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WATER BASED SILICONE ELASTOMER CONTROLLED RELEASE TABLET FILM COATING VI: THE EFFECT OF TABLET SHAPE

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ABSTRACT

The silicone elastomer latex containing colloidal silica and polyoxyethylene glycol 8,000 was shown to produce controlled released film coating on potassium chloride tablets with different shapes. The tablet shape did not affect the zero-order release characteristic of the active ingredient from the coated tablets. With the same coating weight, the capsule shaped tablets exhibited a faster drug release rate as compared to the oval and round deep-cup shaped tablets.

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INTRODUCTION

The use of oval and capsule shaped tablets for oral drug administration has been well received by patients because of the ease of swallowing. The susceptibility of hard gelatin capsules to tampering has further promoted the marketing of capsule shaped tablets (caplets) for over-the-counter medications. Due to the more complex surface contour associated with these tablet shapes, coating of these tablets for controlled drug delivery may face the difficulties of cracking and splitting of the finished coating. The use of a silicone elastomer latex for controlled release tablet coating has been reported (1). The relatively elastic properties of the silicone elastomer latex coating (2) may provide a unique application of this latex for controlled release coating on tablets with various shapes. The major objective of this study is to demonstrate the capability of the silicone elastomer latex to produce acceptable controlled release coatings on three different shaped potassium chloride tablets.

EXPERIMENTAL

Materials:

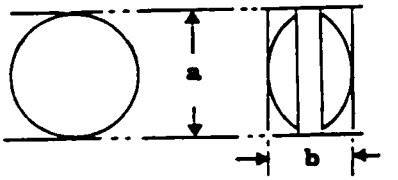
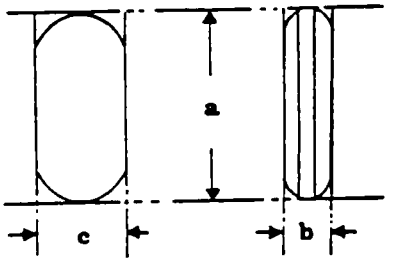
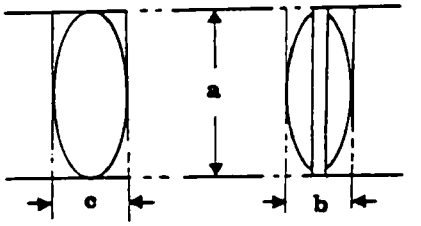
The silicone elastomer latex, the colloidal silica, the polyethylene glycol and potassium chloride used in this study were from the source reported previously (1).

Methods:

Preparation and Coating of Tablets:

Round deep-cup shaped, capsule shaped and oval shaped potassium chloride tablets weighing 600 mg were prepared using a Laboratory Carver Press following the procedures previously reported (1). The dimensions of these tablets are shown in Table 1. Twenty five tablets for each

Table 1. Dimensions for Different Shaped Potassium Chloride Tablets.

Tablet Shape	Dimension in cm		
	a	b	c
Round Deep-cup 	1.18	0.536	-
Capsule 	1.595	0.445	0.643
Oval 	1.308	0.513	0.743

shape were mixed with 1.50 kg of lactose placebo tablets (1/4") and placed in the six-inch Glatt laboratory air suspension column. A coating dispersion consisting of the silicone latex with a silicone to silica ratio of 2 to 1 and 30% PEG 8,000 calculated on the basis of 25% total solids content of the dispersion was used. Coating was conducted under the same conditions reported previously (1). An additional seventy five tablets for each tablet shape were divided into three groups and added into the coating column at three different time intervals during the coating operation to produce tablets with different coating weights. A total of two coating batches were prepared in this study.

Determination of Drug Release Rate:

Three tablets for each tablet shape and weight range from each coating batch were tested for drug release according to the procedures reported previously (1). The slope of the best fitted equation for the linear portion of the cumulative percentage drug released versus time plot was determined as the zero-order drug release rate.

