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WATER BASED SILICONE ELASTOMER CONTROLLED RELEASE TABLET FILM COATING 1: FREE FILM EVALUATION

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ABSTRACT

A latex which is a polymerized and cross-linked product of hydroxyendblocked polydimethylsiloxane and an alkoxysilane has been evaluated as a controlled release tablet film coating system. With adequate reinforcement of colloidal silica, the silicone elastomer latex formed solid elastomeric free films upon drying. Polyethylene glycols of different molecular weights were incorporated in the coating system to enhance the permeability of the silicone elastomer to hydrophilic and ionic species. Free films derived from the three-component silicone elastomer dispersions were evaluated by various physical and chemical methods with respect to their suitability as an aqueous controlled release film coating system.

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INTRODUCTION

Membrane controlled release tablet systems have played a major role in oral controlled drug delivery[1-3]. The controlled release membrane is generally formed on the tablet as a film coating. Polymeric controlled release coatings are usually applied to the tablet core from nonaqueous solvent systems. However, these organic solvents constitute the major drawback of solvent film coating because of the toxicity and inflammability of the solvent. Water has been a viable alternative to organic solvents in controlled release film coating. Currently, water based controlled release coatings have been limited to latex and pseudolatex of acrylate copolymers and ethylcellulose[4].

Because of the physiological inertness and outstanding biocompatibility, silicone elastomers have had a long history of biomedical applications[5]. Presently, silicone elastomers have become the indispensable part for many controlled drug delivery systems[6]. The silicone elastomer latex that has been investigated as a water based controlled release coating consists of a cross-linked hydroxyendblocked polydimethylsiloxane (PDMS). The suitability of this system for controlled release coating is primarily dependent on the permeability of the coating to various drug molecules. Due to the hydrophobic nature of PDMS, silicone elastomers are relatively impermeable to hydrophilic and ionic compounds[7]. The incorporation of water soluble components in a hydrophobic polymeric coating formulation to increase the membrane permeability has been well documented[8,9]. In this study, polyethylene glycols (PEGs) were incorporated into the silicone elastomer dispersions as the water soluble component.

In the development of a film coating system, the free film evaluation has been established as a valuable tool[10,11]. The fundamental material properties of the film system and the complex interactions between the film former and other additives are readily characterized and evaluated using comprehensive and well-controlled free film testing techniques. Additionally, data generated from free film assessment may be correlated with the *in situ* performance of coating formulations applied to the various solid dosage forms. In this study, free films prepared from the polyethylene glycol-silicone elastomer dispersions were characterized with respect to their physicochemical properties. The physical interactions between the film components were investigated and their influence on the free film properties were also determined.

EXPERIMENTAL

Materials:

The formulations for the controlled release coating system investigated in this study contained three major components: the silicone elastomer latex, the colloidal silica and the polyethylene glycol. The silicone elastomer latex was supplied by Dow Corning Company, Midland, Michigan. The latex was formed with a mean particle size of 200 nm, pH of 8.2 and a total solids content of 53.0% (w/w). The colloidal silica was obtained from Nalco Chemical Company, Chicago, Illinois, under the trade name of Nalcoag 1115. It is a silica sol with a mean particle size of 4.0 nm, pH of 10.7 and a solid content of 17.0% (w/w). The polyethylene glycols (PEG 8000, PEG 3350 and PEG 1450) used were NF grade products obtained from Ruger Chemical Company, Irvington, New Jersey.

Methods:

The quantity of each ingredient was measured by weight. Silicone elastomer latex and colloidal silica were well shaken prior to weighing. A predetermined weight of colloidal silica was premixed with a predetermined weight of silicone elastomer latex in a beaker using a stirring bar and a magnetic stirrer. The resultant binary dispersion was sonicated for 5 minutes while it was under continuous stirring. A predetermined weight of PEG was dissolved in an adequate amount of deionized water. The PEG aqueous solution was added to the sonicated binary dispersion. The final weight of the dispersion was adjusted by adding deionized water. The final dispersion was stirred for an additional 5 minutes.

Rheological Evaluation:

The rheological properties of the PEG-silicone elastomer dispersions were evaluated using a bob and cup viscometer system (Contraves Rheomatic 115/Rheoscan 100 Unit, Contraves AG, Zurich). Rheological measurements were done using the DIN 145 bob-cup measuring unit at 25°C. The testing dispersions were equilibrated in a 25°C water bath prior to the measurement. Rheograms for the dispersions were generated and the apparent viscosity values were determined.

Preparation of Free Films:

Silicone elastomer free films with or without PEG incorporated were prepared by a spraying technique. Owing to the extremely strong adhesion of silicone elastomer to most commonly used coating substracts, parafilm (American Can Company, Greenwich, Connecticut) was selected as the coating substract. A piece of

Parafilm was taped onto a glass plate (30 cm X 10 cm). The coating dispersion was applied onto the Parafilm as a fine spray (from a distance of one foot), using a chromatograph spray bottle and compressed air. During the spraying, the glass plate covered with Parafilm was held in a vertical position perpendicular to the spray. The rate of spraying was controlled by making only one pass from the left edge to the right edge of the glass plate. After each application, the glass plate was exposed to a hot air (150°F) stream delivered by a hose (8 cm in diameter), six inches above the plate. Time for each coating cycle (spraying and drying) was of a 1.0 minute duration. The thickness of the film was monitored by measuring the thickness of a small film piece cut and peeled from the middle section of the free film using a hand micrometer. When the desired film thickness was attained(180-200 nm), the free film was cut and peeled from the Parafilm and subsequently dried in a vacuum desiccator for at least 72 hours prior to the free film testing. Dispersions used for the free film preparation contained 25% (w/w) total solids and were freshly prepared.

