Mechanisms to Control Drug Release from Pellets Coated with a Silicone Elastomer Aqueous Dispersion

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The mass transport of two different compounds through polydimethylsiloxane (PDMS)–silica films was investigated to demonstrate qualitatively how this coating system can alter the release of various compounds. Various ratios of PDMS elastomer and silica were used to coat monodisperse particle-sized pellets layered with an ionizable compound (tartrazine) and a nonionized compound (acetaminophen). The 2:1 PDMS–silica composition containing the polyethylene glycol (PEG) 8000 pore former allowed mainly pore transport through void spaces in the PDMS films. Both compounds rapidly diffused through the film as a result of the solubilization and subsequent removal of the PEG 8000 from the film matrix. As the PDMS–silica ratios in the films changed from a 1:1 to a 2:1 to a 4:1 (all without polyethylene glycol 8000) coating formulation, the differences in release rate between acetaminophen and tartrazine changed. The lower ratio of PDMS–silica allowed much faster tartrazine diffusion compared to acetaminophen. As the ratio increased from 1:1 to 2:1, the two compounds were released at similar rates. When the ratio reached 4:1, acetaminophen was released significantly faster than tartrazine. Explanations for these differences and the mechanisms controlling the drug release are discussed in the text. In some circumstances, osmolality and pH affected drug release from dosage forms coated with this polymer system. This study demonstrated that utilization of this polymer system offers a useful tool for the formulation scientist to modify release rates of ionic and nonionic drug substances.

KEY WORDS: acetaminophen; tartrazine; drug release; silicone elastomer dispersion; film-coated pellets; latexes; polydimethylsiloxane; polymeric films; pore former; colloidal silica.

INTRODUCTION

Polyorganosiloxane chemistry has been evaluated for more than 100 years. It has been extensively reviewed and discussed in a recently published textbook (1). Some of the properties of polydimethylsiloxane (PDMS) include good thermal stability, low surface energy, a solubility parameter of approximately 7.4–7.6 $(cal/cm^3)^{1/2}$ (1–3), and a glass transition temperature of $-123°C$ (4).

Although the literature is replete with information about mass transport through PDMS membranes (5–20), only recently was an aqueous-based PDMS polymeric coating system developed for the pharmaceutical industry (21). This controlled-release film coating system is composed of silica and an emulsion, which is a polymerized and cross-linked product of hydroxy end-blocked polydimethylsiloxane and an alkoxysilane (21,22).

The aqueous-based PDMS system has been characterized in a free film form (23) and as a coating system (24–28). Due to the poor mechanical strength of PDMS, colloidal silica is added to the polymer coating suspension to strengthen the coating (1,22). In addition, a pore-forming agent can be added to increase the coating layer permeability to the penetrating species of interest. The purpose of this work is to evaluate how the release mechanism for this coating material can be altered by changing the coating composition. By using tartrazine (TART) and acetaminophen (APAP), ionic and nonionic species, respectively, the dominant mechanisms can be determined.

MATERIALS AND METHODS

Materials

The silicone elastomer X7-2837 latex, hereafter designated PDMS, was supplied by Dow Corning Company, Midland, MI. The latex suspension has a mean particle size of 250 nm, a pH of 7–8, and a total solids content of approximately 52% (w/w). The colloidal silica solution or sol (Nalcoag 1115) was manufactured by Nalco Chemical Company, Chicago, IL, and supplied by the Dow Corning Company. This sol contains an approximately 15% (w/w) solids content, having a mean particle size of 4 nm and a pH of 10.5. The polyethylene glycol 8000 (PEG 8000) was NF grade and obtained from Union Carbide Co., Danbury, CT.

The following chemicals were also used as received: tartrazine or FD&C Yellow No. 5 (Seltzer Chemical, Carlsbad, CA), acetaminophen (Mallinckrodt, Paris, KY), hydroxypropyl cellulose (Klucel LF, Hercules Inc., Wilmington, DE), hydroxypropyl methylcellulose 2910, USP (Methocel E5, Dow Chemical, Midland, MI), anhydrous dextrose, USP (Mallinckrodt, Paris, KY), sodium chloride (J. T. Baker Chemical Co., Phillipsburg, NJ), phosphoric acid, 85% (J. T. Baker Chemical Co., Phillipsburg, NJ), sodium hydroxide pellets (J. T. Baker Chemical Co., Phillipsburg, NJ), and 18/20-mesh nonpareils (Nu-pareils, Ingredient Technology Corp., Pennsauken, NJ).

