DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 15(4), 499-531 (1989)

WATER BASED SILICONE ELASTOMER CONTROLLED RELEASE TABLET FILM COATING II - FORMULATION CONSIDERATIONS AND COATING EVALUATION

Luk Chiu Li[+] and Garnet E. Peck[*]
Purdue University
Department of Industrial and Physical Pharmacy
West Lafayette, Indiana 47906

ABSTRACT

The silicone elastomer latex incorporated with polyethylene glycol and colloidal silica produced controlled release film coating on potassium chloride tablets. The release pattern of potassium chloride from coated tablets was dictated by the composition of the coating. Significant formulation variables included the loading level of polyethylene glycol, the molecular weight of the polyethylene glycol used, and the silicone to silica weight ratio in the coating. Non-formulation variables such as coating weight, drying temperature, dissolution medium pH and aging were shown to alter the release rate of the active ingredient from coated tablets.

* For correspondence
+ Present Address: University of Oklahoma, College of Pharmacy, 1110 N. Stonewall, P.O. Box 26901, Oklahoma City, Oklahoma 73190.

INTRODUCTION

A silicone elastomer latex formulated with colloidal silica and polyethylene glycols (PEG's) was capable of producing elastomeric free films which demonstrated the potential as a rate controlling membrane system for hydrophilic and ionic species [1]. The *in situ* performance of the PEG-silicone elastomer system as controlled release tablet film coatings was further evaluated using potassium chloride as the model drug. Coating formulation variables were evaluated with respect to their effect on the drug release behavior of the resultant coating. The mechanical stability and the aging phenomenon for the tablet coating were examined. The influence of the dissolution medium pH on the release pattern was also determined.

EXPERIMENTAL

Materials:

The silicone elastomer latex, the colloidal silica and the polyethylene glycol were from the same source as reported previously [1]. Potassium chloride powder was USP grade and obtained from Ruger Chemical Company.

Methods:

Preparation and Coating of Potassium Chloride Tablets:

Six hundred mg of potassium chloride powder was weighed and compressed in a 7/16 inch die with deep cup shaped punches using the Carver Laboratory Press [a] at a maximum compression load of 6,000 pounds. The compressed tablets were then numbered on one side using a black medium tip ball point pen. The numbered tablets were subsequently weighed individually and the tablet weights were recorded accordingly. The tablet coating operation was performed using the six-inch Glatt Laboratory air suspension column [b]. The marked

potassium chloride tablets were mixed with 1.5 kg of standard concave, red colored lactose tablets precoated with hydroxylpropylmethyl cellulose. Tablet coating was done using 800.0 g PEG-silicone elastomer dispersions with a 25% (W/W) total solids content. The dispersion spraying rate was set at 20.0 g per minute and the atomization pressure was controlled at 2.5 Kp per cm^2. The inlet air temperature was fixed at 60°C. Coating dispersions were freshly prepared. During the coating operation, the coating dispersion was kept under constant stirring using a magnetic stirrer and stir bar. Coated tablets were dried in a desiccator at room temperature for at least 3 days prior to the drug release studies. Owing to the transparent appearance of the PEG-silicone elastomer film coating, the tablets were easily identified by their number following coating. The coating weight of the tablet was determined by calculating the difference in weight before and after coating.

In Vitro Drug Release Testing:

The in vitro release kinetics of potassium chloride from the controlled release coated tablet was investigated using the standard USP Dissolution Method II, the paddle method. The equipment used was a six-unit dissolution apparatus (c). The dissolution medium was 900 mls of degassed deionized water maintained at 37±0.5°C. The paddle stirring rate was set at 100 rpm. Drug release was monitored for a period of 6 hours or 12 hours, depending on the release rate. A 20.0 ml sample of the dissolution medium was withdrawn at hourly intervals for the first six hours and at two-hour intervals for the remaining six hours. The volume of the dissolution medium was kept constant by adding 20.0 ml of fresh degassed deionized water each time a sample was withdrawn. The conductivity of the sample

was measured using a conductivity meter (d) and the amount of potassium chloride in the sample was calculated by means of a calibration curve. The amount of potassium chloride in a sample withdrawn at each sampling interval was accounted for in the computation of the cumulative amounts of potassium chloride released. The release profile of potassium chloride was obtained by plotting the cumulative percent of total dose released against elapsed time. The cumulative percent release data were correlated with the time elapsed using the least square linear regression method. The slope of the best fitted equation represents the zero order release rate of potassium chloride from the tablet system.

The Effect of Dissolution Medium pH on Release Pattern:

This study was undertaken to investigate the effect of pH on the drug release behavior of the PEG-silicone elastomer controlled release coatings. Three different dissolution media were used in this study. The first medium used was Simulated Gastric Fluid, USP (without enzyme) which has a pH of approximately 1.2. The second medium was a fluid with a pH of 5.0, which was prepared by adjusting the pH of Simulated Intestinal Fluid, USP (without enzyme) to 5.0 by adding 10 percent hydrochloric acid. The third medium was a pH 8.0 fluid, which was prepared by adjusting the pH of Simulated Intestinal Fluid, USP (without enzyme) to 8.0 by adding 10 percent sodium hydroxide solution. These three media were adjusted to be isotonic to the normal saline by adding sodium chloride. The osmolality of each medium was measured and monitored using the Osmette A osmometer (e). The coated tablet sample was placed in the dissolution vessel containing 900 mls of a specific pH medium maintained at $37 \pm 0.5^{o}C$. The stirring rate of the paddle was set at 100 rpm. After

a predetermined time interval, the tablet sample was removed from the medium and the dry weight of the tablet content, which represented the amount of potassium chloride remaining, was subsequently determined. Since the weight of the tablet core was determined before coating, the percent dose released could be calculated.

Stability Studies of Coatings at Room and Elevated Temperatures:

For each coating batch, the coated tablets were divided into two groups. One group was stored at 20°C and the other group was stored at 50°C. The coated tablets were kept in amber colored screw-capped bottles. Three coated tablets were randomly selected from samples stored under different conditions every fifteen weeks for forty-five consecutive weeks. The drug release profiles were determined for the samples withdrawn at each sampling interval.

Evaluation of the Mechanical Stability of Polyethylene Glycol-Silicone Elastomer Coated Tablets:

This study was designed to evaluate the mechanical stability of the PEG-silicone elastomer coated tablets against continuous abrasion and mechanical impact. For each coating formulation evaluated, twenty coated tablets were placed in the Roche Friabilator (f) which was run for four minutes at 25 rpm. Coated tablets without this treatment were used as the control. The drug release profiles for the tested and control coated tablets were determined and compared.

Scanning Electron Microscopy:

The morphology and microstructure of PEG-silicone elastomer tablet coatings were examined using the scanning electron microscope (g). The influence of the coating composition on the structure of the tablet film coating was evaluated and correlated to the drug

release characteristics of the coated product. Scanning electron photomicrographs were also taken of isolated hydrated tablet coatings. Hydrated tablet coating removed from water was first frozen in a dry ice bath and subsequently freeze dried using a suitable freeze dryer [h].

RESULTS AND DISCUSSION

The Effect of Coating Formulation Variables on the Drug Release Characteristics of Coated Potassium Chloride Tablets:

The PEG-silicone elastomer dispersions evaluated in this study exhibited different extents of tackiness during the coating operation as indicated by the degree of fluidization of the tablets in the coating column. Coating dispersions containing lower molecular weight PEG (i.e., PEG 1450) or having a high silicone to silica ratio (i.e., a low silica content) caused tackiness problems during coating. The fluidization of the tablets using these dispersions appeared to be inadequate even at the maximum fluidization air flow. However, the use of high molecular weight PEG (i.e., PEG 8000) and a high silica content in the coating dispersion, resulted in a non-tacky coating. Figure 1 depicts the release profiles of potassium chloride from tablets coated with PEG-silicone elastomer coating formulations containing PEG 8000 at three different loading levels of 20, 30 and 40 percent. The silicone to silica ratio in these formulations was fixed at 2.0 to 1.0. Despite the difference in the slope, these release profiles showed evidence of a membrane-controlled process. The cumulative percent of potassium chloride released showed a linear relationship ($R>0.995$) with the time for up to 80% of the dose released. The slope of the release profile

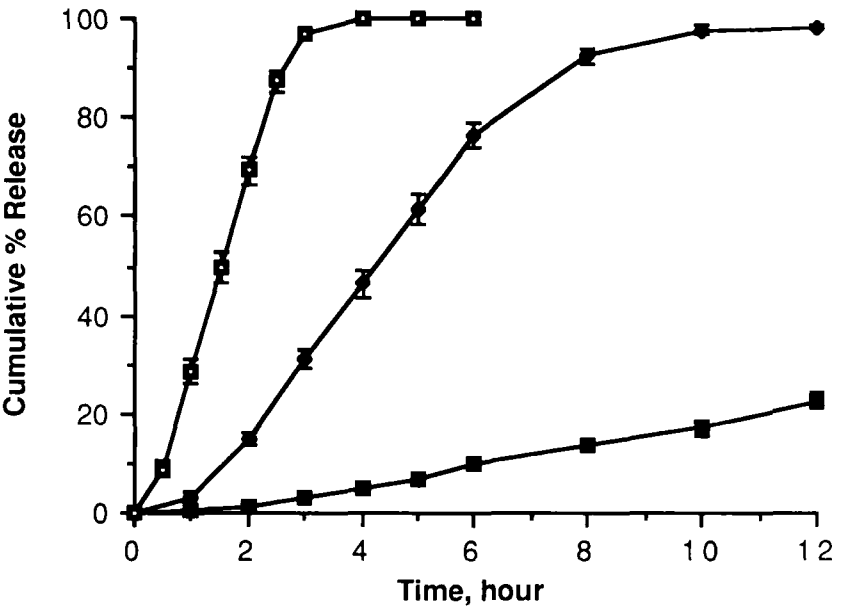

Figure 1. Release Profiles of Potassium Chloride from Tablets Coated with Silicone Elastomer Containing PEG 8000 at Three Different Loading Levels. Key: (■) 20%; (◆) 30%; and (□) 40%.

represented the zero order release rate of potassium chloride from the coated tablets at steady state. Potassium chloride tablets coated with silicone elastomers containing PEG 3350 or PEG 1450 also exhibited zero order release of the active ingredient. Table 1 shows the effect of PEG molecular weight and loading level of PEG in the coating on the release rate of potassium chloride from coated tablets. It should be noted that tablets coated with 10% PEG loaded silicone elastomers showed no sign of potassium chloride release regardless of the molecular weight of PEG used. At 20% PEG loading level, no significant difference was found in the release rate for tablets coated with three different molecular weight PEG's.

