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RESEARCH PAPER

Matrices of Water-Soluble Drug Using Natural Polymer and Direct Compression Method

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ABSTRACT

The objective of this research was to find an optimum Carrageenan matrix formulation with the desired drug release and physical properties prepared by direct compression. In order to achieve this, matrices containing 10% theophylline, different Carrageenan level, and different excipient were prepared and evaluated. A selected matrix containing 40% Carrageenan and lactose fast flo was tested for dissolution in three different dissolution media (distilled water, 0.1 N HCl, and phosphate buffer pH 7.4). The same formulation was also tested for dissolution at 50 rpm, 100 rpm, and 150 rpm, and using different dissolution apparatus (Apparatus 1 and 2).

All matrices showed a decrease in drug release as the polymer level was increased. Only Avicel PH-101 did not show any significant difference between matrices prepared with 30% and 40% polymer. At 10% polymer level, it appears that the type of diluent used controls the drug release. However, at high polymer level, 30% and 40%, it appears that the polymer level controls the drug release. Phosphate buffer pH 7.4 and 0.1 N HCl increase drug release and appear to increase Carrageenan solubility and decrease gel formation. Also, as the rotational speed of the apparatus was increased, the integrity of the gel layer was decreased, and the release of drug was increased. The drug release from Carrageenan matrices appears to follow the diffusion model for inert matrix up to 90 min. After 90 min, the drug release follows a zero-order model.

This study demonstrated that matrices using Carrageenan can be successfully prepared by direct compression.

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INTRODUCTION

Controlled-release drug delivery design involves the application of physical and polymer chemistry to dosage form design to produce a well-characterized and reproducible dosage form that controls drug entry into the body within the specifications of the required drug delivery profile.[1]

Hydrophilic matrices for the past two decades have been popular in the formulation of controlled-release solid dosage forms. A hydrophilic matrix consists of one or more active ingredient(s) with one or more gel-forming agent(s). Many types of polymers[2] have been used as the gel-forming agent in matrices, such as methylcellulose (MC), hydroxypropylmethylcellulose (HPMC), hydroxypropylcellulose (HPC), and sodium carboxymethylcellulose (CMC). Carrageenan, Gelcarin GP 182, is a water-soluble hydrocolloid, the charged nature of the sugar units and their structural arrangements account for its physical properties such as hydration and rapid formation of gel in cold water. Carrageenan, when heated in water, randomly becomes a dispersed polymer. However, upon cooling and in the presence of the appropriate cations, it forms a double helix which builds a matrix.[3]

In order to evaluate the process of drug release from hydrophilic matrices, matrix swelling[4,5] needs to be considered. Wan et al.[6] evaluated the relationship between swelling and drug release in a hydrophilic matrix. Their study was on directly compressed HPMC matrices containing ibuprofen, and drug release appears to be controlled by matrix swelling and polymer dissolution. Most researchers working in the area of controlled drug delivery believe that ideally the drug must be released from the dosage form at zero-order rate.[7,8] Ranga Rao et al.[9] used cellulose ethers to prepare tablets containing water-soluble drugs and a nearly zero-order release was achieved.

The erosion rate of the matrices was studied and they concluded that for formulations that showed zero-order release, the rate of advancement of the swelling front into the glassy polymer and the attrition of the rubbery state polymer might have been nearly equal, resulting in constant diffusional path length for the drug. However, for formulations that showed a decrease in drug release with time, the erosion rate was 2.5 times lower than for other formulations.

Many researchers have shown that the drug release from hydrophilic polymer containing slightly water-soluble and water-soluble drug appears to follow the Higuchi equation for an inert porous matrix.[10] Picker[11] investigated the use of Carrageenan in a mixture with microcrystalline cellulose, and its functionality for making tablets. Little research has been found in the literature related to the use of Carrageenan as a hydrophilic polymer for matrices.[12,13]

The aim of this study was to find an optimum theophylline/Carrageenan matrix with the desirable drug release and physical properties. Controlled-release matrices of theophylline prepared by direct compression using different levels of Carrageenan, Gelcarin GP 812, and different types of excipients were characterized and tested for release behavior.

MATERIALS AND METHODS

Materials

Except when noted, all chemicals were analytical grade and used as received. Carrageenan (Gelcarin GP 812, lot number ZB502, supplied by FMC Marine Colloid Division, Newark, NJ, USA), theophylline anhydrous, lot number 44576G (Boehringer, Ingelheim, Germany), lactose fast flo, lot number 2RL322 (Foremost Ingredient Group, WI, USA), dibasic calcium phosphate, Emcompress, lot number 3108X (Penwest Inc., New York, USA), microcrystalline cellulose, Avicel PH-101, lot number 6206 (FMC Corp., Philadelphia, PA, USA).