Drug Layering Process

The drug suspension formulation is summarized in Table I. Hydroxypropyl methylcellulose (HPMC) was dispersed in the preheated purified water (90°C). The HPMC dispersion was then cooled to 50°C to allow dissolution of the added hydroxypropyl cellulose. PEG 8000 was added followed by tartrazine and acetaminophen to form the suspension. The final suspension was stirred overnight and passed through a No. 80 mesh screen before use.

The drug layering onto the nonpareils was performed in a Versa-Glatt GPCG-1 (Glatt Air Techniques, Ramsey, NJ) equipped with a rotor insert. The drug suspension was continuously stirred. A MasterFlex peristaltic pump (Cole Parmer Instruments, Chicago, IL) was used to deliver the suspension to the Versa-Glatt GPCG-1 unit. A low spray rate (e.g., 6 g/min) was required for the first 10 min to prevent agglomeration and was increased to 12 g/min during the remainder of the coating process. Pellets were layered with

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Table I. Drug Suspension Formulation

Component	Weight (g)	%	% in solids
Tartrazine, USP	510	11.1	66.9
Acetaminophen, USP	170	3.7	22.3
Klucel LF	34	0.7	4.5
Methocel E5	34	0.7	4.5
PEG 8000, NF	14	0.3	1.8
Deionized water	3819	83.4	—
Total	4581	99.9	100.0

drug to an approximately 30% weight gain. The detailed drug layering conditions are given in Table II.

Polymer Coating Process

The coating condition parameters and coating formulations are given in Tables II and III, respectively. The method to prepare the coating suspension involved

(1) dissolving PEG 8000 in purified water if PEG was incorporated, and
(2) mixing the solution from step 1 with the appropriate mixture of PDMS latex and colloidal silica in a stainless-steel beaker.

The PDMS and silica solids ratio ranged from 4:1 to 1:1 in the final suspension. The final suspension contained 20% (w/w) solids. The coating suspension was continuously stirred and pumped via a MasterFlex peristaltic pump to the Versa-Glatt GPCG-1 unit equipped with a rotor insert. A low spray rate (e.g., 6 g/min) was required during the first 10 min but was increased to 11 g/min during the remainder of the coating process. Pellets were coated to an approximately 10% weight gain.

Preparation of Dissolution Media

Five dissolution media composed of various ionic and nonionic species (Table IV) were prepared and used to monitor drug release characteristics. The osmolality of all five dissolution media was confirmed using the Advanced Digi-Matic Osmometer Model 3DII (Advanced Instruments, Inc., Needham Heights, MA).

Table II. Summary of the Drug Layering and Coating Process Conditions

Parameter	Drug layering	Polymer coating
Product load (g)	850	700
Temperatures (°C)		
1. Inlet air	70	55
2. Product	45	36–38
3. Exhaust air	41	34–36
Atomizing air pressure (bar)	2	2
Nozzle orifice (mm)	0.8	0.8
Rotation speed (rpm)	360	180
Spray rate (g/min)	6–12	6–11
Spraying time (min)	140	47
Drying time (min)	3	5
Shaker cycle (shakings/min)	3	Off
Final total weight (g)	1065	783

Table III. Composition of Polydimethylsiloxane (PDMS):Silica:PEG 8000 Coating Formulations

	PDMS–silica–PEG 8000 weight ratio[a] (%)			
Coating component	4:1:0	2:1:0	2:1:0.75	1:1:0
Silicone emulsion X7-2837 or PDMS	80	66.6	53	50
Colloidal silica[b]	20	33.3	27	50
PEG 8000, NF	—	—	20	—

[a] All the weight ratios are based on the solids weight.
[b] Nalcoag 1115.

Dissolution Testing

The USP XXII Apparatus 1 (basket method) dissolution method (29) was employed to prevent the pellets from floating. The basket was rotated at 100 rpm. Each dissolution test was performed on six 200-mg samples of pellets with 900 ml of deaerated deionized water heated to 37°C. The dissolution apparatus (Hanson Research, Northridge, CA) was interfaced to a diode array spectrophotometer (Model HP8451A, Hewlett-Packard Co., Palo Alto, CA). The UV absorbances at 244 and 384 nm were measured at each sampling time point. The amount of tartrazine released was determined from the UV absorbance at 384 nm. The amount of acetaminophen released was then calculated by subtracting the theoretical tartrazine absorbance at 244 nm from the total absorbance measured at 244 nm. Six samples ($n = 6$) were tested per run to obtain the average release profile and demonstrate the drug release reproducibility. Standard deviations are not shown in the figures since they are smaller than the symbol size.