Table 1. Release Rate of Potassium Chloride from Tablets Coated with Silicone Elastomer Containing Three Different Molecular Weights of Polyethylene Glycol at Three Different Loading Levels.

PEG Molecular Weight	Release Rate % Per Hour PEG Loading level (%) 20	30	40
8000	1.95* (0.11)	14.73 (0.56)	39.98 (0.73)
4450	1.95 (0.16)	12.62 (0.47)	22.50 (1.07)
1450	2.12 (0.16)	5.97 (0.18)	12.53 (0.19)

* Mean and standard deviation for six samples.

However, at 30% and 40% loading levels, tablet coatings containing higher molecular weight PEG yielded faster release rate. As the percent of PEG 8000 in the coating increased from 20.0 to 30.0, a nearly seven-fold increase in release rate was achieved. A three-fold increase in release rate was seen when the PEG content increased from 30.0 to 40.0%. However, a much less dramatic change in release rate was observed for coatings consisting of increasing amounts of PEG 3350 and PEG 1450. This result suggests that high molecular weight PEG's were capable of forming more porous and permeable coatings in water, particularly at higher concentrations.

From previous free film studies [1], it was found that in contact with water, PEG-silicone elastomer

mixed films containing 20% and 30% PEG achieved complete leach out of the water soluble polymer within one hour. It is conceivable that rapid leaching of PEG from the tablet coating also takes place readily in water producing a hydrated porous structure. Scanning electron microscopy (SEM) photomicrographs for PEG-silicone elastomer tablet film coatings containing PEG 8000 at 20%, 30% and 40% loading levels are shown in Figures 2 through 4. Despite the slight difference in surface roughness, these tablet film coatings are comparable in surface morphology. Figures 5 through 7 are the SEM photomicrographs for the freeze dried samples for the hydrated tablet film coatings shown in Figures 2 to 4. It is apparent that the PEG levels in the coating exerted a dramatic effect on the appearance of the coating following hydration. For the 20% PEG 8000 loaded film coatings, isolated microscopic pores are discernible in the freeze dried sample. As the PEG percentage increased to 30% and 40%, sponge-like microstructures are seen. These characteristic features of the hydrated coating samples demonstrate the effect of PEG loading on the drug release behaviors of the coated tablets through pore formation. The development of such porous structure further suggests that the drug release from the tablet reservoir is accomplished by a diffusional transport mechanism through the water-filled channels.

The PEG molecular weight effect on the drug release behavior of the resultant tablet coating was investigated by examining and comparing the structure of tablet film coating. Figures 8 and 9 show the SEM photomicrographs for the silicone elastomer tablet film coating containing 30% PEG 1450 and the corresponding freeze dried hydrated sample. A comparison between Figures 3 and 8 confirms that the film coating formed

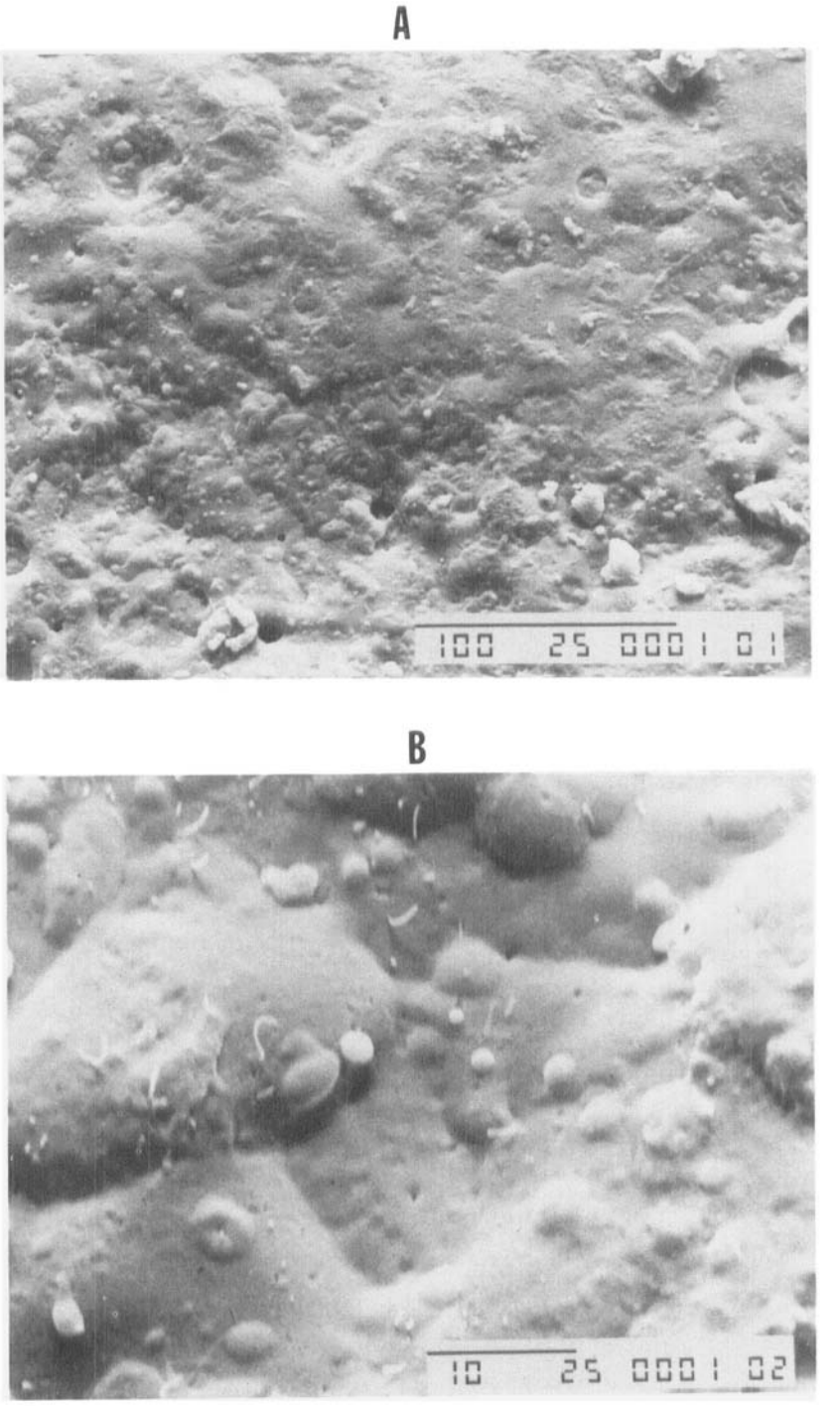

Figure 2. SEM Photomicrographs for Tablet Coating Consisting of Silicone and Silica in a Ratio of 2 to 1 and 20% PEG 8000. Magnification: (A) x350 and (B) x2000.

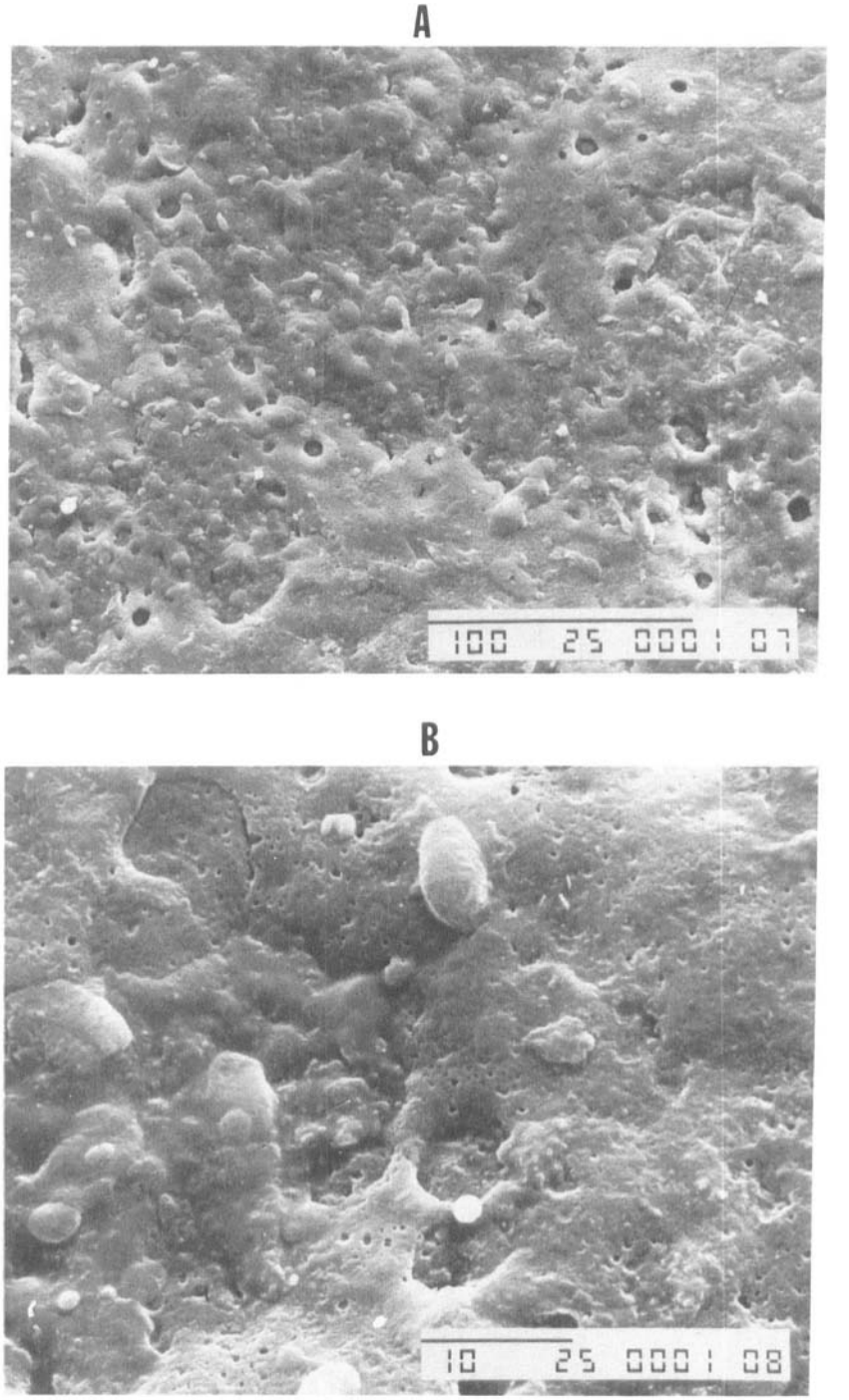

Figure 3. SEM Photomicrographs for Tablet Coating Consisting of Silicone and Silica in a Ratio of 2 to 1 and 30% PEG 8000. Magnification: (A) x350 and (B) x2000.