Data Analysis:

The effect of tablet shape on the drug release rate was evaluated statistically using a covariance analysis method (3). The tablet coating weight was the covariate factor in this analysis. In the covariance data analysis, two models are generated using the multiple regression procedure. The full model including all variables and covariate is first developed as follows:

$$Y_{ij} = b_0 + b_1X_{ij1} + b_2X_{ij2} + b_3X_{ij3} + b_4Z_{ij} + E_{ij} \qquad \text{Eq. 1}$$

where Y_{ij} = drug release rate

X_{ij1} = 1 for samples from batch 1
= -1 for samples from batch 2

X_{ij2} = 1 for oval shaped tablets
= -1 for round deep-cup shaped tablets
= 0 other shape

X_{ij3} = 1 for capsule shaped tablets
= -1 for round deep-cup shaped tablets
= 0 other shape

Z_{ij} = the difference between the overall mean of all tablet coating weights and a specific tablet coating weight

E_{ij} = error term

A reduced model with all terms in the full model except the terms representing tablet shape is then derived as follows:

$$Y_{ij} = b_0 + b_1X_{ij1} + b_4Z_{ij} + E_{ij} \qquad \text{Eq. 2}$$

To test the significance of the tablet shape effect on the drug release rate the following test statistic is used.

$$F_{r-f,r} = \frac{\dfrac{SSE(R)-SSE(F)}{df_r - df_f}}{\dfrac{SSE(F)}{df_f}} \qquad \text{Eq. 3}$$

where SSE(F) = sum of square of the error term with f degree of freedom in the full model

SSE(R) = sum of square of the error term with r degree of freedom in the reduced model

df_r and df_f are the degree of freedom for the error terms associated with the reduced and full model.

RESULTS AND DISCUSSION

The release profiles of potassium chloride from the three different shaped silicone elastomer coated tablets are shown in Figures 1 to 3. In spite of the difference in tablet shape, the release of potassium chloride from all coated tablets exhibited a zero-order

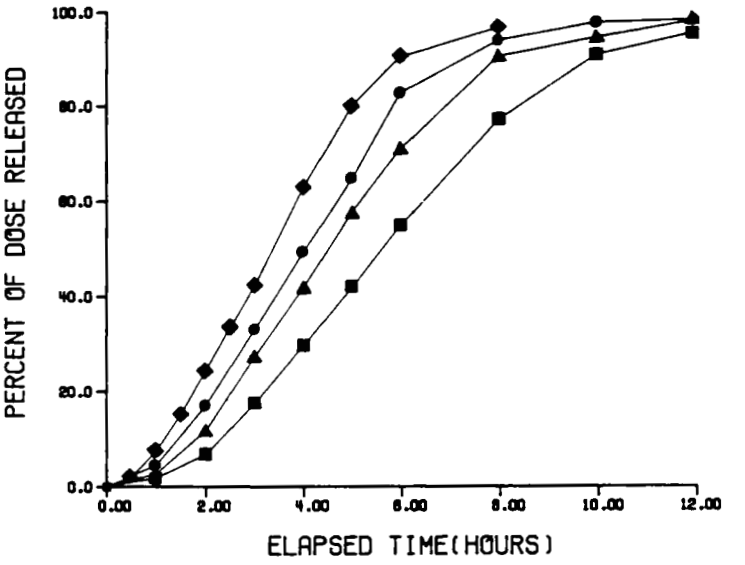


FIGURE 1

Release Profiles for Round Deep-cup Shaped Potassium Chloride Tablets Coated with Different Weights of PEG-Silicone Elastomer.
Key: Mean Coating Weight; (■) 82.2 mg; (▲) 70.7 mg; (●) 60.3 mg and (◆) 48.6 mg.