RESULTS AND DISCUSSION

Effect of Film Composition on Drug Release

Figure 1 shows the influence of PDMS–silica films containing a pore former (top set of curves) and films without a pore former (bottom set of curves).

When the film contained 20% PEG 8000 (2:1:0.75 film), tartrazine (MW 465.42) and acetaminophen (MW 151.16) began to appear immediately in the deionized water without any significant lag time. The percentage acetaminophen released at each time point was about 10% higher than that of tartrazine until 90% of the drug was released. This is presumably due to the smaller molecular volume of the acetaminophen compared to tartrazine. More than 90% of the acetaminophen and tartrazine were released from the coated pellets in approximately 3 hr.

Figure 2 illustrates the change in the physical appearance of the coated pellets as a function of time in water. Note how quickly the color disappears from the PDMS–silica–PEG 8000 (2:1:0.75)-coated pellet core compared to the other coating systems at the 1-hr time point.

Table IV. Composition of Dissolution Media Used for Mass Transport Studies

Component[a]	Dissolution medium				
	Deionized water	Dextrose solution	Dextrose/ sodium chloride solution	Buffer solution (pH 1.8)	Buffer solution (pH 8.0)
$[H_3PO_4]$[b]	—	—	—	0.034	0.034
[NaOH]	—	—	—	0.004	0.063
[NaCl]	—	—	0.149	0.106	0.047
[Dextrose]	—	0.377	0.128	0.136	0.141
μ[c]	0.00	0.00	0.15	0.14	0.14
mOs[d]	0	400	400	400	315[e]
pH	~6	~6	~6	1.8	8.0

[a] Molar concentrations.
[b] Total phosphoric acid concentration in the solution.
[c] Ionic strength.
[d] Milliosmoles.
[e] The theoretical osmolality (i.e., 400 mOs) was unachievable due to the physicochemical properties of dextrose in an alkaline medium.

Figure 3a represents the internal structure of the 2:1:0.75 film as hypothesized in this laboratory. Note that the silica and PEG 8000 are incompatible with the PDMS. As a result, domains containing silica–PEG create channels that are available for drug transport. Li and Peck (23) have commented on the immiscibility of PEG and silica in the PDMS film as well as the intensive interaction between PEG and silica. Similar trends in drug release have been previously demonstrated by Li and Peck (24). They incorporated different molecular weights and concentrations of PEG in the PDMS–silica films to control the release of potassium chloride.

Returning to Fig. 1, note that the 2:1 PDMS–silica film without the pore former exhibits a lag time of approximately 1 hr. Although the release rates for both tartrazine and acetaminophen through the 2:1 PDMS–silica film are similar, their release rates were significantly slower than the value observed for the 2:1 PDMS–silica film containing PEG 8000. The steady-state slope of the 2:1 PDMS–silica film containing PEG 8000 was 0.9% min^{-1}, compared to 0.4% min^{-1} for

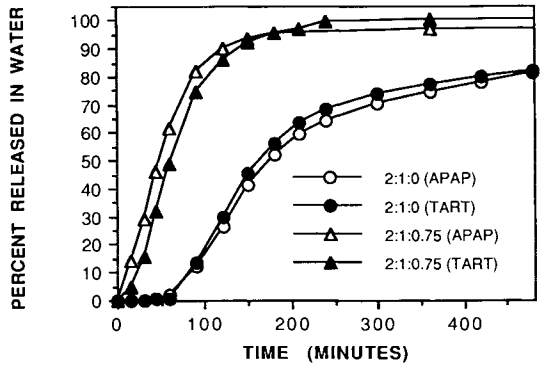


Fig. 1. Effect of the pore former (PEG 8000) in the PDMS elastomer film on acetaminophen (open symbols) and tartrazine (filled symbols) release. Drug release through films composed of 2:1-weight ratio PDMS–silica containing 20% PEG 8000 (△ and ▲) and 2:1 PDMS–silica film without the pore former (○ and ●). Drug release experiments were performed in deionized water.

the 2:1 PDMS–silica film without film former. Figure 2 shows the physical appearance of the coated pellets while immersed in water. In the first time frame the pellets have a dark orange hue. By the third time frame the color has leveled off to a light orange hue.