Differential Scanning Calorimetry:

Differential Scanning Calorimetry was employed to investigate the interactions between PEG and the other two film components. Dispersions containing colloidal silica, silicone elastomer and a mixture of colloidal silica and silicone elastomer (1:1) in a concentration of 10% (w/w) were prepared separately. Each of the above dispersions was divided into five equal portions. To these divided portions, adequate amounts of a 10% (w/w) PEG 8000 aqueous solution were added to yield dispersions containing dissolved PEG and the insoluble dispersed phase(s) in five different ratios (1:1, 1:1.5, 1:2, 1:3

and 1:4). The final dispersion was mixed thoroughly. Ten grams of each of these dispersions were transferred to a plastic petri dish and placed in a 50°C oven overnight. The dried solid sample was subsequently powdered. The powdered samples represented dried solid mixtures of PEG 8000 in colloidal silica, silicone elastomer and a mixture of silicone and silica. The weight fractions of PEG 8000 in these solid mixtures were 0.5, 0.4, 0.33, 0.25 and 0.2, respectively. Samples containing 5.0 mg of PEG 8000 were accurately weighed and encapsulated in flat-bottom aluminum pans with crimped-on lids. These samples were heated and the thermograms were obtained using a Perkin-Elmer DSC-4 Differential Scanning Calorimeter connected to a strip chart recorder. The instrument was operated at a constant heating rate of 10°C per minute, with a constant range setting of 10 mcal per second and a chart speed of 10 mm per minute. The measurement of the area under the transition peak provides the direct base for the calculation of the energy associated with the phase transition. In the present study the area was determined by cutting out and weighing the traces of the transition profile[12] and the area determined was converted to the heat of transition[13]. Thermograms were also obtained from PEG-silicone elastomer mixed free films containing different molecular weight PEGs at different loading levels.

Determination of Polyethylene Glycol Leach Out and Film Hydration:

Free film disks which were cut from the free film sample using a cork borer were soaked in 300 mls of deionized water maintained at 37°C in a 400 ml water-jacketed beaker. Mixing was achieved using a magnetic stirrer and a floating magnetic stirring bar. At a predetermined time interval, soaked film disks were removed from the water. Surface adhering water droplets were blotted using a piece of filter paper and the soaked film disks were weighed immediately. The wet film disks were subsequently oven dried at 60°C for 24 hours and placed in a vacuum desiccator until a constant weight was reached. The percent weight loss from the dry film samples was calculated as follows:

$$\%\ \text{weight loss} = \frac{(\text{weight of dry film} - \text{weight of dry soaked film})}{\text{weight of dry film}} \times 100 \qquad \text{(Eq. 1)}$$

Since PEG was the major water soluble component in the mixed films, the percent weight loss from the dry films in water actually represented the amount of PEG leached out. The percent of water in a hydrated film sample was calculated as follows:

$$\%\ \text{water in hydrated film} = \frac{(\text{weight of soaked film} - \text{weight of dry soaked film})}{\text{weight of soaked film}} \times 100 \qquad \text{(Eq. 2)}$$

The percent of water in the hydrated film represented the extent of film hydration.

Stress-Strain Analysis for Dry and Hydrated Free Films:

Instron tensile testing has been extensively utilized in the evaluation of the mechanical properties of polymeric films systems[14]. The Instron Tensile Tester (Model 1130) equipped with a 2.0 Kg tension load cell was used in this study. Film specimens (9 cm X 1 cm) were cut from the dry and hydrated free film samples using a razor blade and a plexiglass template which was 1 cm in width and 9 cm in length. The hydrated free films were prepared by soaking the dry films in water maintained at 37°C for 12 hours. The thickness of each film specimen was the mean of five separate measurements taken in the middle 4 cm section of the specimen using a hand micrometer. The film specimen was clamped by an upper and lower flat-faced grip. The dimension of the grip face was 1 cm in width and 2.5 cm in length. To avoid any damage to the film specimens by the sharp edge of the metal grips, a piece of silicone rubber with a thickness of 2 mm was affixed to the grip surface with epoxy glue. The instrument gauge length was set at 4.0 cm. Perfect alignment of the film specimen between the upper and the lower grips was checked visually before the test started. The instrument was calibrated using a 500.0 g weight and the full scale of the strip output was set at 500.0 g or 1,000 g with the sensitivity setting, depending on the breaking load of the specimen. The cross-head speed was 1.0 cm/min. and the strip chart recorder speed was set at 10 cm/min. From the recorder output of applied load versus displacement, stress-strain profiles were generated. Stress-strain data were only accepted from those specimens which ruptured in the middle section of the stressed films. Stress-strain parameters, including the ultimate tensile length, the Young's modulus and the elongation at break were determined for each film specimen[14].

RESULTS AND DISCUSSION

Rheological Evaluation:

The undiluted silicone elastomer latex exhibited distinctive pseudoplastic flow behavior with an apparent viscosity of 58 cps determined from the linear portion of the rheogram. As the latex was diluted, the viscosity decreased dramatically. Newtonian flow was noticed for samples with latex concentration below 40.0%. Due to the low solids content, the colloidal silica used in this study yielded a viscosity of 4.0 cps. The polyethylene glycols (PEGs) formed aqueous solutions with varying viscosities which increased with increasing molecular weight and concentration. Solution of PEG 8000 yielded the highest viscosity and showed the most pronounced concentration dependent rheological properties. In order to study the concentration dependent rheological properties of the PEG-silicone elastomer coating dispersions, three different coating formulations which contained a total solids consisting of silicone elastomer and colloidal silica in a ratio of 2 to 1 and 30% (w/w) PEG of three different molecular weights were evaluated. Dispersions with a total solids content equal to or less than 30% exhibited Newtonian flow. Figure 1 depicts the effect of the PEG molecular weight and the total solids content on the apparent viscosities of the PEG-silicone elastomer dispersions. With the same total solids content, dispersions containing PEG of higher molecular weight was shown to be more viscous. As the solids content increased, a more pronounced viscosity build-up was also observed in dispersions formulated with high molecular weight PEG. The relatively low viscosity associated with the PEG-silicone elastomer dispersions with the compositions evaluated in this study is an obvious advantage in tablet film coating because the use of concentrated coating dispersions allows the reduction in coating time, in labor and energy consumption as well as less exposure of the tablet core to moisture and heat during the coating process.

Differential Scanning Calorimetry Studies of Polyethylene Glycol-Silicone Elastomer Mixed Films:

Characteristic endothermal transition peaks were shown in the thermograms for the three different