Preparation of Blends

Nine formulations and three controls were prepared. The batch size for each formulation was 500 g. A 10% w/w anhydrous theophylline was used as model drug, Carrageenan as hydrophilic polymer at three levels (10% w/w, 30% w/w, and 40% w/w),

magnesium stearate (1% w/w) as lubricant, and three different excipients (lactose fast flo, Emcompress, and Avicel PH-101). All materials were sifted manually through screen #12 and the lubricant was sifted through screen #30.

The powder mixing was performed by pre-blending the drug and the polymer in a Turbula mixer (Willy A. Bachafen, model T2c, Switzerland) at a speed of 90 rpm for 10 min. The lubricant was added before compression and the blend was mixed for an additional 5 min.

Tablet Compression

The blends were compressed into tablets using a rotary machine, Manesty B-3B (Manesty Machine Ltd.) equipped with 12/32-inch round, flat-faced tooling. The target tablet weight was 450 mg±5% and the target hardness was 6–9 kp.

Weight, Thickness, and Hardness of Tablets

A total of 10 tablets were evaluated for weight (Analytical Sartorius balance, model 1412), thickness using a portable dial hand gauge (L.S. Starnet Co.) and hardness using an Erweka hardness tester, model TBH-28. Means and standard deviations were calculated.

Disintegration Time

A total of six tablets were tested separately for disintegration (Erweka disintegration apparatus, model ZT3-2). The test was performed using 900 mL distilled water maintained at 37±2°C as immersion fluid. The disintegration test was stopped at 60 min and the disintegration time for tablets that had not disintegrated was recorded as more than 60 min.

Dissolution Testing

The dissolution of theophylline from all tablet formulations was measured in 900 mL distilled water, phosphate buffer pH 7.4 or 0.1 N HCl at 37±0.5°C using a rotating basket apparatus (Hanson Research model SR2) at speeds of 50 rpm, 100 rpm, or 150 rpm. Filtered samples were withdrawn and assayed using an ultraviolet spectrophotometer (Bechman instrument, model DU 65) at 272 nm. The number of replicates for each formula was six tablets.

RESULTS AND DISCUSSION

All blend formulations were successfully compressed into tablets and all tablet formulations were within the acceptable range of uniformity of weight, thickness, and hardness.

Table 1 shows uniformity of weight, thickness, hardness, and disintegration for all formulations. The tablet weight for all formulations varied from 448 mg to 464 mg and the hardness varied from 5.75 kp to 8.97 kp.

Avicel and lactose tablet formulations containing 30% and 40% polymer did not disintegrate up to 1 hr, while formulations containing 10% polymer or Avicel disintegrate in 36.8 and 34.2 min, respectively. All Emcompress formulations did not disintegrate up to 1 hr of testing disintegration.

Figures 1–3 depict the effect of polymer level on drug release from tablets prepared with different diluents (lactose fast flo, Avicel PH-101, and Emcompress) and different polymer levels. In general, tablets containing a low level of polymer (10% w/w) gave higher drug release than those containing high levels (30% or 40%).

Avicel PH-101 tablets containing 10% polymer gave 89.6% drug release, while Avicel PH-101 tablets containing 30% and 40% polymer gave 62.8% and 61.6%, respectively, at 3 hr of testing dissolution (Fig. 1). No significant difference in drug release was observed between Avicel PH-101 formulations containing 30% polymer and 40% polymer. Fisher's statistical analysis test supported these data (Table 2).

Emcompress tablet formulations containing 10% polymer gave 83.2% drug release, for tablets containing 30%, the drug release was 60.8%, and Emcompress formulations containing 40% polymer gave 45% drug release at 3 hr of testing dissolution (Fig. 2). As the level of polymer was increased in the formula, the drug release was decreased. Analysis of variance showed significant difference between Emcompress formulations containing different levels of polymer (Table 3).

Figure 3 depicts the dissolution data for lactose fast flo formulations containing different polymer levels. At 3 hr of testing dissolution, lactose fast flo tablet formulations containing 10% polymer

Table 1

Physical Properties of Tablets Prepared with 10% w/v Theophylline, Different Carrageenan Level, and Different Diluents

Test ($n = 10$)	10% w/w Carrageenan	30% w/w Carrageenan	40% w/w Carrageenan
Mean weight (g)±SD			
Avicel PH-101	0.454±0.006	0.456±0.007	0.458±0.009
Lactose fast flo	0.448±0.007	0.457±0.008	0.464±0.005
Emcompress	0.461±0.003	0.448±0.004	0.459±0.004
Mean thickness (mm)±SD			
Avicel PH-101	6.7±0.015	6.5±0.014	6.67±0.010
Lactose fast flo	4.92±0.058	5.17±0.062	5.36±0.023
Emcompress	3.67±0.03	4.05±0.06	4.25±0.05
Mean hardness (kp)±SD			
Avicel PH-101	7.12±0.46	6.21±0.67	5.78±0.85
Lactose fast flo	6.00±0.93	5.78±0.67	5.75±0.75
Emcompress	8.38±0.67	7.67±0.42	8.32±0.56
Mean disintegration time (min)±SD			
Avicel PH-101	3.68±1.72	>60	>60
Lactose fast flo	3.42±2.79	>60	>60
Emcompress	>60	>60	>60