Figure 3b represents the hypothesized internal structure of the 2:1 PDMS–silica film system, which has significant quantities of the dispersed silica filler attached to multiple PDMS latex spheres. As the film is formed during the coating process, silica coats the PDMS particles. The excess silica then forms contact points which create silica channels. Due to the charged surface of the colloidal silica particles (30), the channels hydrate when exposed to an aqueous environment. These channels are hydrophilic and probably swell after the films are immersed in an aqueous media. It is reasonable to assume that the silica leads to formation of the hydrated channels because polar solvents such as water are normally excluded from the pure, hydrophobic PDMS polymer membranes (19,20). As a result these hydrophilic channels preferentially allow the ionized tartrazine to penetrate.

The 1:1 PDMS–silica weight ratio film allowed faster tartrazine release through the film than acetaminophen (Fig. 4). In fact, 20 to 25% more tartrazine is released at most of the time points. This is an interesting finding because of the differences between the molecular volumes of the two permeants. For instance, tartrazine and acetaminophen have molecular volumes of approximately 930 and 140 $Å^3$, respectively (31). Therefore the higher release rate for tartrazine is most likely due to the high load of silica in the film. Figure 3c illustrates this hypothesis.

As a result of the high concentration of charged silica, there may either be some exclusion of the nonionic acetaminophen from the silica channels or a strong chemical interaction between the silica and the acetaminophen. Based on previous work in the literature (8,10,12) it is unlikely that a strong interaction exists between the acetaminophen and the silica. The absence of a strong interaction can also be supported by the lack of a lag time for the 1:1 PDMS–silica coating system. Therefore, it appears that the ionic tartrazine tends to penetrate the charged, hydrophilic silica chan-