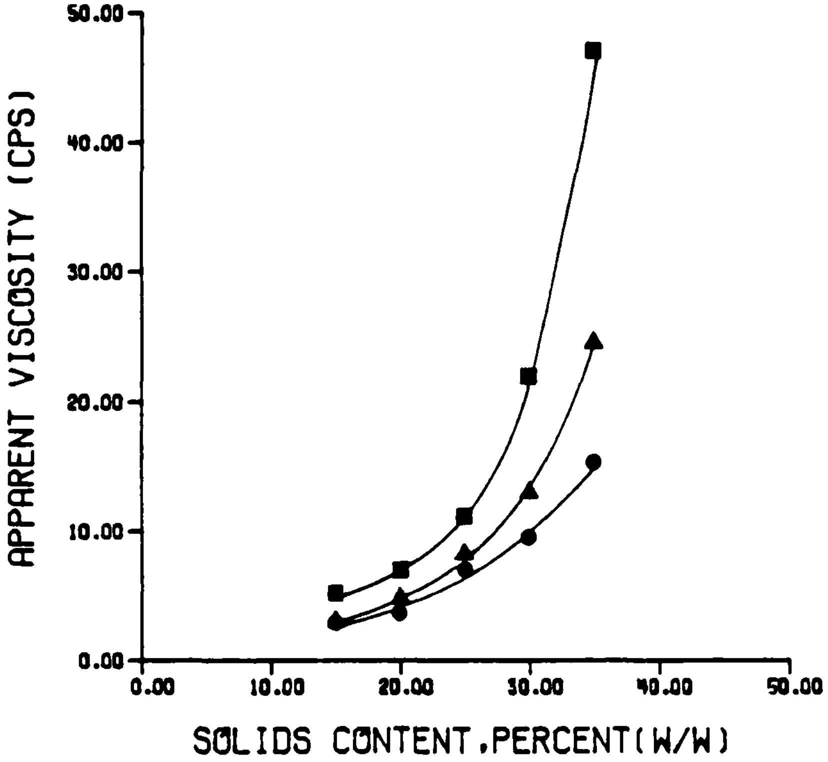

FIGURE 1

The Effect of Total Solids Content on the Apparent Viscosity of Dispersions with a Total Solids Consisting of Silicone and Silica in a Ratio of 2 to 1 and 30% Polyethylene Glycol. Key: (■) PEG 8000; (▲) PEG 3350; and (●) PEG 1450.

molecular weight PEGs used in this study. The melting points determined from the transition peaks for PEG 8000, 3350 and 1450 were 60°C, 56°C and 42°C, respectively. No thermal change was detected for silica and silicone elastomer over the temperature scanning range used for the PEGs. These characteristic transition peaks provide the best reference for the detection of solid interaction between PEG(s) and the other film forming components. Figure 2 shows the thermograms for various PEG-silicone elastomer mixed films containing PEG at three different loading levels.

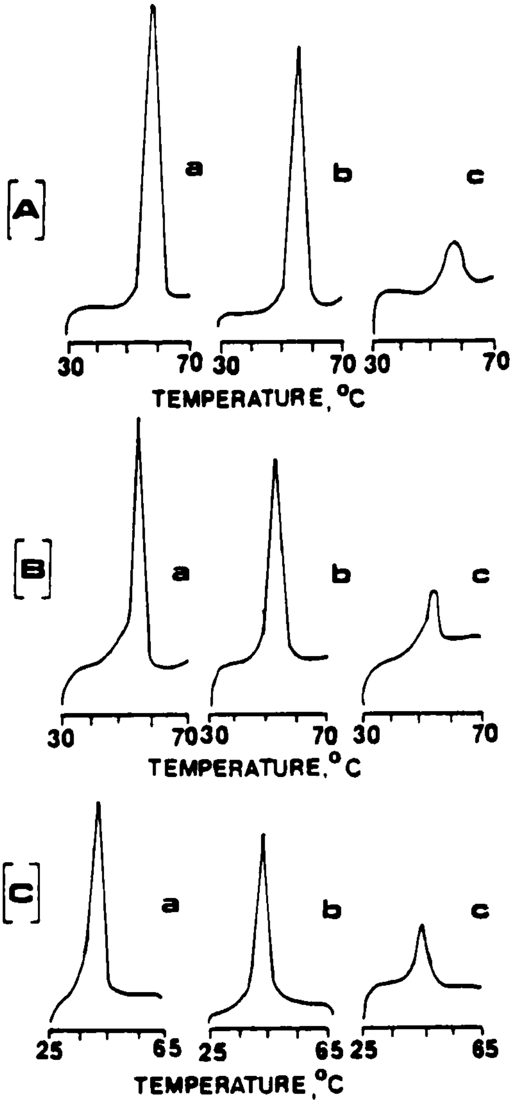

FIGURE 2

DSC Thermograms for Polyethylene Glycol-Silicone Elastomer Mixed Films Containing Three Different Molecular Weights of Polyethylene Glycol at Three Different Loading Levels. Key: (A) PEG 8000; (B) PEG 3350; and (C) PEG 1450. Polyethylene Glycol Loading Levels, (a) 30%; (b) 20%; and (c) 10%.

Since the sample weight of each mixed film was adjusted to contain the same amount of PEG (5 mg), the reduction in the PEG transition peak as observed in the low PEG loaded films indicated significant interaction between PEG and the other film components.

Thermograms obtained from sample of PEG 8000 and silicone elastomer dried mixtures with PEG weight fractions of 0.5, 0.4, 0.33, 0.25 and 0.2 showed no noticeable alteration of the position and size of the transition peak. Thermograms for dried mixtures of PEG 8000 and colloidal silica showed that the PEG phase transition peak shifted to a lower temperature and the size of the peak decreased as the proportion of PEG in the mixtures decreased. The enthalpy changes (ΔH) as measured by the area of the PEG transition peak in these thermograms were determined and used to quantitate the extent of interaction between these components. Figure 3 shows the relationship between the enthalpy change for PEG 8000 and the weight fraction of PEG in the mixtures. A ΔH value corresponding to 5.0 mg of free PEG 8000 was obtained from all PEG-silicone elastomer mixtures regardless of the PEG weight fractions. This result indicates that interaction between PEG and silicone polymer is insignificant. The pronounced interaction between PEG 8000 and silica is substantiated by the drastic decrease in the H values associated with the PEG-silica mixtures. It is evident that when PEG weight fraction was below 0.33, no thermal response of the PEG in the mixture was recorded. A more gradual decrease in the ΔH value for samples composed of PEG 8000 and a 1:1 mixture of silicone and silica is also seen in Figure 3. The hydroxyl groups on the colloidal silica surface have been shown to interact with polymers with hydroxyl functionality through hydrogen bonding[15].