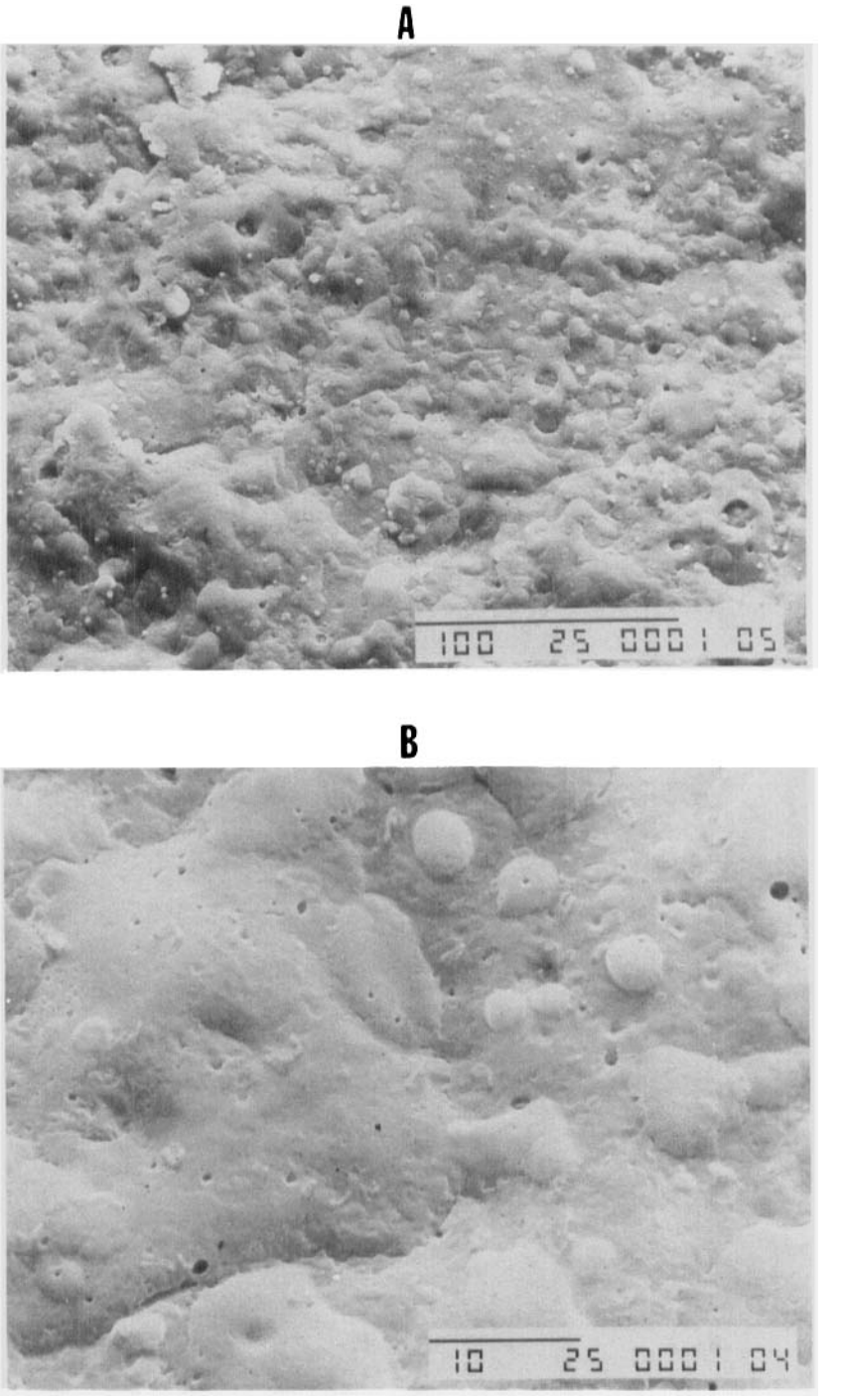

Figure 4. SEM Photomicrographs for Tablet Coating Consisting of Silicone and Silica in a Ratio of 2 to 1 and 40% PEG 8000. Magnification: (A) x350 and (B) x2000.

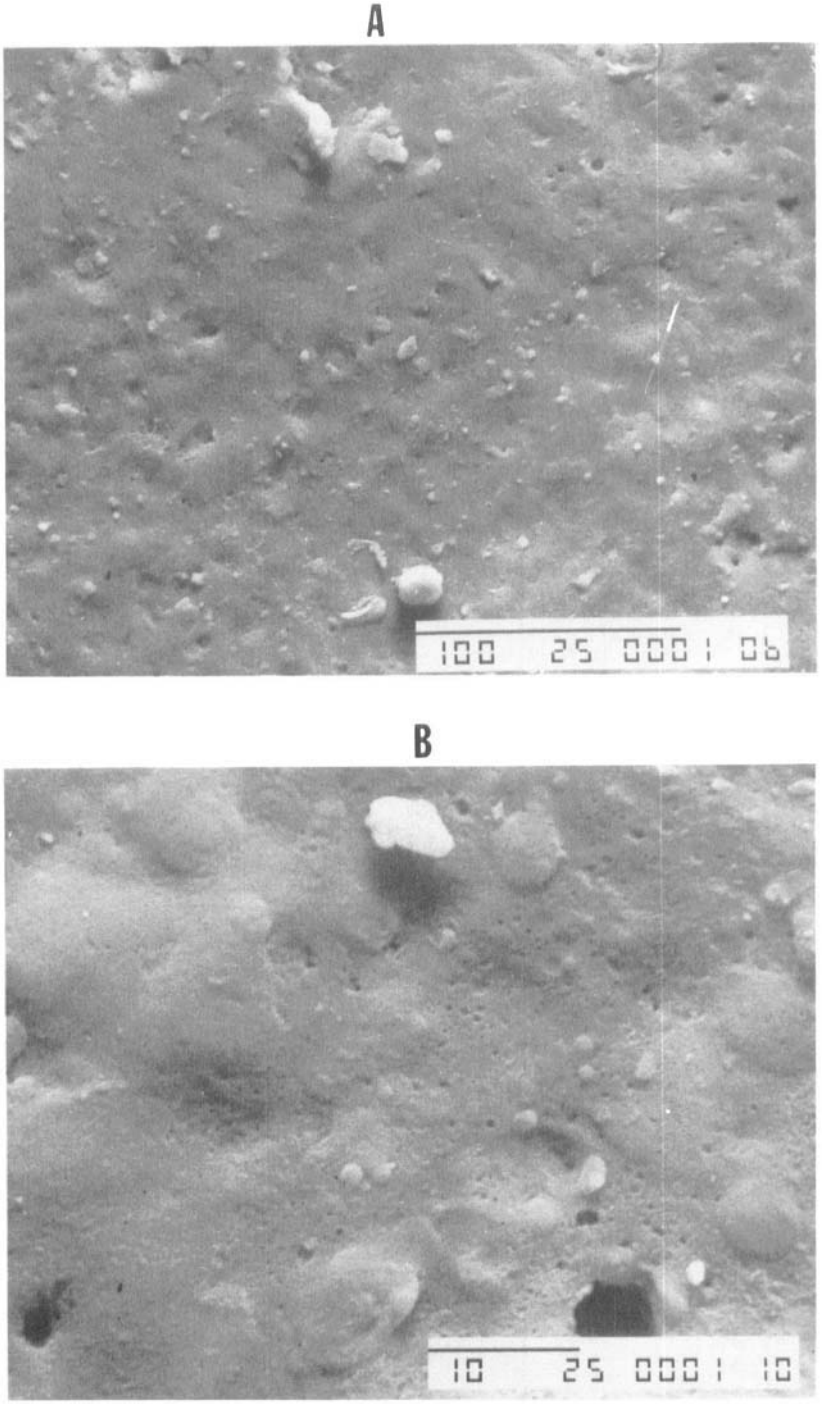

Figure 5. SEM Photomicrographs for Freeze Dried Silicone Elastomer Coating Containing 20% PEG 8000, after Hydration. Magnification: (A) x350 and (B) x2000.