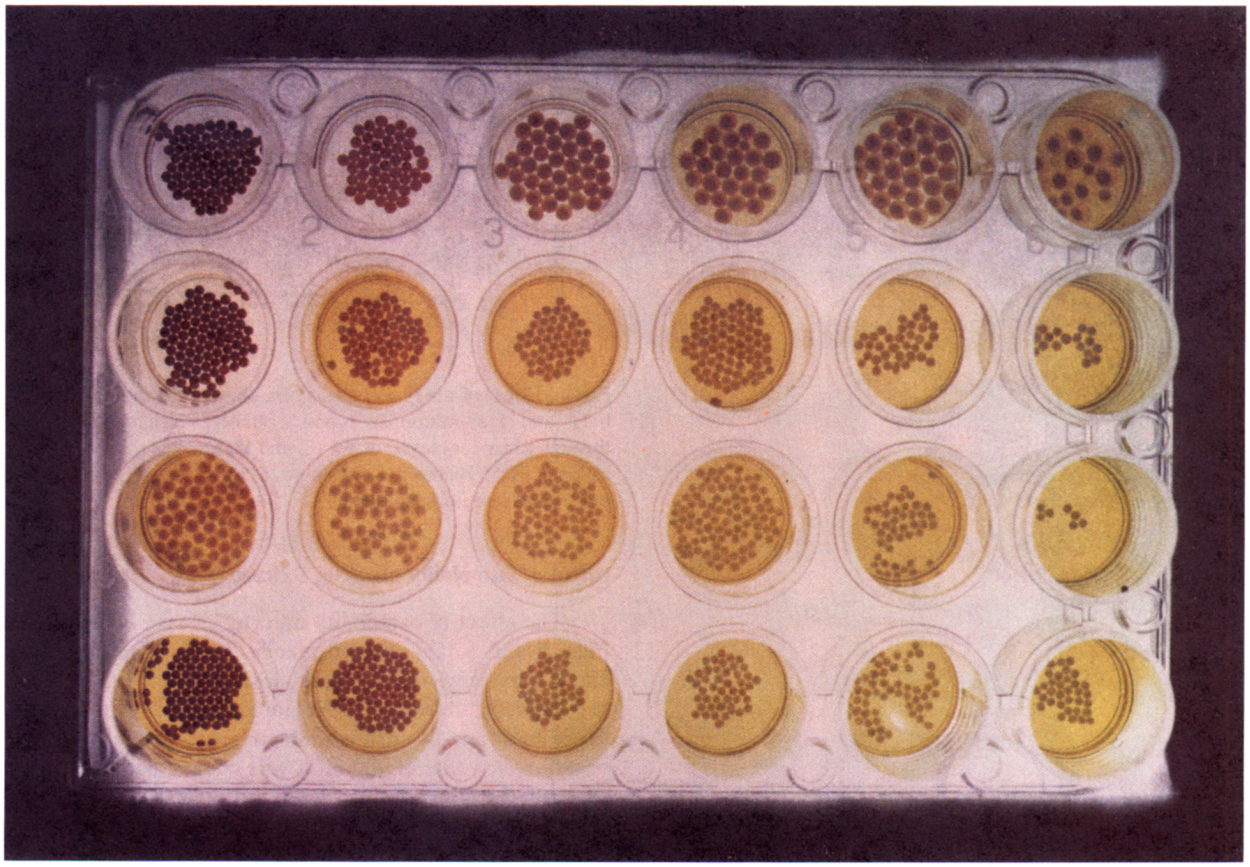


Fig. 2. Appearance of the four coating formulations of PDMS–silica–PEG 8000-coated pellets as a function of time after exposure to deionized water. The six time points (left to right) are 1, 4, 27, 32, 42, and 98 hr. From top to bottom the film coatings are 4:1:0, 2:1:0, 2:1:0.75, and 1:1:0 PDMS–silica–PEG 8000 ratios.

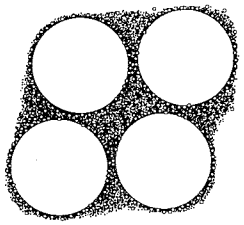
nels faster than the nonionic acetaminophen despite the fact that tartrazine has a threefold higher molecular weight and a severalfold larger molecular volume.

The physical appearance of the 1:1 film also was unique. All coating formulations gave clear films except the 1:1 formulation, which gave a milky appearance due to the high proportion of the silica.

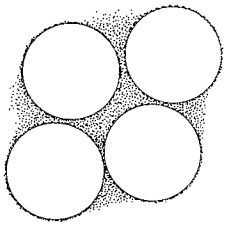
Figure 4 also illustrates the release characteristics in deionized water of both tartrazine and acetaminophen through a 4:1-weight ratio PDMS–silica system (Table III). Virtually no tartrazine permeated the 4:1 PDMS–silica film coating due to the large amount of hydrophobic PDMS in the film and the ionic nature of tartrazine. As shown in Fig. 2, the core of the 4:1 PDMS–silica-coated pellets remains orange for a period longer than 98 hr. One can also observe the significant swelling of the 4:1 PDMS–silica film, which results in an appearance much like that observed with fish eggs. This phenomenon is addressed further in the next section.

The PDMS–silica film composition can be envisioned as in Fig. 3d, where the silica is uniformly dispersed in a noncontinuous manner. As a result there may be some submicroscopic void spaces in the film due to the coating process and the physical interaction between silica and the rigid PDMS latex particles. If it is assumed that water is excluded from PDMS films (19,20), then the small water molecules must traverse a very circuitous or tortuous pathway to penetrate the film and initiate dissolution of the drug core. Since acetaminophen diffuses through the film, it follows that the water molecules must be able to penetrate the hydrophobic film. However, essentially no tartrazine was released from these coated pellets. Silicone is impermeable to ionic species (5,7,32), therefore the difference between acetaminophen and tartrazine release rates suggests that the silica particles in the film may be close enough to one another to form some tortuous channels. These tortuous channels are large enough to allow diffusion of water but too small for the diffusion of the larger tartrazine molecules. There does not seem to be this impact with acetaminophen, which is nonionized due to its low ionization constant or high pK_a (pK_a° = 10.1) (33). Therefore, acetaminophen can partition into the nonporous, highly hydrophobic 4:1 PDMS–silica polymer film. Note also that after a lag time of approximately 2 hr, acetaminophen was released at a constant rate of 0.05% min^{-1} to a total of approximately 48% at the 16-hr time point.

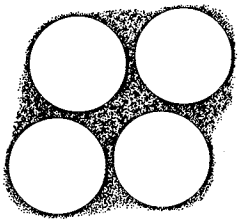
Drug transport of ionic solutes such as tartrazine through the aqueous-based PDMS system is unlike that observed with cured PDMS films containing a fumed silica as an inert filler (10). Silica found in cured polydimethylsiloxane films may be hydrophobic and more uniformly dispersed such that few, if any, contact points among silica particles form continuous channels to allow drug transport. The dif-



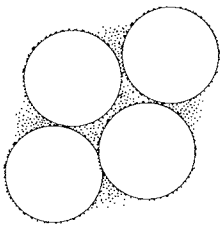
2:1:0.75
(a)



2:1:0
(b)



1:1:0
(c)



4:1:0
(d)

Fig. 3. Hypothesized internal structures of the films composed of (a) 2:1-weight ratio PDMS–silica containing 20% PEG 8000, (b) 2:1-weight ratio PDMS–silica, (c) 1:1-weight ratio PDMS–silica, and (d) 4:1-weight ratio PDMS–silica. The small black dots are colloidal silica particles, the open squares are PEG 8000 domains, and the large open circles are PDMS spheres.

ferences between the two types of PDMS film systems (cast/cured versus aqueous dispersion of PDMS) are magnified because cured PDMS films are permeable only to nonionic species. Also, it has been shown that the inert filler actually reduces a cured film's transmission or flux rate (8,10,12), whereas the silica in the aqueous coating system actually enhances a compound's transmission rate through the film.