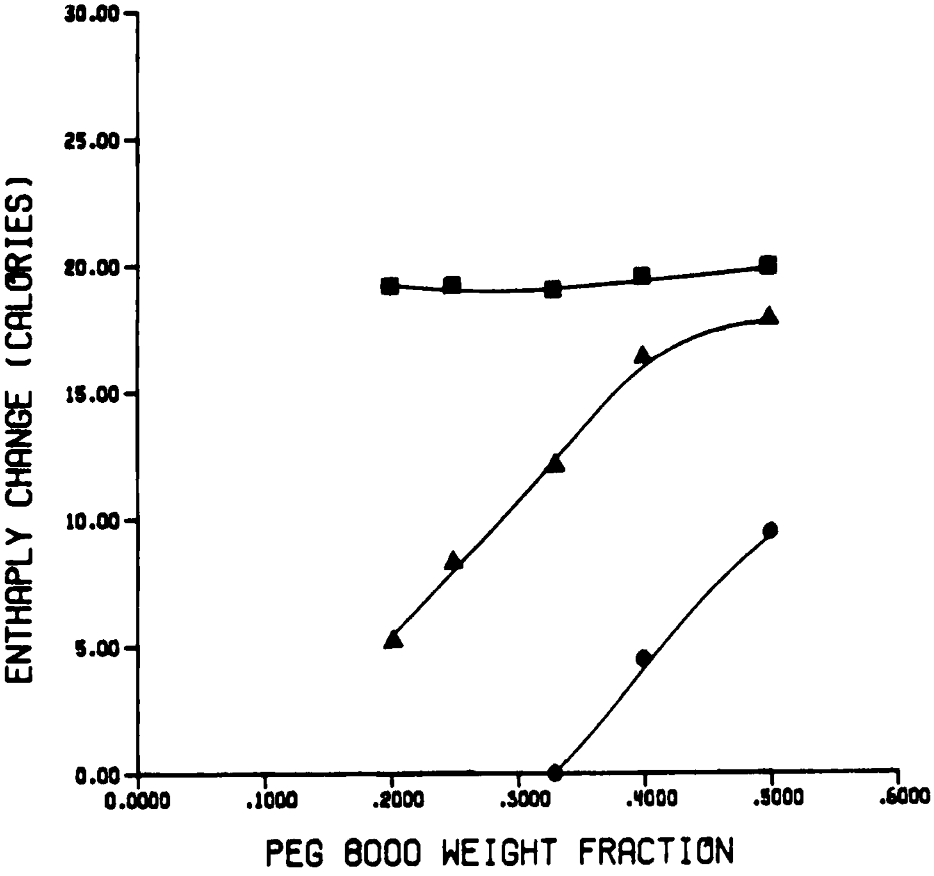

FIGURE 3

The Effect of Polyethylene Glycol 8000 Weight Fraction on the Enthalpy Change for Various Dried Mixtures. Key: (■) PEG 8000-Silicone Elastomer; (▲) PEG 8000-Silica Filled Silicone Elastomer; and (●) PEG 8000-Colloidal Silica.

With the two end hydroxyl groups and the repeating ether linkages, PEG 8000 is probably capable of hydrogen bonding to the surface silanol groups of the colloidal silica. At low PEG weight fractions, the majority of the PEG 8000 present is likely hydrogen bonded to the silica. This molecular interaction would result in the loss of crystallinity and the consequent lack of thermal response of PEG 8000 in the mixture. This preferential interaction between PEG and silica may significantly disrupt the filler-polymer linkages between silica and silicone polymer, leading to a considerable attenuation of the mechanical reinforcement of the elastomer networks.

The Extent and Rate of Polyethylene Glycol Leachout and Film Hydration:

After soaking in deionized water (37°C) for 12 hours, the percent weight loss from the silicone elastomer free films prepared with different silicone to silica ratios was found varying from 2.5% to 3.0%. The water leachable substances may consist of the soluble silicate and alkali stabilizer from the colloidal silica dispersion as well as the surfactant and pH modifier present in the silicone elastomer latex. Although there was negligible weight loss in water, silicone elastomer free films absorbed significant amounts of water. Figure 4 represents the hydration (water uptake) profiles for various silicone elastomer free films in deionized water during a 12-hour test period. These profiles showed a rapid initial water uptake phase within the first hour followed by a slow linear increase. This extensive swelling behavior of this film system could be attributed to the presence of the hydrophilic silica phase in the film matrix.

Figure 5 shows the rate and extent of the percent weight loss from PEG-silicone elastomer mixed films containing 10%, 20% and 30% PEG 8000, respectively. The leaching of water soluble ingredients from the 10% PEG loaded mixed films occurred at a comparatively slower rate and only about 9% loss in the dry film weight was obtained after soaking in water for 12

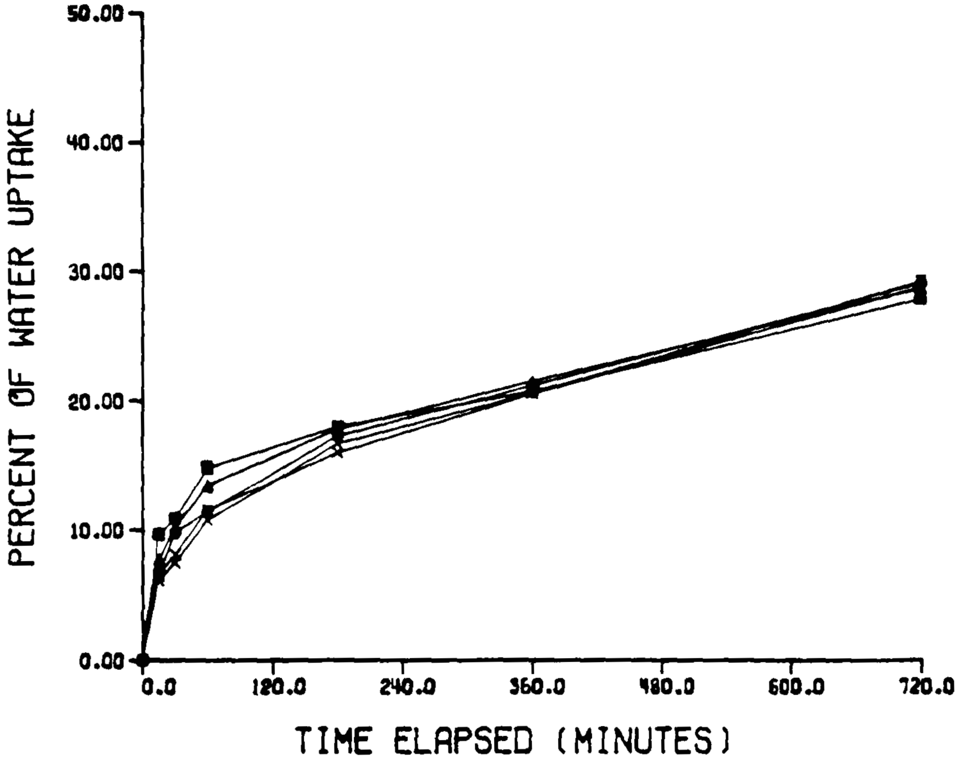

FIGURE 4

The Percent Water Uptake by Hydrated Silicone Elastomer Free Films with Five Different Silicone to Silica Ratios. Key: (■) 2 to 1; (▲) 3 to 1; (●) 4 to 1; (X) 6 to 1; and ($\overline{\text{X}}$) 9 to 1.