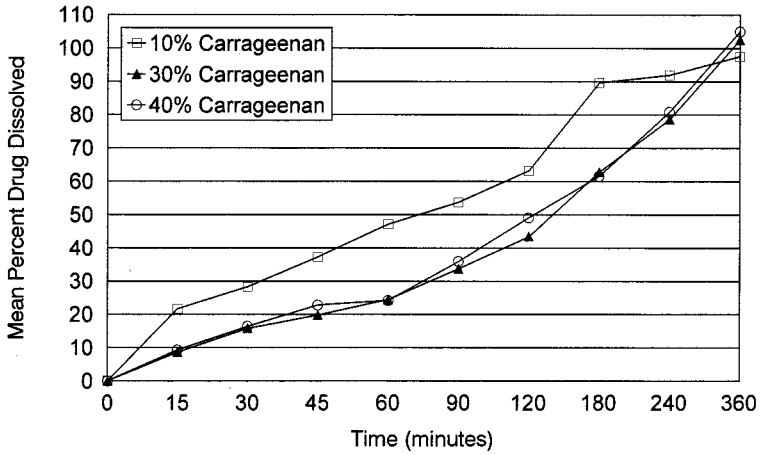

Figure 1. Effect of polymer level on drug release from tablets prepared with Avicel PH-101.

released 94.1% drug, lactose fast flo tablets containing 30% released 59.2%, and lactose fast flo tablets containing 40% polymer released 48%. These data indicate that as the level of polymer in the formula was increased, the drug released from tablets was decreased. A possible explanation for these results is that at low polymer level, the rate of advancement of the swelling front into glassy polymer and the attrition of the rubbery state polymer may have been nearly equal, resulting in a constant diffusional path length for the drug until the entire drug is released from the tablets. At higher polymer levels, the diffusional path length of the drug is increased, resulting in a slower release because of the polymer swelling. Fisher's *T*-test supported these data and showed no significant difference between lacose fast

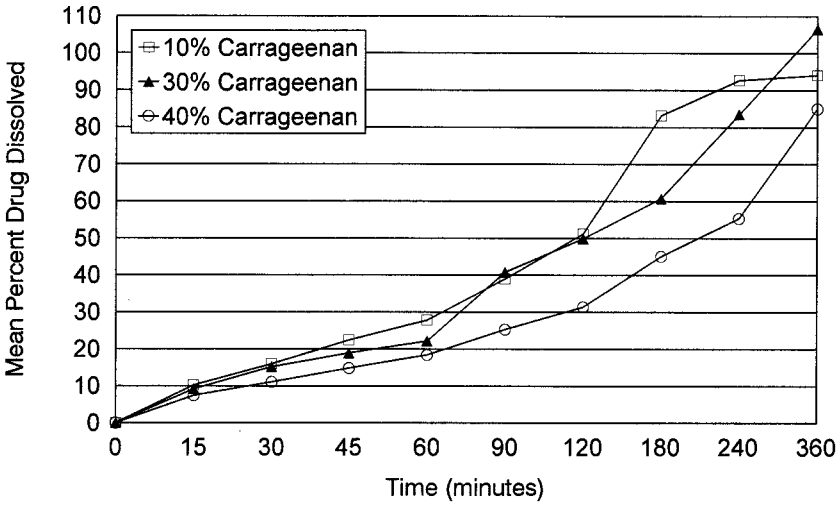

Figure 2. Effect of polymer level on drug release from tablets prepared with Emcompress.

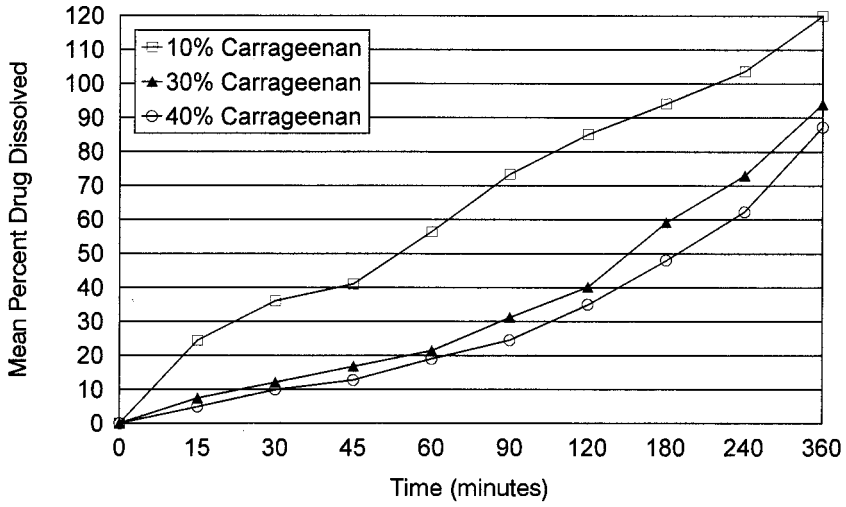

Figure 3. Effect of polymer level on drug release from tablets prepared with lactose fast flo.

flo formulations containing 30% and 40% polymer level (Table 4).