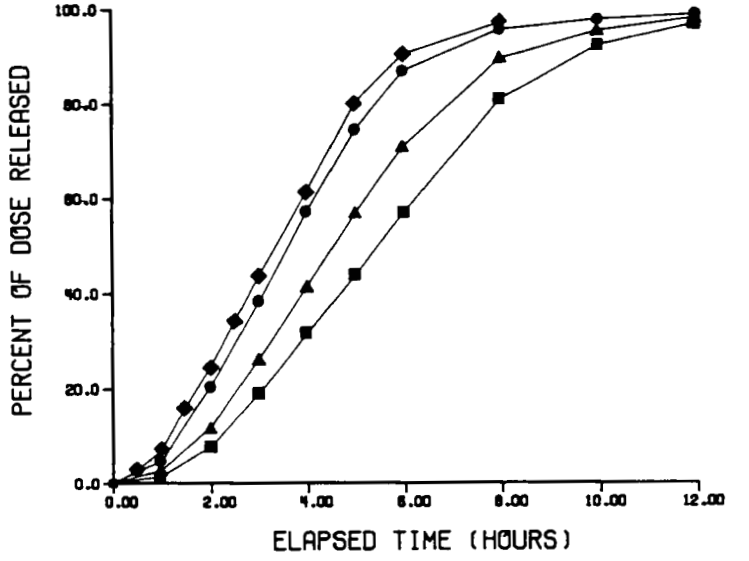


FIGURE 2

Release Profiles for Oval Shaped Potassium Chloride Tablets Coated with Different Weights of PEG-Silicone Elastomer.
Key: Mean Coating Weight; (■) 83.3 mg; (▲) 71.9 mg; (●) 60.2 mg and (◆) 48.0 mg.

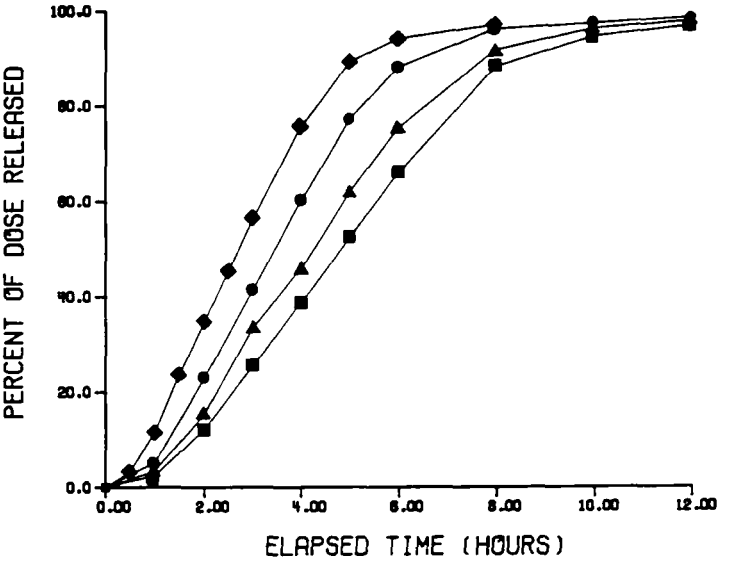


FIGURE 3

Release Profiles for Capsule Shaped Potassium Chloride Tablets Coated with Different Weights of PEG-Silicone Elastomer.
Key: Mean Coating Weight; (■) 83.1 mg; (▲) 70.4 mg; (●) 60.3 mg and (◆) 47.9 mg.

release profile. During the time course of drug release, due to the development of an appreciable osmotic pressure inside the coated tablets, a significant swelling of the coated tablet was seen and the shape of the coated tablets changed markedly. The coated round deep-cup tablets became spherical in shape while the capsule shaped tablets changed into a sasuage-like shape and the oval tablets attained a football shape. The effect of coating weight on the drug release rate was also shown in Figures 1 to 3. Coated tablets with a higher coating weight (thicker coating) released the active ingredient at a slower rate

Table 2 Drug Release Rate for Different Shaped Potassium Chloride Tablets Coated with Different Weights of Silicone Elastomer Coating.