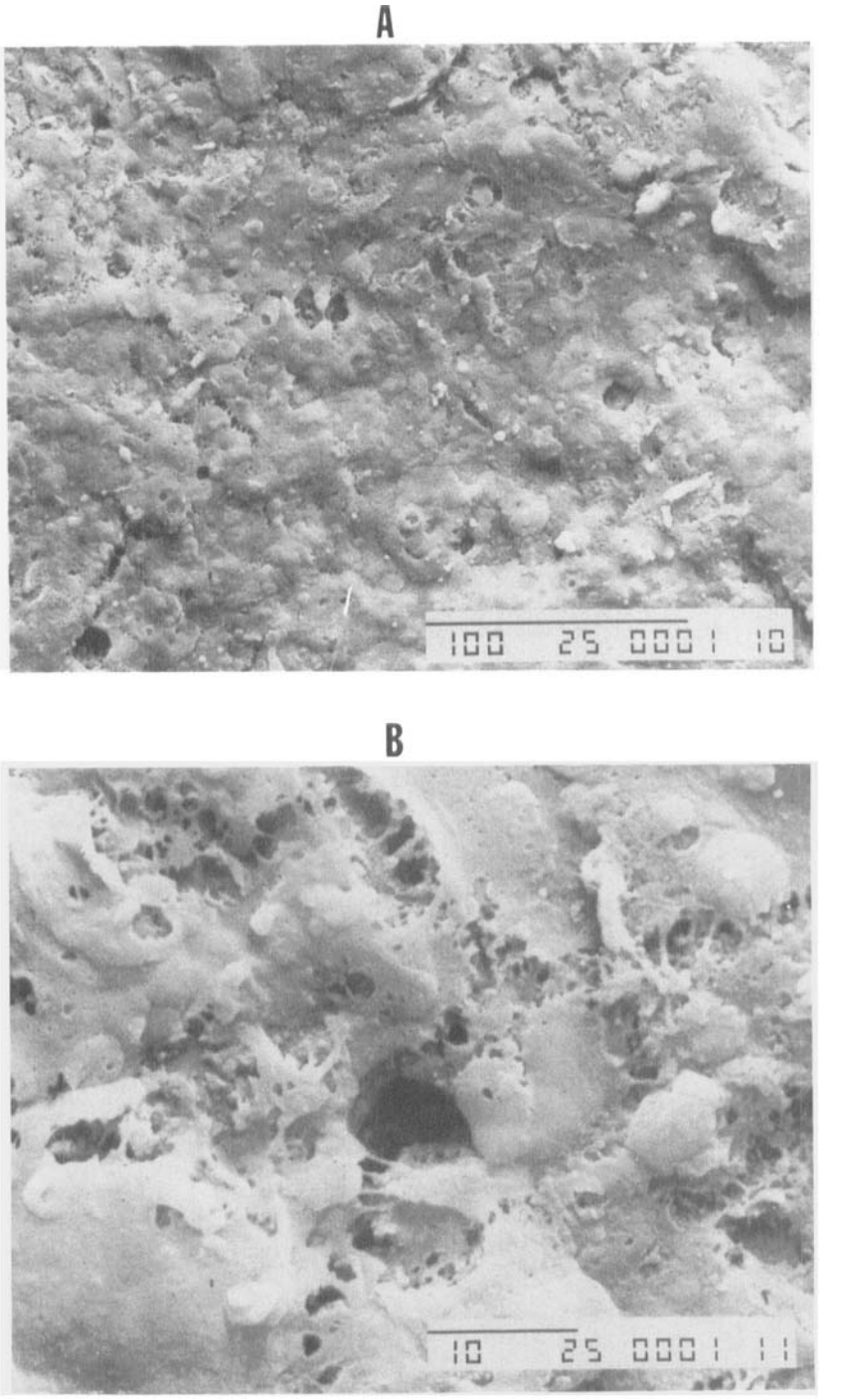

Figure 6. SEM Photomicrographs for Freeze Dried Silicone Elastomer Coating Containing 30% PEG 8000, after Hydration. Magnification: (A) x350 and (B) x2000.

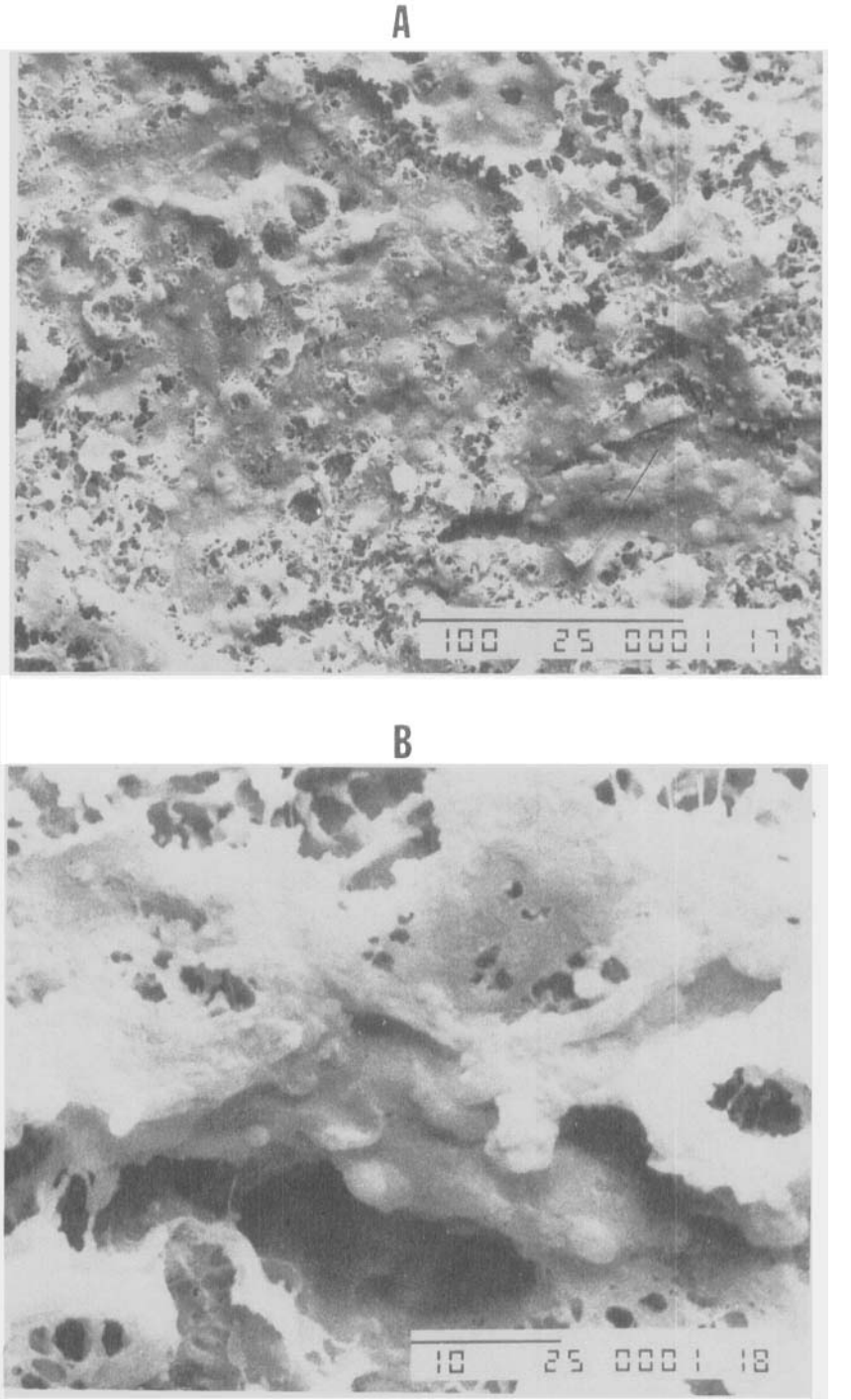

Figure 7. SEM Photomicrographs for Freeze Dried Silicone Elastomer Coating Containing 40% PEG 8000, after Hydration. Magnification: (A) x350 and (B) x2000.

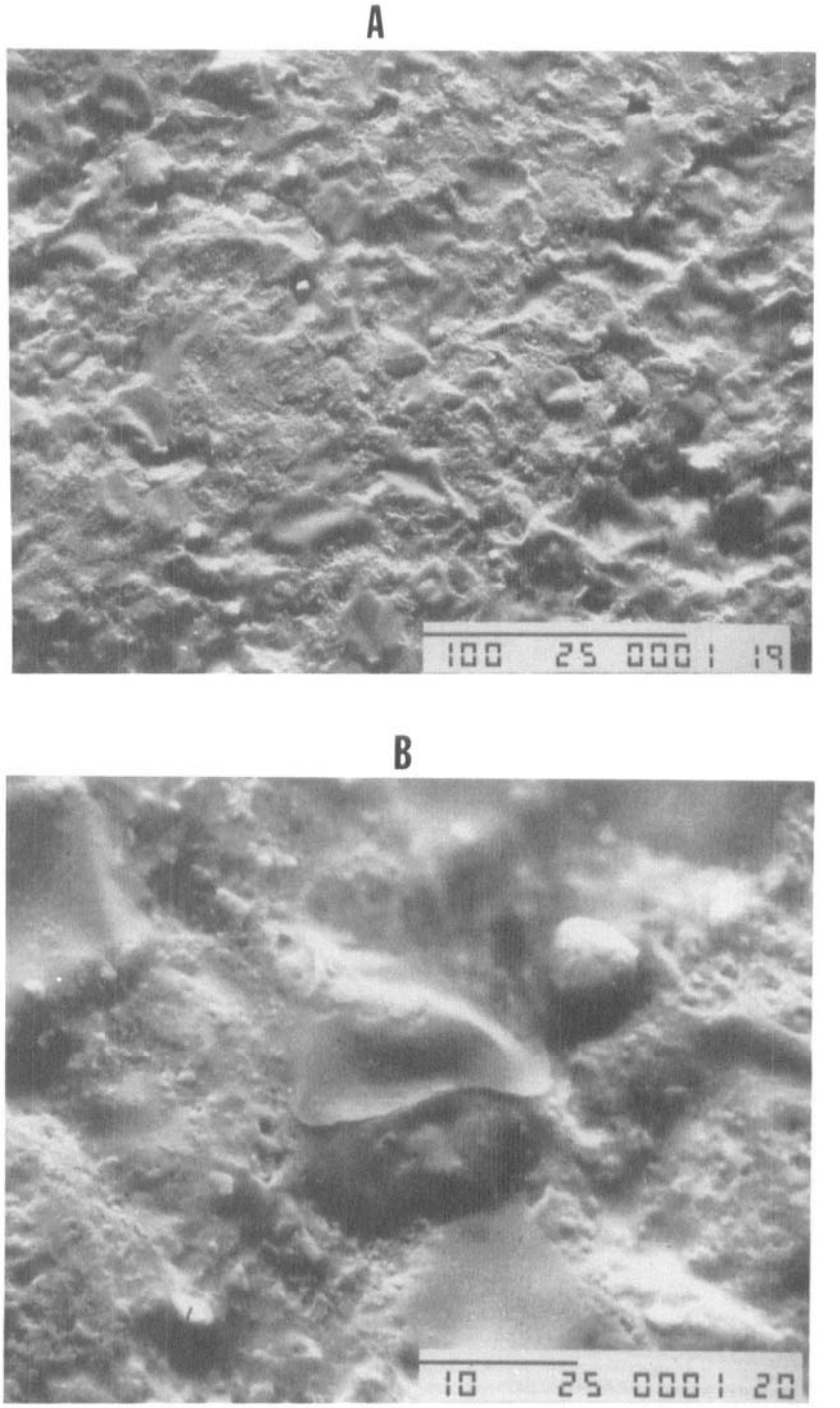

Figure 8. SEM Photomicrographs for Tablet Coating Consisting of Silicone and Silica in a Ratio of 2 to 1 and 30% PEG 1450. Magnification: (A) x350 and (B) x2000.