hours. As the PEG loading level of the film increased to 20% and 30%, the rate of leaching was considerably faster and the extent of leaching approached completion after the first hour. Since PEG 8000 is the major water soluble ingredient in the mixed film, particularly at the high PEG loading levels, the percent weight loss of the film in water actually represents the amount of PEG leached out. Therefore, a comprehensive consideration of the data presented in

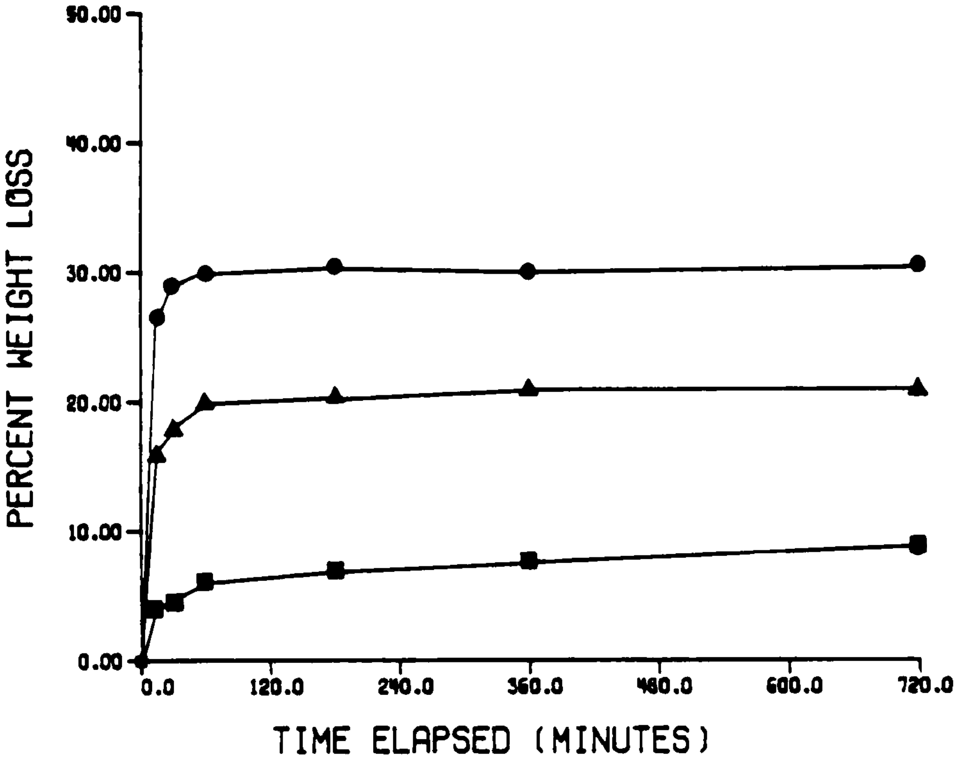

FIGURE 5

The Percent Weight Loss from Polyethylene Glycol-Silicone Elastomer Mixed Films Containing Silicone and Silica in a Ratio of 2 to 1 and Polyethylene Glycol 8000 at Three Different Loading Levels. Key: (■) 10%; (▲) 20%; and (●) 30%.

Figure 5 leads to the conclusion that nearly complete leaching of PEG 8000 was achieved in water for films with 20% and 30% PEG content, within the first hour. For the 10% PEG loaded mixed films, considering the amount of leachables that are also available from the silicone elastomer matrix, only about 70% of the PEG incorporated was released in 12 hours. The leaching of PEG 3350 and PEG 1450 from mixed silicone elastomer films was shown to follow the same pattern as PEG 8000.

TABLE 1

The Effect of Polyethylene Glycol Molecular Weight and Level on the Maximum Percent Weight Loss for Various Mixed Films Soaked in Water for 12 Hours.

	Percent Weight Loss		
	PEG Loading Level (%, w/w)		
PEG Molecular Weight	10	20	30
8000	8.95* (0.34)	21.45 (0.33)	31.85 (0.45)
3350	9.27 (0.18)	22.18 (0.23)	32.05 (0.24)
1450	10.43 (0.20)	21.95 (0.33)	32.23 (0.34)

* Mean and standard deviation for six samples.

Table 1 presents the maximum percent weight loss from various PEG-silicone elastomer mixed films. The leaching of PEG from the mixed films can be considered as being a matrix-controlled diffusion process which 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. Therefore, water penetration into the PEG-silicone elastomer matrix should take place prior to the PEG leaching. Figure 6 illustrates the rate and extent of water uptake (film hydration) for silicone elastomer films comprised of three different loading levels of PEG 8000. After a relatively slow initial phase, the 10% PEG loaded films yielded a higher water content than the 20% PEG loaded films. It is conceivable that the entrapped PEG in the