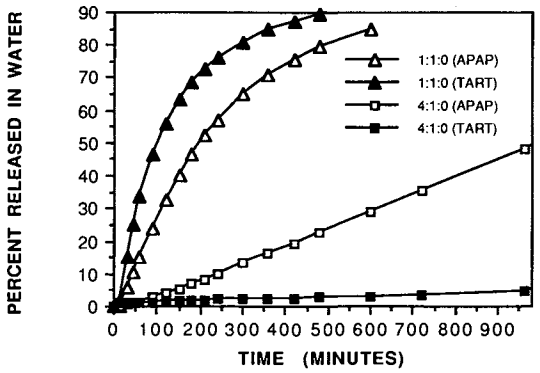


Fig. 4. Effect of the film composition on both tartrazine (filled symbols) and acetaminophen (open symbols) release. Drug release through films composed of 4:1 (□ and ■) and 1:1 (△ and ▲) weight ratios of PDMS–silica are presented. Drug release experiments were performed in deionized water.

Effect of Osmolality on Drug Release

The effect of osmolality on drug release is presented in Figs. 5 and 6. Dissolution media (Table IV) composed of either pure water or dextrose, which were 0 and 400 mOs, respectively, were used. No ionic species were added to these solutions to ensure that the ionic strength would be constant. A value of 400 mOs was chosen because it represents the highest possible value in the gastrointestinal tract (34). Only the most and least permeable coating formulation cases are shown in these figures. Osmolality had no effect on drug release from the 1:1 and 2:1 PDMS–silica-weight ratio coating formulations; therefore these are not shown.

Figure 5 illustrates that osmolality decreased both tartrazine and acetaminophen diffusion through the 2:1 PDMS–silica film with PEG. Osmolality effects should be most pronounced on the porous film containing 20% PEG 8000, because drug release is due not to partitioning but to a combination of passive pore diffusion and osmotic pumping. The slowing of drug release from the porous film can be attributed to the osmotic pressure in the dissolution medium containing dextrose. Thus a film with less pore surface area resulted from a decrease in the net internal osmotic pressure

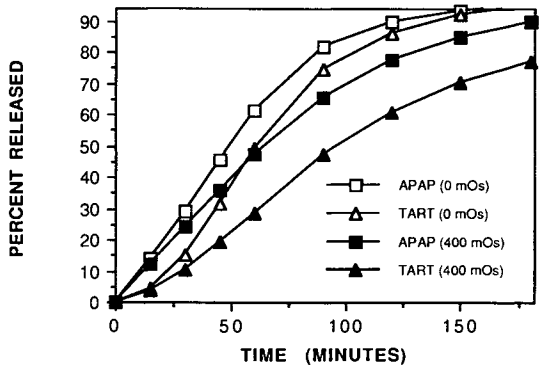


Fig. 5. Effect of solution osmolality on both tartrazine (△ and ▲) and acetaminophen (□ and ■) release through films composed of 2:1 PDMS–silica with 20% PEG 8000. Open and filled symbols represent the drug dissolution in deionized water (0 mOs) and dextrose solution (400 mOs), respectively.

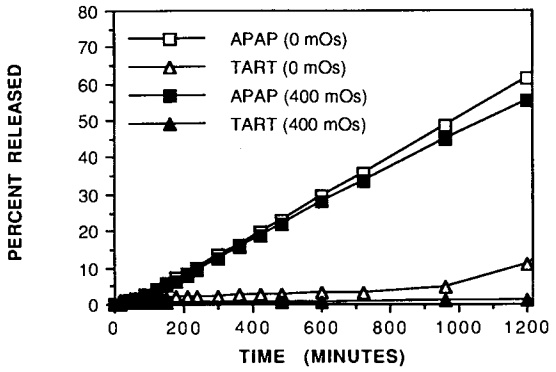


Fig. 6. Effect of solution osmolality on tartrazine (△ and ▲) and acetaminophen (□ and ■) release through 4:1 PDMS–silica films. Open and filled symbols represent the drug dissolution in deionized water (0 mOs) and dextrose solution (400 mOs), respectively.

difference and the reduced ability of the film to swell. The release rate should decrease when a film has enough porosity to prevent the buildup of osmotic pressure and subsequent stretching of the film but not enough core osmotic force to override the osmotic influence of the dissolution medium.