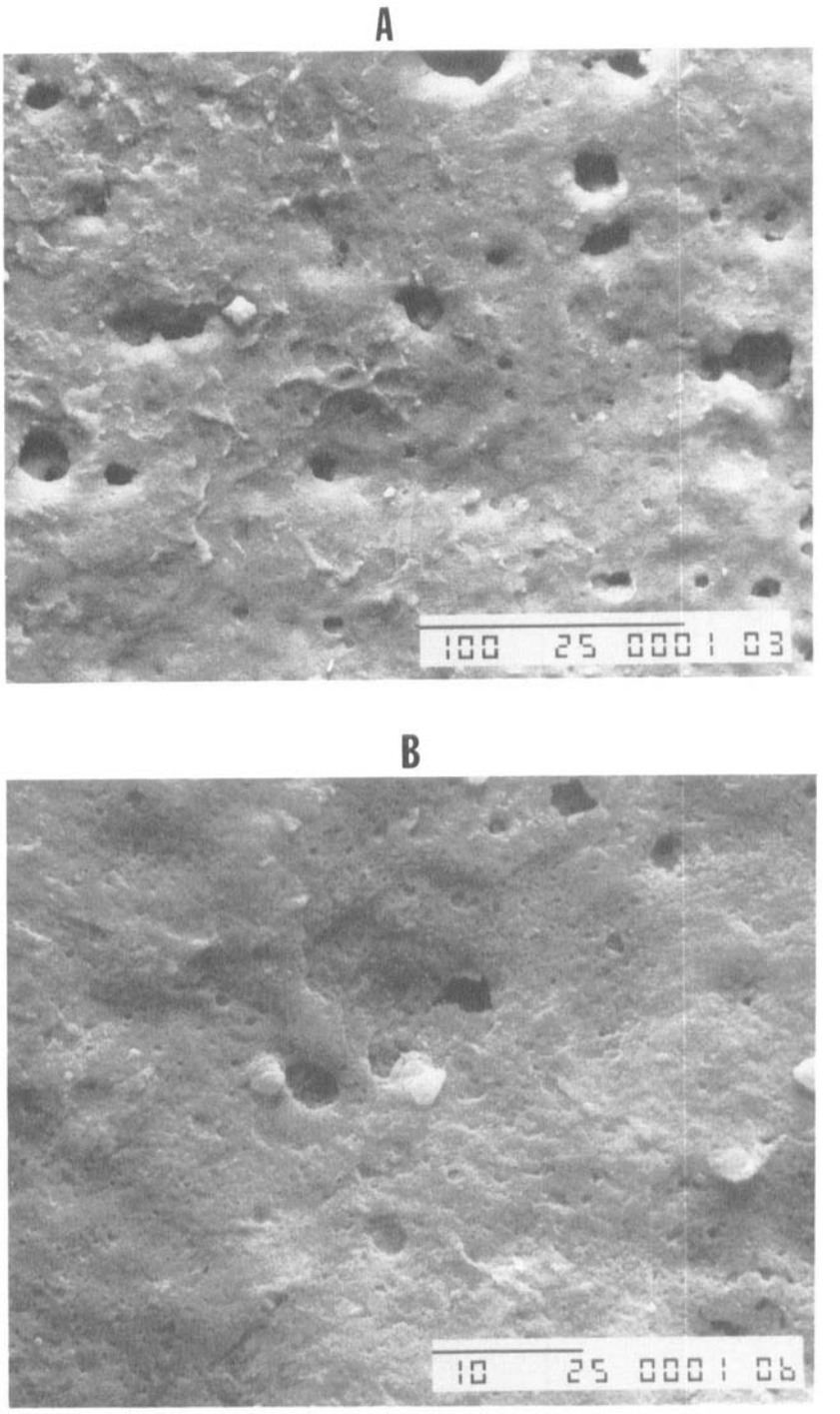

Figure 9. SEM Photomicrographs for Freeze Dried Silicone Elastomer Coating Containing 30% PEG 1450, after Hydration. Magnification: (A) x350 and (B) x2000.

with low molecular weight PEG was more continuous and less porous. The significant difference between the structure of freeze dried hydrated samples is illustrated by Figures 6 and 9. It is evident that the leaching of PEG 1450 produced a microporous hydrated film structure in water, whereas sponge-like structures were formed in 30% PEG 8000 loaded coating. Based on this observation, it can be concluded that the sponge-like structures developed in the hydrated film coating contribute to the higher drug release rate associated with the silicone elastomer coating containing 30% PEG 8000, while the tortuous microporous structures of the hydrated film coating may be responsible for the relatively slow rate of drug release obtained from tablet coating containing 30% PEG 1450.

The striking difference between the structure of the dried and hydrated coating samples of these two formulations could be a process related phenomenon. It is generally accepted that the evaporation of water and coalescence of the film formers present in the coating dispersion take place concurrently on the tablet surface during the film coating process[2]. Since the coating was applied at 60°C in this study, the tablet surface temperature was well above the melting point of PEG 1450 (42°C). Thus, upon the removal of water, the PEG 1450 would probably remain as a liquid in the silicone elastomer matrix. This liquified PEG may allow the close packing of the silicone elastomer and lead to the formation of a more continuous coating. The solidification of the molten PEG may take place gradually in the dried silicone elastomer matrix after the coated tablets were removed from the coating column. Furthermore, the melting of PEG 1450 during the coating process may provide a suitable explanation for the tackiness problems observed during the coating

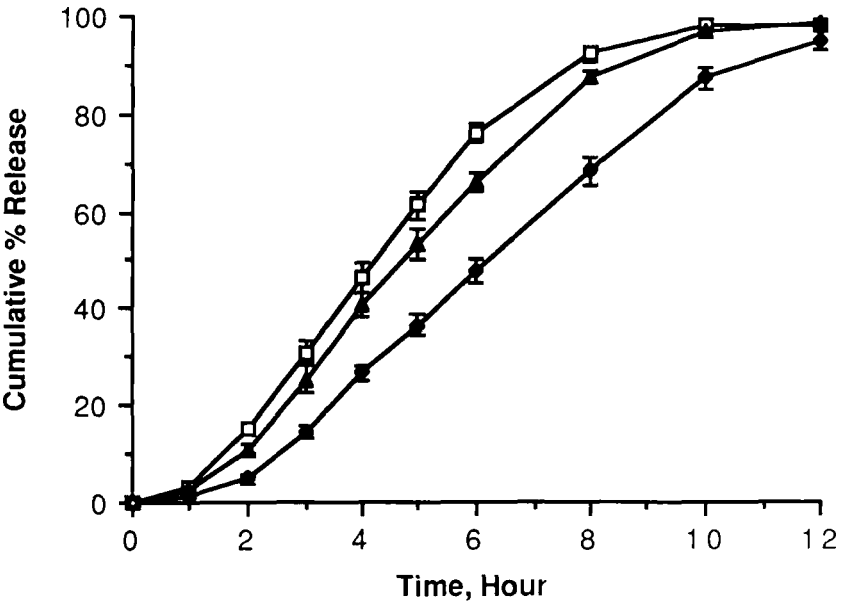

Figure 10. Release Profiles of Potassium Chloride from Tablet Coated with Silicone Elastomer Containing 30% PEG 8000 and Silicone and Silica in Three Different Ratios. Key: (□) 2 to 1; (▲) 3 to 1; and (◆) 4 to 1.

process using formulations containing this low molecular weight PEG. On the other hand, when using coating formulations containing PEG 8000 which has a high melting point, the water soluble polymer would crystallize in the silicone elastomer film matrix upon the removal of water. The existence of the hard solid PEG 8000 in the coating may prevent close packing of the film formers and result in a more discontinuous and porous film structure. Also, due to the more pronounced viscosity build-up of PEG 8000 in water, the rapid evaporation of water would cause the instantaneous gelling of the coating dispersion and a loss of fluidity, which may further limit the spreading of the

Table 2. Release Rate of Potassium Chloride from Tablets Coated with Silicone Elastomer Containing Three Different Molecular Weights of Polyethylene Glycol at 30% Loading Level and Silicone and Silica in Three Different Ratios.

PEG Molecular Weight	Release Rate % Per Hour PEG Loading level (%) 20	30	40
8000	14.73* (0.56)	12.26 (0.44)	10.78 (0.51)
4450	12.62 (0.47)	10.45 (0.49)	9.30 (0.63)
1450	5.97 (0.18)	3.63 (0.22)	3.06 (0.23)

* Mean and standard deviation for six samples.

coating dispersion. The rough and porous surface morphology of the silicone elastomer coating formed with 30% PEG 8000 would confirm this conclusion.

Figure 10 illustrates the release profiles of potassium chloride from tablets coated with PEG-silicone elastomers containing 30% PEG 8000 and silicone and silica in three different ratios. Table 2 shows the effect of PEG molecular weight and silicone to silica ratio on the release rate of potassium chloride from coated tablets. It is apparent that the influence of PEG molecular weight on the drug release rate was not significantly altered by the change of the silicone to silica ratio of the coating. Tablet coatings containing higher molecular weight PEG yielded a faster drug release rate for the three silicone to silica ratios evaluated in this study. Tablets coated

with formulations having a low silicone to silica ratio released potassium chloride at a faster rate. Figure 11 contains the SEM photomicrographs of the tablet film coating formed with 30% PEG 8000 and a silicone to silica ratio of 4.0. The SEM photomicrographs of the corresponding freeze dried hydrated coating sample are seen in Figure 12. In comparison with the film coating formed with a low silicone to silica ratio as shown in Figures 3 and 6, it is apparent that an increased silicone content in the coating (i.e., a high silicone to silica ratio) produced a more compact tablet coating which formed a hydrated film with a more continuous microporous structure. The structural difference in the hydrated coating samples as shown in Figure 6 and 12 may account for the difference in drug release characteristic of these two tablet coating samples.

