film have structure similar to that when immersed in pH 1.2 alone, so that they had similar release profiles until about 8 h. When the swelling media was changed to pH 6.8 after 2 h, the condensation reactions could have occurred and taken effect around 8 h, which made the release rate and amount decrease.

## CONCLUSION

PDMS latex was found to be suitable for applications in tablet coating processes. Addition of PEG to PDMS was successful in achieving a film coating to control drug release at zero-order over a period of 24 h. A 100% drug release was achieved in 72 h for coated tablets with 50% PEG loading, but the drug release profile was not linear. Formation of coated tablets without colloidal silica was possible, and resulted in increased release rates and amounts released. The pH values had effects on drug release by changing the PDMS film structure. A more condensed film structure could be formed if the coated tablets were soaked in pH 6.8 media, which would decrease the drug release through the film.

It is a pleasure to acknowledge the financial support provided JEM by the National Science Foundation through Grant DMR-0314760 (Polymers Program, Division of Materials Research). We also wish to thank the Dow Corning

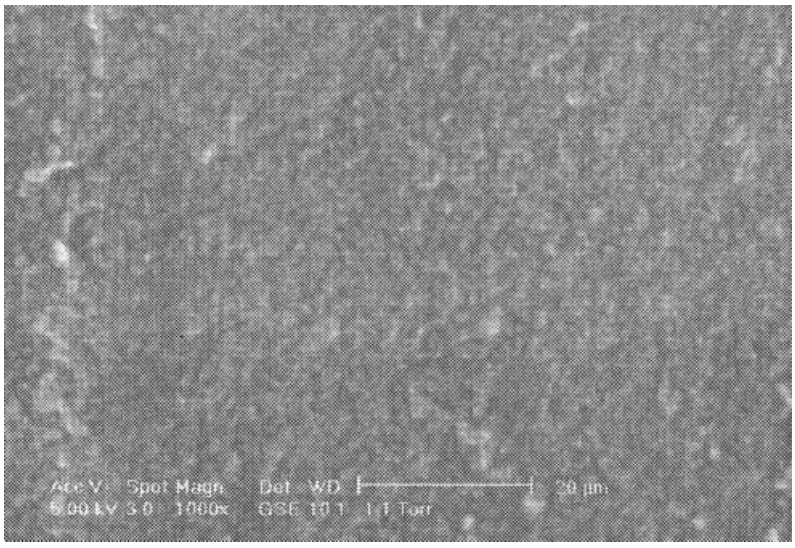


**Figure 8** The cross section of a PDMS free film after swelling in pH 6.8 media.

**TABLE IV**
**Density Changes for the Free Films Before and After Swelling**

| PEG contents (%) | Before swelling ($g/cm^3$) | After swelling ($g/cm^3$) | |
|---|---|---|---|
| | | pH 1.2 | pH 6.8 |
| 0 | 1.0233 (± 0.0034) | 0.9998 (± 0.0058) | 1.0176 (± 0.0033) |
| 10 | 1.0548 (± 0.0008) | 0.9753 (± 0.0044) | 0.9911 (± 0.0039) |

Corp. for providing one of the polymer samples.

## REFERENCES


1. McGinity, J. W. Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms, 2nd ed.; Marcel Dekker: New York, 1997.
2. Warrick, E. L.; Pierce, O. R.; Polmanteer, K. E.; Saam, J. C. Rubber Chem Technol 1979, 52, 437.
3. Compton, R. A. J Long-Term Med Implants 1997, 7, 29.
4. Tan, E. L.; Liu, J. C.; Chien, Y. W. Int J Pharm 1988, 42, 161.
5. Saam, J. C. US Patent 4,244,849, 1981.
6. Liles, D. T. US Patent 4,962,153, 1990.
7. Li, L. C.; Peck, G. E. Drug Dev Ind Pharm 1989, 15, 65.
8. Li, L. C.; Peck, G. E. Drug Dev Ind Pharm 1989, 15, 499.
9. Li, L. C.; Peck, G. E. Drug Dev Ind Pharm 1943 1989, 15.
10. Dahl, T. C.; Sue, I. T. Drug Dev Ind Pharm 1990, 16, 2097.
11. Dahl, T. C.; Sue, I. T. Pharm Res 1992, 9, 398.
12. Gao, Z. M.; Schulze Nahrup, J.; Mark, J. E.; Sakr, A. J Appl Polym Sci 2003, 90, 658.
13. Gao, Z. M.; Schulze Nahrup, J.; Mark, J. E.; Sakr, A. J Appl Polym Sci 2004, 91, 2186.
14. Schulze Nahrup, J.; Gao, Z. M.; Mark, J. E.; Sakr, A. Int J Pharm 2004, 270, 199.
15. Schulze Nahrup, J. Ph.D. Thesis, The University of Cincinnati, Cincinnati, OH, 2003.
16. Brinker, C. J.; Scherer, G. W. Sol-Gel Science: The Physics and Chemistry of Sol-Gel Processing; Academic Press: San Diego, CA, 1990.
17. Hench, L. L.; West, J. K. Chem Rev 1990, 90, 33.
18. Kim, G. D.; Lee, D. A.; Moon, J. W.; Kim J. D.; Park, J. A. Appl Organometal Chem 1999, 13, 361.
19. Huang, H.; Orler, B.; Wilkes, G. L. Macromolecules 1987, 20, 1322.
20. Esquena, J.; Solans, C. Colloids and Surfaces A: Physicochem Eng Aspects 2001, 533, 183.
21. Esquena, J.; Pons, R.; Azemar, N.; Caelles, J.; Solans, C. Colloids and Surfaces A: Physicochem Eng Aspects 1997, 575, 123.