Tablet Shape	Coating Batch 1		Coating Batch 2	
	Coating Weight (mg)	Release Rate (%/hr)	Coating Weight (mg)	Release Rate (%/hr)
	83.5	12.42	77.9	12.86
	80.3	12.00	77.5	12.37
	82.7	12.44	78.8	12.52
	71.1	14.01	69.6	13.46
	70.5	15.05	68.0	13.89
Oval	70.4	15.44	67.9	14.00
	60.0	16.35	62.4	14.13
	59.6	17.60	63.1	15.00
	61.3	16.78	62.6	16.26
	48.2	18.18	49.9	19.32
	49.1	18.87	46.8	21.53
	48.6	17.94	46.7	21.01
	83.8	13.74	77.3	14.12
	85.8	14.08	76.1	13.57
	80.4	12.50	75.7	14.04
	73.1	14.97	75.7	13.16
	74.9	14.47	64.9	16.28
	67.6	16.28	67.0	16.04
Capsule	60.1	18.25	62.8	17.91
	59.6	17.60	62.5	16.99
	61.3	16.78	61.4	17.59
	48.2	18.18	52.4	19.31
	49.1	18.87	50.9	17.33
	48.6	17.94	46.6	21.19
	83.9	10.71	86.5	10.52
	82.7	11.72	84.3	11.70
	82.6	12.82	81.9	12.07
	70.0	14.71	73.5	13.11
	70.6	14.07	72.1	13.11
Round Deep-cup	70.5	15.92	72.8	13.95
	61.7	16.21	63.0	14.92
	60.5	15.68	62.1	14.42
	61.4	16.51	62.4	15.89
	47.4	17.62	52.4	19.31
	47.1	19.49	50.9	17.33
	49.3	18.35	46.6	21.19

Table 3. Analysis of Variance and Test Results for the Covariance Analysis for the Effect of Tablet Shape on the Zero-Order Release Rate of Potassium Chloride from Coated Tablets.

(A) ANOVA Results

	Full Model		Reduced Model	
Source	df	SS	df	SS
Regression	4	497.26	2	455.86
Error	67	55.52	69	96.92

(B) Test Results

Effect	Test Statistic	F	F (α=0.01)
Tablet Shape	$\frac{SSE(R) - SSE(F)}{df_r - df_f} / \frac{SSE(F)}{df_f}$	24.97*	4.98

* Significant at = 0.01

which is explained by the membrane controlled release as well as the osmotic pressure driven drug release mechanisms (4).

Table 2 shows the zero-order release rate for different shaped tablets with various coating weights. The two multiple regression models (Eqs. 1 & 2) were developed using the REG Procedure in SAS. Table 3 gives the ANOVA results for the two models and the test results performed according to Eq. 3. The test results indicate that the tablet shape effect is significant at α = 0.01. A paired comparison between the tablet shape effect using the Scheffé multiple comparison procedure with a 99 percent family confidence coefficient (α = 0.01), concludes that, for all the coating weights evaluated, coated capsule shaped

tablets released the active ingredient at a higher zero-order rate than the oval and round deep cup shaped tablets, but no significant difference was shown between the drug release rate from the other two tablet shapes. For the same coating weight, a thinner coating will be formed on tablets with a larger surface area. As predicted by the transpore diffusion and osmotic pumping drug release models, a decrease in coating thickness and an increase in surface area of a coated tablet will result in a faster drug release rate (4). The result of this study suggests that the capsule shaped tablets used in this study may have the largest surface area as compared to the other two tablet shapes.

CONCLUSION

This study has demonstrated that the silicone elastomer latex containing colloidal silica and PEG can be used to produce controlled release film coating on potassium chloride tablets with different shapes. The tablet shape did not affect the zero-order release characteristics of the active ingredient. Amongst the three tablet shapes evaluated, the capsule shaped tablets exhibited a higher drug release rate as compared to the round deep-cup and oval shaped tablets. This was probably attributed to a large surface area associated with the capsule shaped tablets.

ACKNOWLEDGEMENT

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