During the coating process using the PEG-silicone elastomer dispersions with a high silicone to silica ratio, it was observed that the degree of tablet fluidization was significantly reduced because of the tackiness of the coating dispersion. In a less expanding tablet bed inside the coating column, it is conceivable that tablet to tablet contact would be enhanced and the rate of water removal would be reduced. The decreased rate of drying may facilitate the close packing of the coating and the contact between tablets may produce an additional smoothing effect on the coating. It is proposed that the slower drug release rate for high silicone content coating formulations could also be a process related effect.

The Effect of Tablet Coating Weight:

Potassium chloride tablets coated with PEG-silicone elastomer dispersions were prepared with different coating weights. Figure 13 shows the release profiles of potassium chloride from coated tablets with three

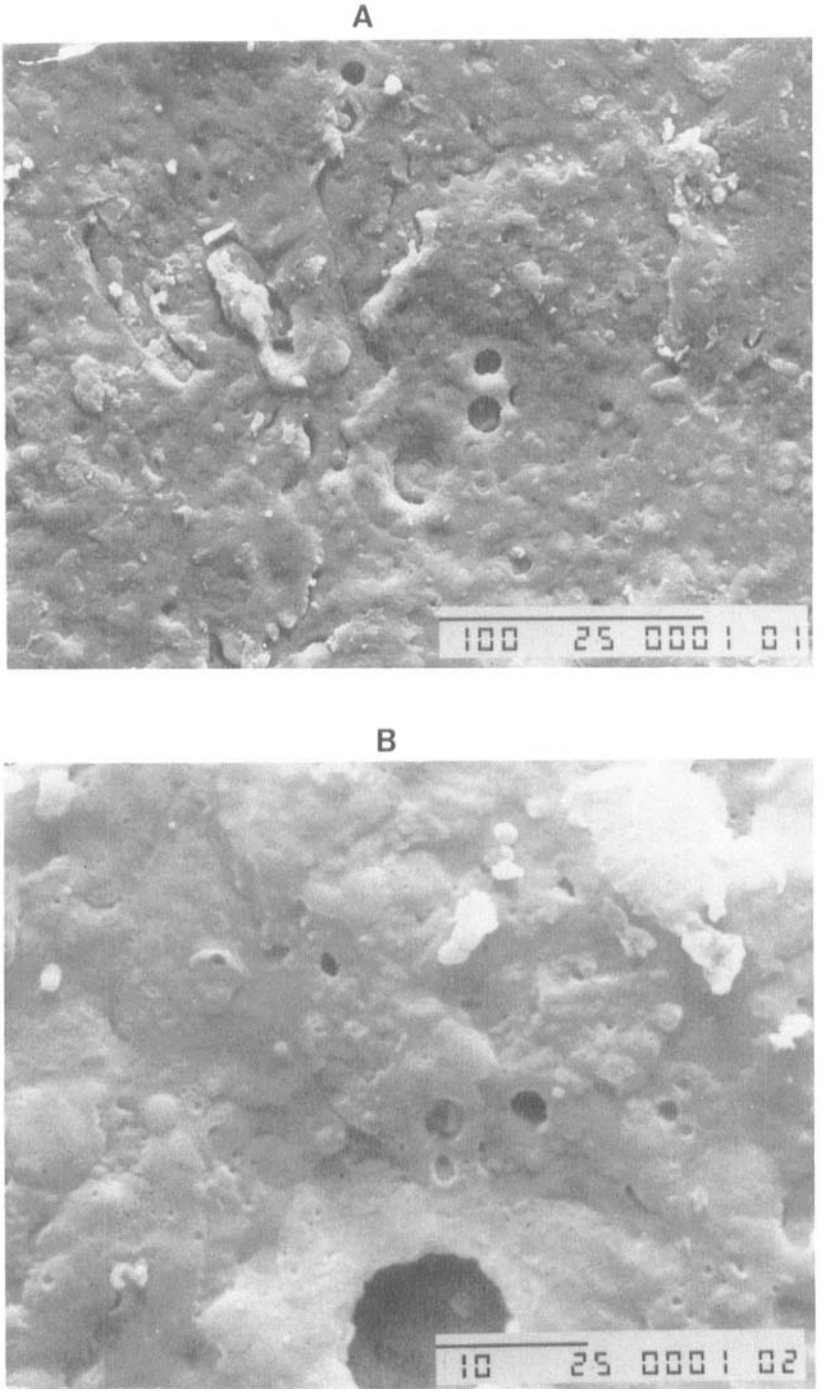

Figure 11. SEM Photomicrographs for Tablet Coating Consisting of 30% PEG 8000 and Silicone and Silica in a Ratio of 4 to 1. Magnification: (A) x350 and (B) x2000.

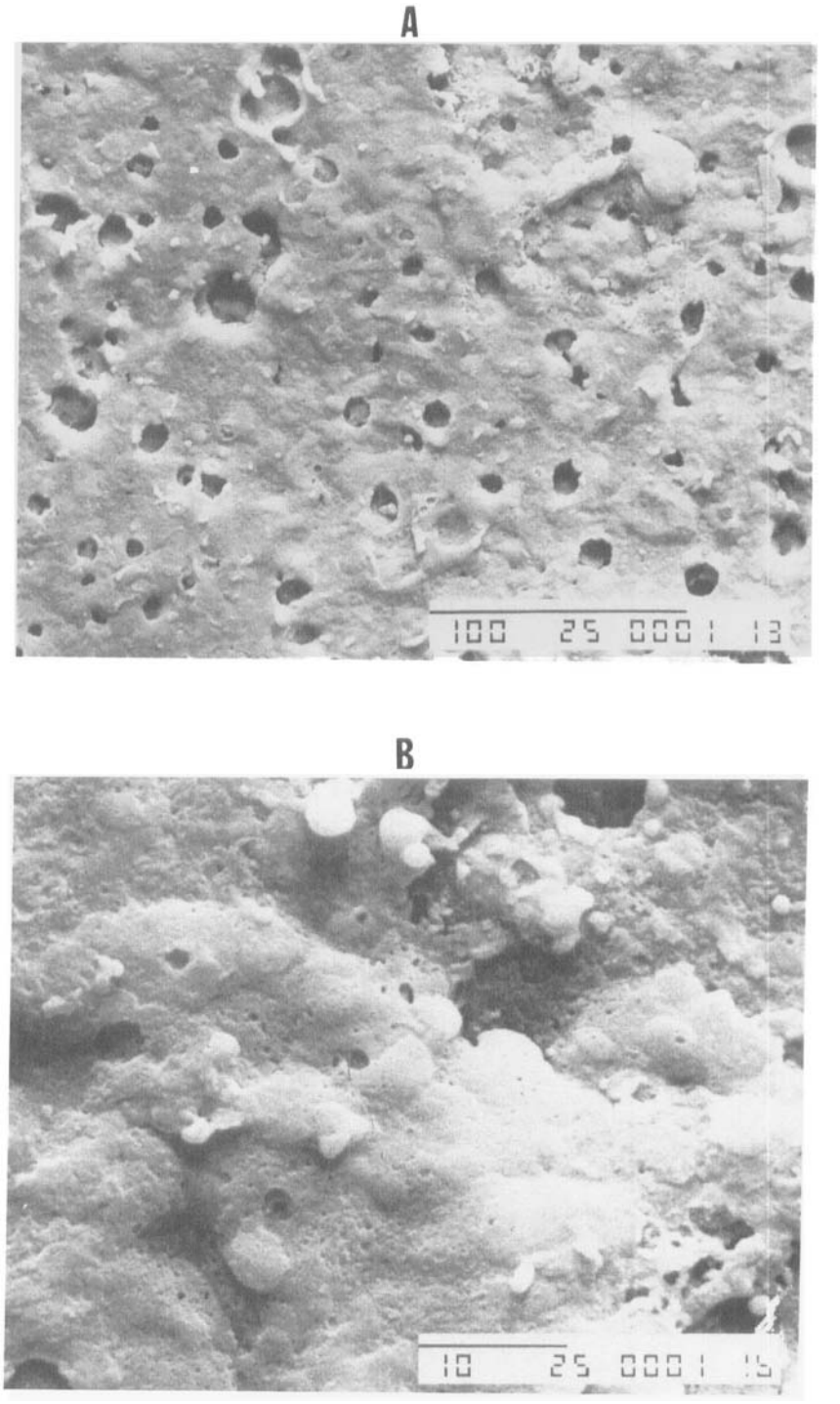

Figure 12. SEM Photomicrographs for Freeze Dried Silicone Elastomer Coating Containing 30% PEG 8000 and Silicone and Silica Ratio of 4 to 1, after Hydration. Magnification: (A) x350 and (B) x2000.

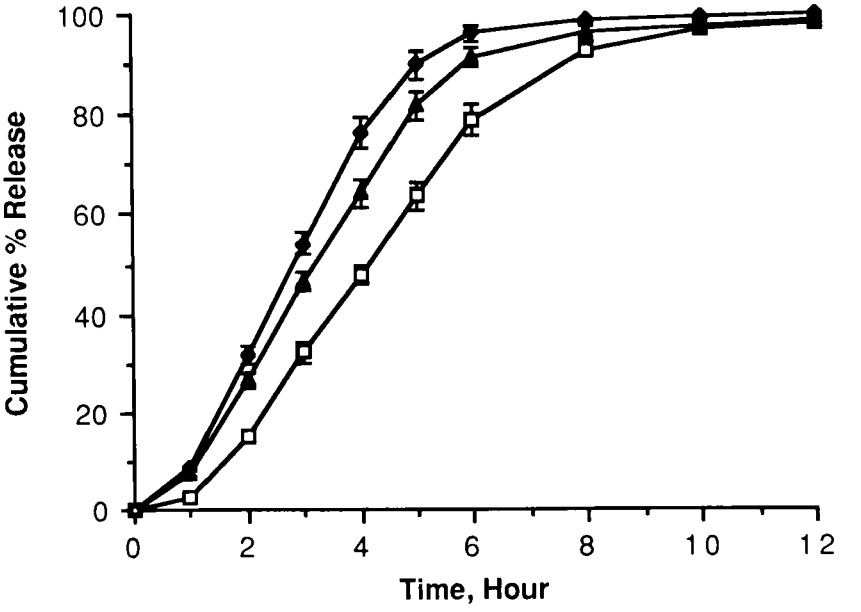

Figure 13. The Effect of Coating Weight on the Release of Potassium Chloride from Tablets Coated with Silicone Elastomer Containing 30% PEG 8000. Key: (□) 60.9 mg; (▲) 51.3 mg; and (◆) 45.3 mg.

different coating weights. As the tablet coating weight increased, the release rate of the active ingredient from the coated tablet decreased. With a constant tablet surface area, it is conceivable that increased coating weight yields thicker coating with fewer open pores and increased tortuosity. These factors probably contribute to the observed decreased release rate.