Figure 6 demonstrates the influence of increasing the dissolution medium osmolality from 0 to 400 mOs on tartrazine and acetaminophen release through the film comprised of a 4:1 PDMS–silica ratio. In the majority of release rate experiments, the 4:1 PDMS–silica polymer-coated pellets typically swelled to approximately eight times their original volume. This change can be seen in Fig. 2. This magnitude of film swelling is due to a combination of the high drug and sucrose solution (suspension) concentration inside the core, which increased the water flux across the film from outside the pellet coating to inside the coating. Figure 6 shows that tartrazine and acetaminophen were released faster in purified water (0 mOs) than in the 400-mOs dextrose solution after 16 hr of immersion. The sudden increase in release rate at 16 hr was very possibly a result of the swelling phenomenon. Swelling created some water channels or pores due to film expansion (stretching), allowing the ionic tartrazine and the nonionized acetaminophen to permeate. The experiment using an osmotic pressure of 400 mOs demonstrated relatively constant release profiles for acetaminophen and tartrazine through the 4:1 silicone–silica nonporous film. The lack of tartrazine release and slight slowing of acetaminophen release through this nonporous film in solutions with osmotic pressure support the hypothesis that the core builds up a high pressure, leading to film stretching in purified water (0 mOs).

Effect of Ionic Strength on Drug Release

Silica particles are presumed to contain ionic groups on the surface (30). Therefore the influence of increasing the ionic field around the silica particle environment (i.e., the ionic strength in dissolution medium) was evaluated to determine the impact on drug release from the coating system containing silica. Using solutions with constant osmotic pressure, the effect of ionic strength on drug release was investigated by comparing the release profiles in dextrose solutions with or without sodium chloride (Table IV). Ionic strength (μ = 0.15 and 400 mOs) did not significantly alter drug release profiles compared to the dextrose solution (μ = 0.0 and 400 mOs) for all four film-coated pellets.

Effect of pH on Drug Release

The effect of pH was evaluated by comparing drug release profiles of coated pellets immersed in pH 1.8 buffer, pH 8 buffer, and dextrose/NaCl solution (~pH 6). Changes in the pH did not significantly alter drug release profiles for pellets coated with the 1:1 PDMS–silica coating formulations (Fig. 7).

Figure 8 illustrates that the 2:1 PDMS–silica films shows more pH sensitivity. During the early time points in the pH 1.8 dissolution medium, the tartrazine and acetaminophen were released faster through the film. This result indicates that as the ratio of PDMS to silica increases, the effect of pH on drug release becomes more evident. This type of effect was not observed with the 1:1 PDMS–silica system because the hydration and porosity effects of the film appear to override the subtle charge effects seen in a film with higher PDMS levels. Hence, the sensitivity of the coating system is apparently magnified as the level of silica, which is needed for drug transport, becomes less and less.

It was found that for the 4:1 PDMS–silica film, both acetaminophen and tartrazine release rates were enhanced after 12 hr of immersion in the pH 1.8 buffer (Fig. 9). The results showing the effect of low pH on drug release from the 4:1 formulation are interesting for two reasons. First, although acetaminophen is nonionized (pK_a° = 10.1) at all pH's used in this study, acetaminophen release increased at about 12 hr. This increase may indicate that pH 1.8 influences the silica charge and the silica physically hydrates in a manner different from that observed at other pH's. This effect was also observed with the 2:1 PDMS–silica film. This result also indicates that the 4:1 PDMS–silica film could be the optimum polymer–filler ratio to detect pH effects on the silica. Interestingly, Li and Peck (25) found maximal differences at the higher pH's.