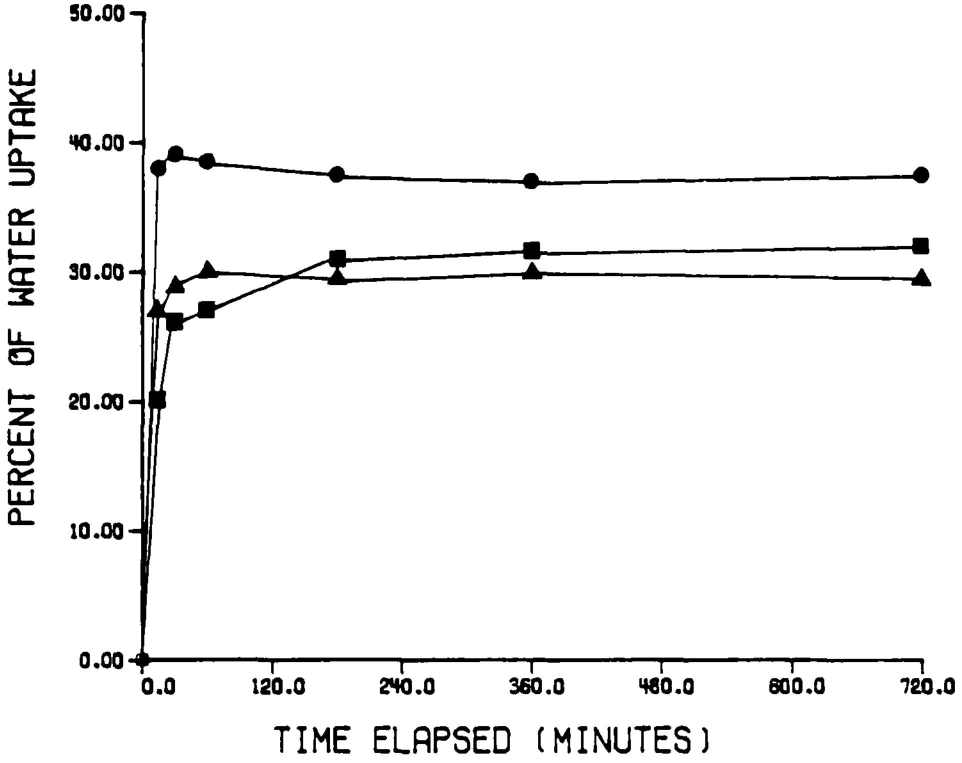

FIGURE 6

The Percent Water Uptake by Hydrated Polyethylene Glycol-Silicone Elastomer Mixed Films Containing Silicone and Silica in a Ratio of 2 to 1 and Polyethylene Glycol 800 at Three Different Loading Levels. Key: (■) 10%; (▲) 20%; and (●) 30%.

10% PEG loaded films would dissolve in the imbibed water and form vesicles of concentrated solution which subsequently generated an osmotic pressure gradient within the hydrated film matrix. The osmotically driven flow of water into the film may account for the higher equilibrium water content in the resultant hydrated films. Silicone elastomer mixed films containing 20% and 30% PEG 8000 achieved the maximum hydration within the first hour in water. From the

TABLE 2

The Effect of Polyethylene Glycol Molecular Weight and Loading Level on the Maximum Percent Water Uptake by Various Mixed Films Soaked in Water for 12 Hours.

PEG Molecular Weight	Percent Water Loss PEG Loading Level (%, w/w) 10	 20	 30
8000	32.10* (0.61)	28.27 (0.50)	37.63 (1.55)
3350	32.10 (1.24)	26.12 (0.31)	31.65 (1.27)
1450	25.83 (0.61)	20.22 (0.51)	26.77 (1.53)

* Mean and standard deviation for six samples

comparison of the PEG leaching profiles with the film hydration profiles, it is evident that these two processes appear to occur simultaneously. The film hydration profiles for silicone elastomer mixed films containing PEG 3350 and PEG 1450 exhibited the same pattern as those presented in Figure 6. The equilibrium water contents for various hydrated films are given in Table 2. At all three loading levels, films incorporated with PEG 8000 and PEG 3350 attained a higher equilibrium water content than those containing PEG 1450. Furthermore, it is also noted that no significant difference in the extent of hydration was found for films containing PEG 8000 and PEG 3350 at 10% and 20% loading levels; however, a significantly higher water content was shown in the 30% PEG 8000 loaded film. It is conceivable that the free water present in a hydrated PEG-silicone elastomer mixed film is located in the void space generated by the leaching of PEG, the pores existing in the dry film as well as the interstitial space within the swollen silicone elastomer matrix. The difference between the water content of the hydrated film and the amount of PEG leached out from the dry mixed film may actually represent the porosity of the dry film and the extent of swelling of the hydrated film. Since the water content of the hydrated 10% PEG loaded films was considerably higher than the amount of PEG leached out from the dry film and was also greater than the water content of the 20% PEG loaded films, appreciable swelling of the low PEG loaded silicone elastomer matrix was demonstrated. Furthermore, the extent of film hydration associated with the PEG 1450 containing mixed films was significantly less than those achieved by the mixed films containing the other two high molecular weight PEGs. This result may indicate that the PEG 1450 loaded dry films were more compact and/or the extent of swelling of the silicone elastomer matrix was less dramatic in water.

The PEG leaching and film hydration data from this study appear to support the speculation that incorporation of PEG in the silicone elastomer film facilitates the formation of a porous film structure in an aqueous medium, which may be essential to the transport of hydrophilic and ionic species through the hydrophobic silicone film matrix. The significant influence of PEG molecular weight on the extent of film hydration may suggest that the use of different molecular weight PEGs may be an effective formulation approach to produce silicone elastomer tablet coatings with varying drug release characteristics.

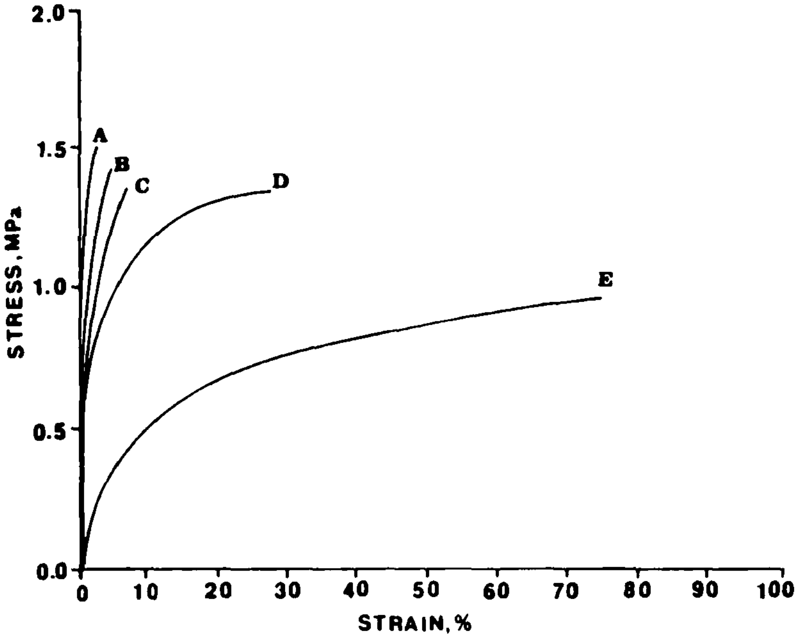

FIGURE 7

Stress-Strain Profiles for Silicone Elastomer Free Films with Five Different Silicone to Silica Ratios. Key: (A) 2 to 1; (B) 3 to 1; (C) 4 to 1; (D) 6 to 1; and (E) 9 to 1.

Stress-Strain Analysis of Dry and Hydrated Free Films:

The silicone elastomer latex formed a gummy material after the evaporation of water. The addition of colloidal silica in the latex converted the silicone to an elastomeric material upon drying. The effect of the addition of silica to the silicone elastomer is illustrated in Figure 7. Samm et al.[16] suggested that cast films derived from dispersions of colloidal silica and silicone elastomer latex consist of a silicone hydrophobic phase and a silica hydrophilic phase. Biphasic stress-strain curves for silica filled silicone elastomer cast films were obtained. They suggested that the initial high modulus part of the

TABLE 3

The Effect of Silicone to Silica Ratio on the Stress-Strain Parameters for Dry Free Films.