The Effect of Heat Treatment:

Figure 14 depicts the release profiles of potassium chloride from coated tablets dried at room temperature and at 60°C, respectively. The heat treated coated tablets exhibited slower drug release profile. Since the melting point of PEG 8000 is about 60°C, when the coated

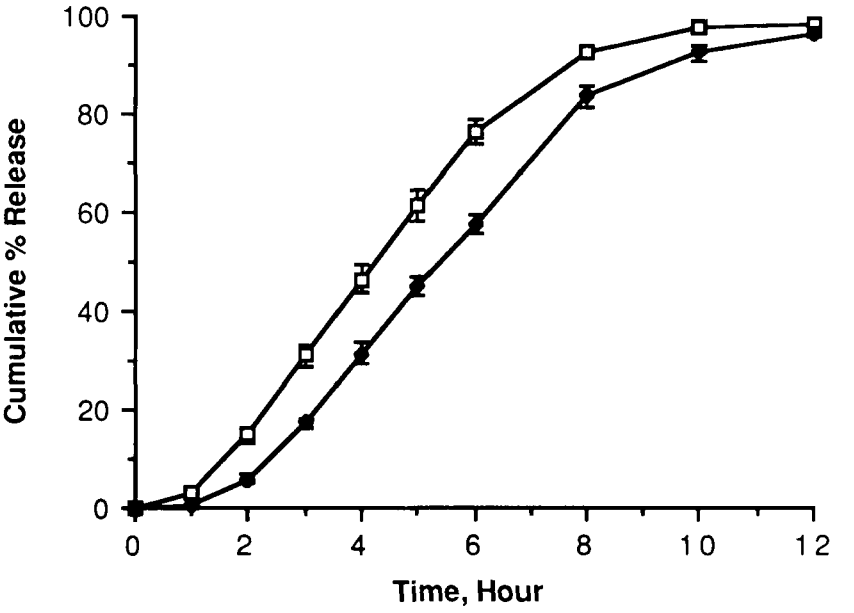

Figure 14. The Effect of Heat Treatment on the Release of Potassium Chloride from Tablets Coated with Silicone Elastomer Containing 30% PEG 8000. (Key: (□) Dry at Room Temperature and (◆) Heat at 60°C for 24 Hours.

tablets were subjected to prolong heating at 60°C, the PEG within the coating would probably soften, which may facilitate the coalescence of the silicone elastomer matrix. The coalescence of latex particles has been shown to be a temperature dependent process [2]. Therefore, at an elevated temperature a more continuous but less permeable PEG-silicone elastomer coating may be produced. Figure 15 shows the SEM photomicrographs of the surface of unheated and heated coated tablets. It is apparent that without heat treatment the coating appears to be somewhat rough and porous. The heat treated tablets showed a coating that is more coalesced and less porous.

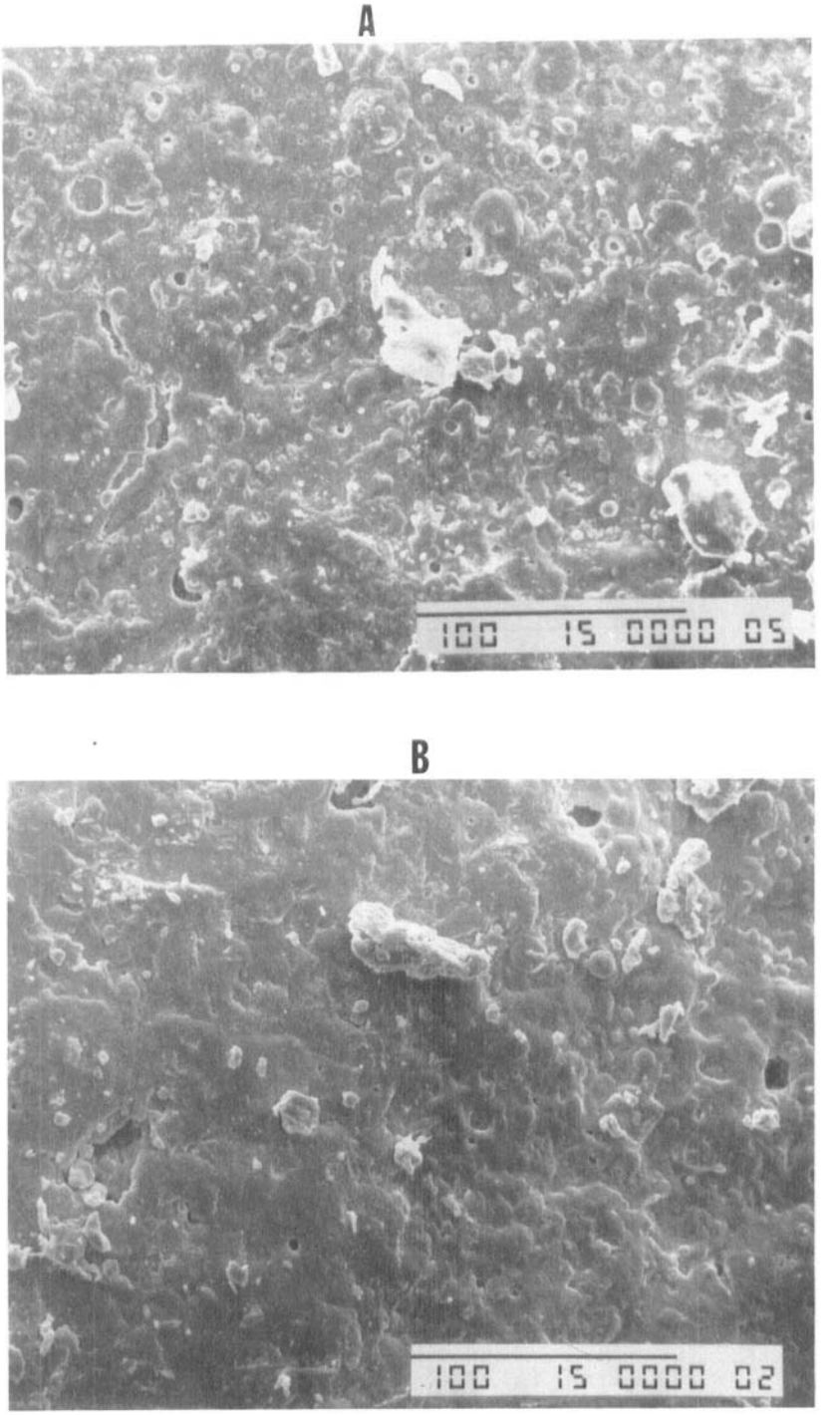

Figure 15. SEM Photomicrographs for Silicone Elastomer Coating Containing 30% PEG 8000 and Silicone and Silica in a Ratio of 2 to 1. Key: (A) Dry at Room Temperature and (B) Heat at 60°C. Magnification: x350.

Table 3. Comparison of the Release of Potassium Chloride from Coated Tablets Before and After the Friability Testing.

	Cumulative Percent Release					
	Time (Hour)					
	0.5	1.0	1.5	2.0	2.5	3.0
Control	8.05* (1.03)	29.33 (2.97)	50.47 (3.19)	69.18 (1.78)	88.50 (1.90)	98.40 (0.67)
Tested	7.58 (1.39)	28.32 (2.04)	49.31 (1.87)	69.90 (1.88)	88.60 (1.37)	98.60 (0.69)

* Mean and standard deviation for six samples.

Evaluation of the Mechanical Stability of Coated Tablets:

Potassium chloride tablets coated with PEG-silicone elastomer containing 40% PEG 8000 were subjected to a friability test as described in the experimental section. Table 3 gives the cumulative percent of potassium chloride released from coated tablet before and after friability testing. It is apparent that the friability test has no significant effect on the release characteristics of the coated tablets. This result suggests that the PEG-silicone elastomer film coatings are sufficiently strong to withstand mechanical shock and continuous abrasion. In the free film evaluation, it was noted that with increasing PEG loading levels, the silicone elastomer free films became more brittle [1]. At the 40% PEG loading level, the free films cracked upon drying. However, as shown in the present study, PEG-silicone elastomer tablet coatings with 40% PEG loading were free of any physical defect and were capable of resisting intensive mechanical stresses. This result

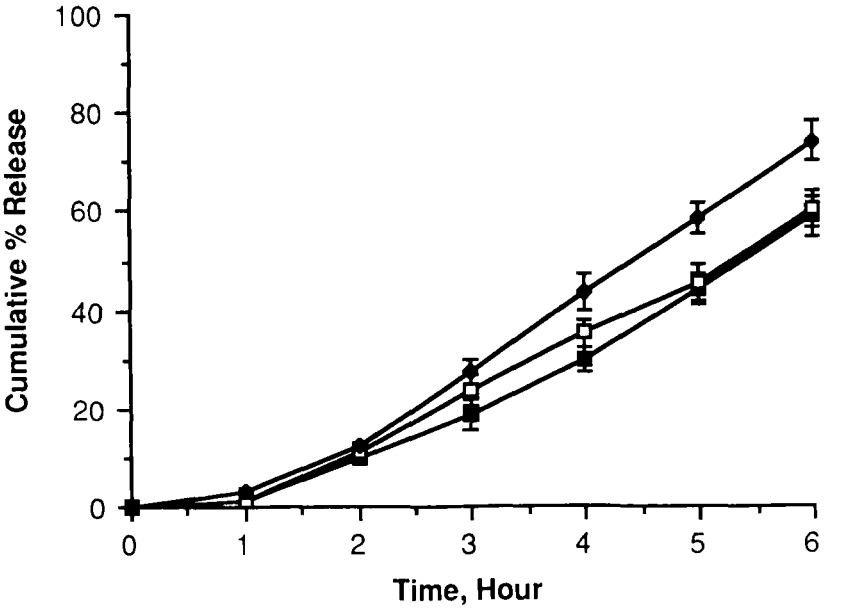

Figure 16. The Effect of Dissolution Medium pH on the Release Profiles of Potassium Chloride from Tablets Coated with Silicone Elastomer Containing 30% PEG 8000. Key: (◆) pH 8.0; (□) pH 5.0; and (■) pH 1.2.

further demonstrates the basic difference between a free film and an applied tablet film coating with respect to the resultant film properties. Since low PEG loaded silicone elastomer free films are mechanically stronger than the high PEG loaded film [1], the ability of the high PEG loaded silicone elastomer tablet coating to resist external mechanical impact would suggest that low PEG loaded tablet coatings are also durable and mechanically stable under the same testing conditions.