Second, tartrazine release also increased at the lower pH value, which indicates that protons permeate the coating and neutralize the ionic tartrazine. However, this would be a

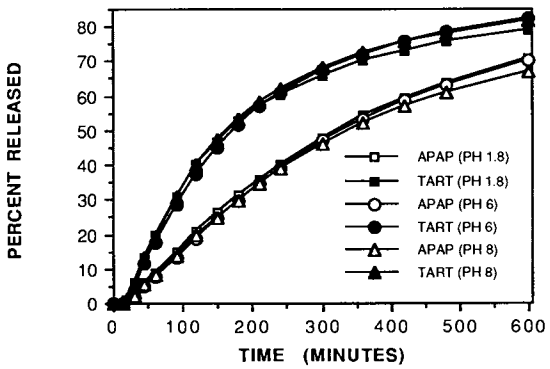


Fig. 7. Effect of dissolution medium pH (μ = 0.15 and 400 mOs) on tartrazine (filled symbols) and acetaminophen (open symbols) release through 1:1 PDMS–silica films: pH 1.8 buffer (□ and ■), pH 6 dextrose/NaCl solution (○ and ●), and pH 8 buffer (△ and ▲).

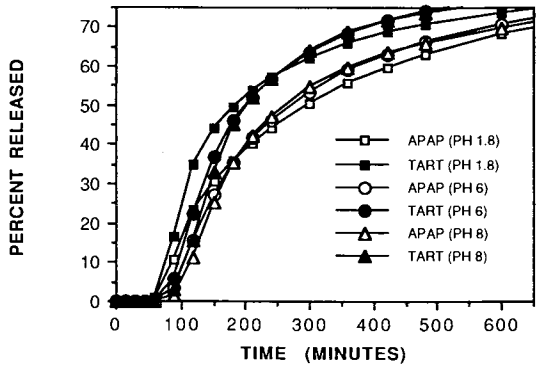


Fig. 8. Effect of dissolution medium pH (μ = 0.15 and 400 mOs) on tartrazine (filled symbols) and acetaminophen (open symbols) release through 2:1 PDMS–silica films: pH 1.8 buffer (□ and ■), pH 6 dextrose/NaCl solution (○ and ●), and pH 8 buffer (△ and ▲).

very slow process due to the tortuous diffusional pathway required to follow the silica channels. The tartrazine sulfonate groups should have an ionization constant very close to that of the sulfonate group of sulfanilic acid (pK_a = 3.22) (35). Therefore, protonation of the sulfonate groups and protonation of the carboxylate groups allow tartrazine to partition through the film at low pH's.

As a point of interest, the pellets coated with PDMS–silica–PEG 8000 2:1:0.75 demonstrated a constant acetaminophen release rate over the pH range studied due to its nonionic charge. The release rate of tartrazine was lower at pH 1.8 compared to the other pH values. The decrease in tartrazine release rate can be attributed to the decreased tartrazine solubility at low pH, which is a result of protonation of the carboxylate and a fraction of the sulfonate groups.

CONCLUSION

By comparing the *in vitro* release profiles of both ionized and nonionized compounds through the PDMS elastomer film, differences in the drug transport mechanisms can be demonstrated. The dissolution results illustrated that ionized tartrazine release was mainly through the water filled pores. However, nonionized acetaminophen can be released through either membrane pores or partitioning. Therefore, by changing the PDMS–silica ratio of the film, the desired release rate for either ionized or nonionized compounds can be achieved. Ionic strength and species in the dissolution media did not show significant effect on drug release rates. Osmolality appeared to inhibit the swelling of the nonporous 4:1 PDMS–silica film and, therefore, decreased drug release from this highly hydrophobic polymer film. Osmolality also demonstrated some effect in decreasing drug release from the film containing 20% PEG 8000. Except for coating systems composed of the 2:1 and the 4:1 PDMS–silica film tested in pH 1.8 buffer, the dissolution medium pH did not significantly alter the release profiles of either compound through the other coating systems at higher pH's.

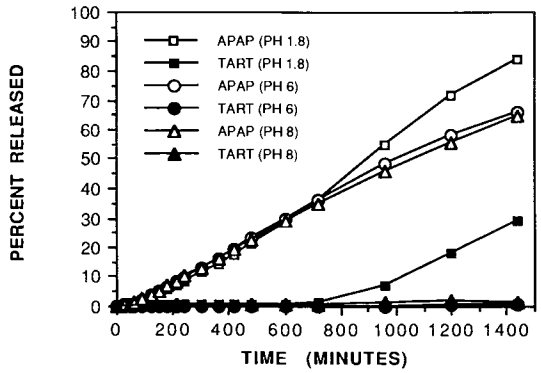


Fig. 9. Effect of dissolution medium pH (μ = 0.15 and 400 mOs) on both tartrazine (filled symbols) and acetaminophen (open symbols) release through 4:1 PDMS–silica films: pH 1.8 buffer (□ and ■), pH 6 dextrose/NaCl solution (○ and ●), and pH 8 buffer (△ and ▲).

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