	Silicone to Silica Ratio				
	2	3	4	6	9
Tensile Strength (MPa)	1.65* (0.043)	1.62 (0.099)	1.36 (0.063)	1.56 (0.053)	1.82 (0.147)
Young's Modulus (MPa)	68.65 (2.864)	63.37 (5.406)	45.80 (3.416)	32.61 (2.363)	11.36 (2.049)
Elongation (%)	2.68 (0.531)	3.42 (0.662)	6.58 (0.917)	23.33 (3.525)	85.67 (6.676)

* Mean and standard deviation for six samples.

curve corresponded to the response of the hydrophilic silica and the region of lower modulus at high strain was the response of the rubber-like hydrophobic silicone. As illustrated in Figure 7, stress-strain curves with the biphasic characteristics were only obtained from films with a high silicone to silica ratio (low silica content). As the proportion of silica increased, the expanding hard silica region rendered the films more brittle. From each stress-strain profile, three parameters were determined. Table 3 shows the effect of the silicone to silica ratio of the film on the ultimate tensile strength, the Young's modulus and the percent of elongation. Ultimate tensile strength fell from 1.65 MPa for films with a silicone to silica ratio of 2 to 1, to 1.36 MPa for films with a 4 to 1 ratio. However, beyond this

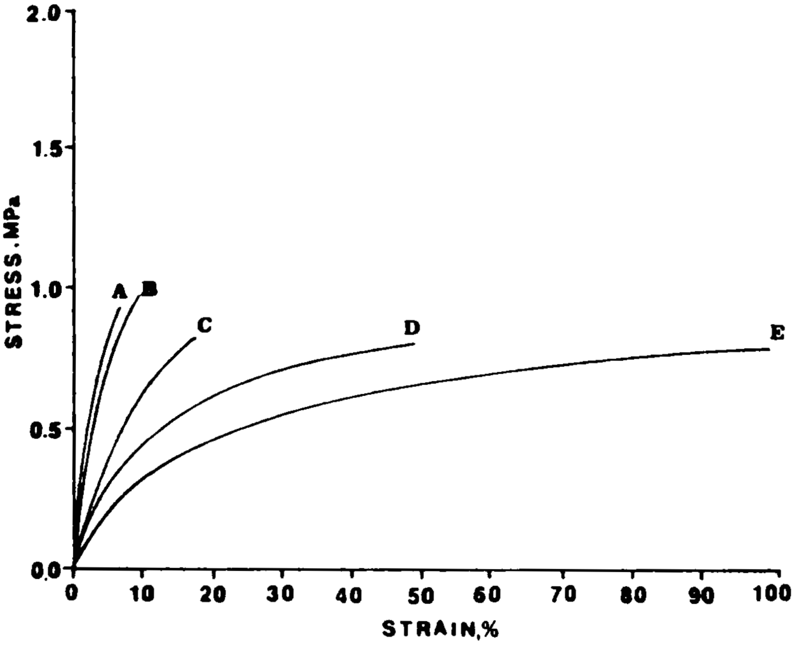

FIGURE 8

Stress-Strain Profiles for Hydrated Silicone Elastomer Free Films with Five Different Silicone to Silica Ratios. Key: (A) 2 to 1; (B) 3 to 1; (C) 4 to 1; (D) 6 to 1; and (E) 9 to 1.

ratio, higher tensile strength was shown with increasing silicone content in the films. Over the same range of silicone to silica ratio, the Young's modulus decreased from 70 MPa to 10.0 MPa, while the percent elongation increased from 2.7% to 85.7%. It has been stated that silica reinforcement of a silicone elastomer involves the formation of filler-polymer linkages of different natures[6]. In a silicone elastomer latex film system, the interaction between the polymer and the added silica filler may be confined to the surface of the elastomer latex particles since

TABLE 4

The Effect of Silicone to Silica Ratio on the Stress-Strain Parameters for Hydrated Free Films.

	Silicone to Silica Ratio				
	2	3	4	6	9
Tensile Strength (MPa)	0.96* (0.034)	1.09 (0.085)	0.88 (0.068)	1.12 (0.091)	1.66 (1.603)
Young's Modulus (MPa)	17.10 (1.351)	16.95 (2.294)	10.62 (0.879)	5.93 (0.466)	2.23 (0.243)
Elongation (%)	6.38 (0.981)	10.42 (1.656)	17.45 (0.718)	48.83 (3.573)	118.03 (6.304)

* Mean and standard deviation for six samples.

the penetration of the colloidal silica particles into the interior of the latex particles is very unlikely. Therefore, a silica filled silicone elastomer derived from a latex system is markedly weaker than the conventional silica filled vulcanized silicone elastomer[17]. Figure 8 shows the stress-strain responses of various hydrated silicone elastomer films. When compared to the stress-strain profiles for the dry films (Figure 7), it appears that water uptake (film hydration) considerably reduced the tensile strength and the Young's modulus, but markedly increased the percent elongation (Table 4). Owing to the hydrophobic nature of polydimethylsiloxane, water present in the hydrated films was probably excluded from the silicone polymer and primarily associated with the hydrophilic silica. Through the polar interaction between water and silica,

silica to silicone linkages as well as silica to silica linkages were effectively weakened, resulting in the pronounced plasticization effect of water.

Table 5 presents the stress-strain parameters for PEG-silicone elastomer mixed films consisting of PEG 8000, PEG 3350 and PEG 1450 at three different loading levels. The silicone to silica ratio in these films was fixed at 2 to 1. It is evident that an increase in PEG loading level of the mixed films from 0 to 20% resulted in a steady increase of the tensile strength. It should also be noted that little difference was found between films formed with different molecular weight PEGs. However, at 30% PEG level, the tensile strength for films consisting of PEG 8000 and PEG 3350 declined, while the PEG 1450 loaded mixed film showed no appreciable change. When the films contained 10% PEG, they showed no significant change in the Young's modulus as compared with the silicone elastomer free film. A dramatic increase in Young's modulus was observed for mixed films containing 20% and 30% PEG. It is also apparent that films formed with low molecular weight PEG consistently yielded lower Young's moduli. The incorporation of 10% PEG in the silicone elastomer film was shown to achieve more than three-fold increase in percent of elongation. As the PEG content increased, the extent of elongation decreased considerably. The results of this experiment support the concept that, at low loading levels, the PEGs functioned as a plasticizer in the silicone elastomer mixed films, and reduced the brittleness and restored the ductility of the silica filled silicone elastomer. The plasticizing effect of PEG may be attributed to the polar interaction between this polymer and silica as illustrated in the DSC results. At higher PEG levels, the plasticizing effect of PEG was possibly prevented because of the brittleness of the

TABLE 5

The Effect of Polyethylene Glycol Molecular Weight and Loading Level on the Stress-Strain Parameters for Dry Mixed Films.