The Effect of Dissolution Medium pH on the Release Pattern of Potassium Chloride:

Figure 16 illustrates the release profiles of potassium chloride from tablets coated with 30% PEG

Table 4. Liquid Uptake Data for Hydrated Silicone Elastomer Coating Evaluated in Different Dissolution Media.

Medium pH	Liquid Uptake % (W/W)
8.0	36.2* (0.35)
5.0	32.9 (0.49)
1.2	33.1 (0.61)

* Mean and standard deviation for six samples.

8000 loaded silicone elastomer in three different pH media. The release of potassium chloride was faster in the pH 8.0 fluid than in the other two acidic fluids. The pH effect on the drug release characteristics of silicone elastomer coating was further investigated with respect to its influence on the extent of hydration of the film coating. The dissolution apparatus was used for this experiment. Three coated potassium chloride tablets were soaked in the dissolution medium (900 mls, 37 $\pm$ 0.5°C) for 30 minutes. The tablets were removed from the medium and the film coatings were separated from the remaining potassium chloride tablet core. The isolated tablet film coatings were returned to the medium and the experiment was continued for one hour at a paddle stirring rate of 100 rpm. The percent of liquid uptake by the hydrated film coating was determined following the same procedures as used for the free film hydration

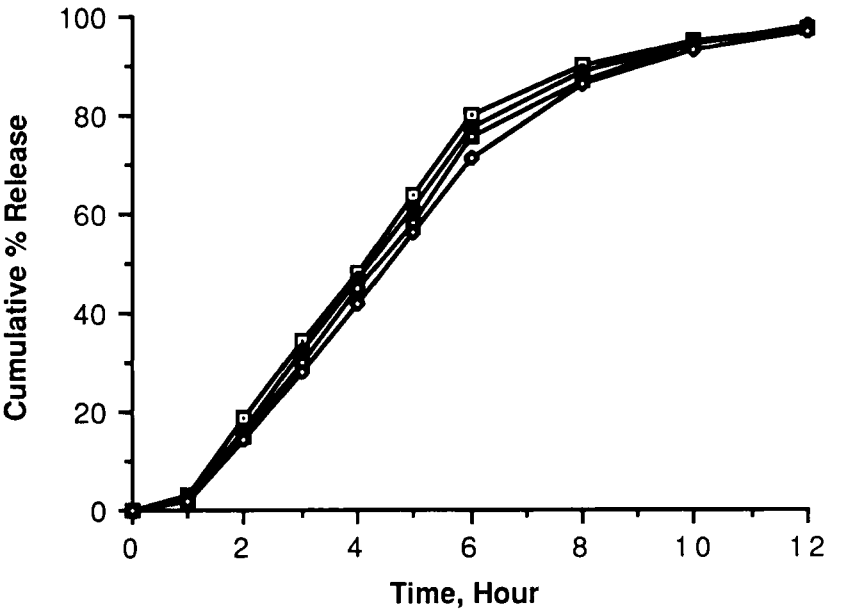

Figure 17. The Effect of Aging at 20°C on the Release Profiles of Potassium Chloride from Tablets Coated with Silicone Elastomer Containing 30% PEG 8000. Key: (⊡) 0 Week; (◆) 15 Weeks; (□) 30 Weeks; and (◇) 45 Weeks.

studies [1]. Table 4 gives the percent liquid uptake data for the hydrated tablet film coatings in different media. Since there was no increase in the percent of liquid uptake by the hydrated tablet film coatings after soaking in the media for an additional hour, it was concluded that the hydration of the tablet film coating reached equilibrium within the first one and one-half hours. As shown in Table 4, the liquid uptake in the pH 8.0 medium was significantly higher than those in the two acidic media.

This result suggests that the hydrated silicone elastomer tablet film coating swelled more extensively in the alkaline medium resulting in a more porous structure which may explain the higher drug release rate.

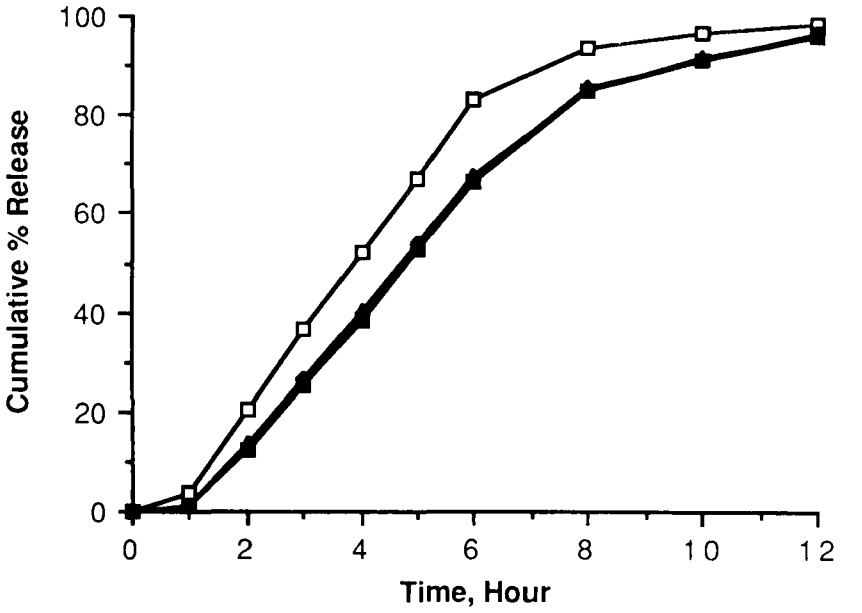

Figure 18. The Effect of Aging at 50°C on the Release Profiles of Potassium Chloride from Tablets Coated with Silicone Elastomer Containing 30% PEG 8000. Key: (⊡) 0 Week; (◆) 15 Weeks; (□) 30 Weeks; and (◇) 45 Weeks.

The Effect of Temperature and Time on the Release Pattern of Potassium Chloride from Stored Coated Tablets:

The release profiles of potassium chloride from tablets coated with 30% PEG 8000 loaded silicone elastomer, before and after aging at 20°C and 50°C for different time intervals are shown in Figures 17 and 18. Coated tablets aged at 20°C exhibited gradual decrease in the extent of drug release during the 45 weeks of storage. However, at 50°C, a dramatic decrease in the release of potassium chloride was noticed after the first 15 weeks of aging. The release profile remained unchanged for the remaining 30 weeks. This result indicates that after 15 weeks of elevated temperature storage, the coating matrix may achieve the

maximum coalescences leading to the consistent drug release profiles. In spite of the continuous decrease in the drug release from coated tablets stored at 20°C, the relatively moderate reduction in the extent of drug release observed during the 45 weeks of storage may not be a concern for the suitability of the coated tablets as a reliable drug delivery system over the shelf life of the product.

CONCLUSION

The release profiles of potassium chloride from tablets coated with PEG-silicone elastomers showed evidence of a zero order membrane controlled process. Studies of the effect of coating composition on the release rate of potassium chloride from coated tablets indicated the significance of the molecular weight of PEG used, the PEG loading level and the silicone to silica ratio in the coating. Scanning electron photomicrographs for tablet coating before and after hydration showed the existence of a porous structure which was formed during the coating process and after the leaching of the PEG in water. The influence of the coating components on the processing behavior of the coating dispersion was shown to play a significant role in determining the drug permeability of the resultant coating. The release rate of potassium chloride was a function of the coating weight. The heat treatment on the coated tablets resulted in slower release of the active ingredient. The effect of dissolution medium pH and room temperature aging on the drug release characteristics of the coated tablets was also demonstrated.

ACKNOWLEDGMENT

The study was supported by a grant from the Dow Corning Corporation.

NOTES

(a) Carver Laboratory Press, Model C, Fred S. Carver, Inc., Menomonee Falls, Wisconsin.

(b) Unit-Glatt Laboratory Six-Inch Coating Column, Glatt 7859 Holtinger/Brinzer (Germany).

(c) Dissolution Test Station, Model 72, Hansen Research Corporation, Northridge, California.

(d) Barnstead Conductivity Bridge Model PM-70C13, The Barnstead Company, Boston, Massachusetts.

(e) Osmette A Automatic Osmometer, Precision Systems, Inc., Sudbury, Massachusetts.

(f) Roche Friabilator, Model TA3R, Erweka, West Germany.

(g) Jeol Scanning Electron Microscope, Model JSM-T300, Jeol-Technics Company, Ltd., Tokyo, Japan.

(h) Freeze Dryer, Model 517C, The Virtis Company, Gardina, New York.

REFERENCES

(1) L.C. Li and G.E. Peck, Drug Dev. Ind. Pharm., in press (1988).

(2) G. Zografi, "Wetting, Adhesion and Polymer Coating", Presentation at the Arden House Conference, February, 1987.

(3) F.W. Goodhart, M.R. Harris, K.S. Murthy and R.U. Nesbitt, Pharm. Technol. 8(4), 64 (1984).