PEG Molecular Weight	Loading Level (%)	Tensile Strength (MPa)	Young's Modulus (MPa)	Elongation (%)	T/E* X 100
8000	10	2.32** (0.141)	72.72 (5.054)	6.71 (1.571)	3.20 (0.345)
	20	3.36 (0.373)	147.75 (4.972)	3.33 (0.876)	2.27 (0.226)
	30	2.40 (0.325)	190.55 (7.011)	1.18 (0.286)	1.26 (0.153)
3350	10	2.66 (0.407)	71.51 (5.43)	7.30 (1.476)	3.78 (0.775)
	20	3.06 (0.282)	121.63 (8.625)	4.50 (0.447)	2.53 (0.212)
	30	2.49 (0.380)	153.72 (11.50)	1.88 (0.531)	1.61 (0.210)
1450	10	2.42 (0.429)	58.95 (4.376)	6.50 (0.707)	4.10 (0.832)
	20	3.13 (0.098)	99.47 (6.643)	6.00 (0.949)	3.15 (0.183)
	30	3.22 (0.276)	135.50 (6.566)	3.15 (0.455)	2.38 (0.125)

* Ratio of tensile strength and Young's modulus.

** Mean and standard deviation of six samples.

unbound crystalline PEGs. In comparison with PEG 8000 and PEG 3350, PEG 1450 yielded mixed films with improved mechanical properties at all three loading levels. Two probable causes exist for this molecular weight effect. First, PEG 1450, with its smaller molecular size and high diffusivity, may interact more strongly with silica, resulting in a more efficient plasticization. Second, the relatively soft nature of PEG 1450 may confer a moderate degree of plasticity to the resultant mixed films.

The three stress-strain parameters discussed above are good indicators for the mechanical properties of the film. However, the separate consideration of these parameters may have less significant implication to the in situ performance of the film on a tablet surface. Rowe proposed that the in situ performance of a film was better reflected by the ratio of the tensile strength and the Young's modulus (T/E). A decrease in this ratio was shown to highly correlate with the increase in the incidence of coating defects[18]. Table 5 also shows the T/E ratios for various PEG-silicone elastomer mixed films. It is apparent that an increase in the PEG loading level in the mixed film lead to a decrease in this ratio indicating that the high PEG loaded silicone elastomer tablet coating may be more susceptible to physical defect. Mixed films loaded with PEG 1450 yielded a larger T/E ratio than those prepared with the high molecular weight PEGs.

The physical integrity of a controlled release tablet coating in an aqueous medium is of utmost importance in providing and maintaining a consistent and reliable drug delivery rate. Therefore, the mechanical properties of the hydrated film system are of practical interest. In water, the leaching of PEG and the uptake of water dramatically altered the

TABLE 6

The Effect of Polyethylene Glycol Molecular Weight and Loading Level on the Stress-Strain Parameters for Mixed Films After Hydration.

PEG Molecular Weight	PEG Loading Level (%)	Tensile Strength (MPa)	Young's Modulus (MPa)	Elongation (%)
8000	10	1.21* (0.208)	5.88 (0.538)	24.33 (4.262)
	20	1.31 (0.131)	9.84 (1.034)	24.50 (2.430)
	30	0.57 (0.023)	5.57 (0.471)	16.08 (1.304)
3350	10	1.56 (0.136)	6.82 (0.525)	27.17 (3.342)
	20	1.72 (0.150)	13.90 (0.760)	18.50 (1.049)
	30	0.66 (0.061)	6.77 (1.096)	10.98 (1.360)
1450	10	1.65 (0.153)	6.65 (0.431)	28.92 (2.354)
	20	2.41 (0.213)	27.99 (4.847)	19.17 (2.229)
	30	1.25 (0.093)	18.14 (1.445)	11.83 (1.169)

* Mean and standard deviation for six samples.

stress-strain responses for PEG-silicone elastomer mixed films. Table 6 presents the stress-strain parameters for hydrated films obtained from PEG-silicone elastomer mixed films. The comparison between Tables 5 and 6 indicates that the hydrated films were considerably more elastic but relatively weaker than the dry films. Amongst the three PEG loading levels, 20% PEG loaded mixed films yielded hydrated films with the highest tensile strength and Young's modulus, whereas the greatest percent of elongation was seen in the hydrated films derived from 10% PEG loaded dry films. Furthermore, at the same PEG loading level, mixed films consisting of lower molecular weight PEG yielded hydrated films with higher tensile strength and Young's modulus, while the greatest percent of elongation was demonstrated by hydrated films of mixed films containing PEG 8000. The complex relationship between the stress-strain parameters for the hydrated films and the PEG molecular weight and loading level may be explained in the light of PEG leaching and film hydration associated with these mixed films. As noted in the previous section, the 10% PEG loaded mixed films exhibited the most extensive swelling in water. It is conceivable that the swelling of the elastomer reduced cohesive strength of the elastomer networks resulting in a considerable decrease in both tensile strength and Young's modulus, and an increase in elongation. For the 30% PEG loaded mixed films, the mechanical properties of the dry films were weakened because of the presence of a brittle and crystalline PEG solid phase. The mechanical properties of the hydrated films were further weakened by the extensive leaching of PEG which would produce a sponge-like microstructure in the film. At 20% PEG loading level, the hydrated films exhibited improved mechanical properties because of the moderate degree of hydration and less PEG leaching. The influence of PEG molecular weight on the stress-strain responses for the hydrated films can also be related to its effect on the extent of film hydration. At the same loading level, mixed films containing high molecular weight PEG hydrated more extensively in water resulting in weaker hydrated films.

CONCLUSION

Silicone elastomer latex formulated with colloidal silica and polyethylene glycol (PEG) produces solid continuous free films. The silica content, the molecular weight of PEG used and the PEG loading level of the mixed films are formulation variables which dictate the physical properties of the mixed films. The complete leaching of PEG(s) from the mixed films and the extensive film hydration in water indicates that the film forms a highly porous structure which may provide water filled diffusion channels for polar or ionic molecules.

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