Figures 4 and 5 show the effect of type of diluent on drug release from tablets containing different levels of polymer. In general, Emcompress formulations gave the slowest drug release. This is due to the nature of this diluent. Emcompress is insoluble in water, will not create pores in the matrix and can create a barrier to retard the drug release.

At 10% polymer level (Fig. 4), the drug release from Avicel formulation was 63.2%, from Emcompress formulation was 51.2%, and from lactose fast flo formulation was 85.1% at 2 hr of testing dissolution.

The difference in drug release between formulations containing a low level of polymer (10%) and different diluents may be due to the fact that at low level of polymer, the drug release from the matrix appears to be controlled by the diluents, indicating that the drug release depends on the type of diluents used. Avicel PH-101 is water-dispersible, Emcompress is water-insoluble, and lactose fast flo is water-soluble. Analysis of variance statistical analysis showed significant difference between formulations containing 10% polymer level and different diluents (Table 5).

Table 2

Fisher's Least Significant Difference (LSD) for Avicel PH-101 Formulations Containing Different Polymer Levels

Time (min)	Polymer % Comparison	Mean Difference	Fisher's LSD Limit	Results[a]
15	10 vs. 30	13.13		S
	10 vs. 40	12.43	8.57	S
	30 vs. 40	−0.70		NS
30	10 vs. 30	12.53		S
	10 vs. 40	11.97	6.06	S
	30 vs. 40	−0.57		NS
45	10 vs. 30	17.53		S
	10 vs. 40	14.53	5.94	S
	30 vs. 40	−3.0		NS
60	10 vs. 30	22.63		S
	10 vs. 40	22.93	10.05	S
	30 vs. 40	0.30		NS
90	10 vs. 30	20.03		S
	10 vs. 40	17.77	11.62	S
	30 vs. 40	−2.27		NS
180	10 vs. 30	26.77		S
	10 vs. 40	28.03	19.73	S
	30 vs. 40	1.27		NS
360	10 vs. 30	−5.27		NS
	10 vs. 40	−7.53	13.29	NS
	30 vs. 40	−2.27		NS

[a]S = Significant difference. NS = No significant difference.

Figure 5 shows the dissolution data from tablets containing 30% polymer and different diluents. At 180 min, the percent drug released from Avicel PH-101 was 62.8%, the percent drug released from Emcompress was 60.8%, and the percent drug released from lactose fast flo was 59.2%. There was no significant difference in drug release between formulations containing 30% polymer and different diluents. The same results were true for matrices containing 40% polymer and prepared with different diluents. These data indicate that at high polymer level (30% or 40%), the drug release is controlled more by the polymer level and the diluent appears to have little effect on drug release. Analysis of variance statistical analysis showed no significant difference between formulations containing high level of polymer and different diluents (Table 6).

Tablets containing 40% polymer and prepared with lactose fast flo diluent were tested for dissolution at different rotational speeds, 50 rpm, 100 rpm, and 150 rpm. Figure 6 shows the effect of rotational speed of dissolution apparatus on drug release. At 4 hr of testing dissolution, the percent drug released at 50 rpm was 62.3%, at 100 rpm was 77.5%, and at 150 rpm was 83.6%. As the rotational speed was increased, the drug release was increased. A possible explanation for this is that when tablets are exposed to the dissolution medium at high rotational speed, surface erosion and gel disruption can occur faster and consequently drug release is increased. These results were confirmed by Fisher's *T*-test analysis (Table 7).

The drug release from tablets containing 40% polymer and lactose fast flo was tested in different dissolution media (distilled water, 0.1 N HCl, and phosphate buffer pH 7.4). The effect of dissolution medium on drug release is shown in Fig. 7. The highest percent drug released was in phosphate

Table 3

Analysis of Variance for Emcompress Formulations Containing Different Polymer Levels

Time (min)	Polymer (%)	Mean Percent Drug Dissolved	Variance	*F* (Mean Square of Treatment/ Mean Square of Error)	P^a	Results
15	10	10.2	0.13			
	30	9.2	0.64	16.48	0.0037	S
	40	7.4	0.30			
30	10	16.0	0.39			
	30	15.2	1.7	26.83	0.0010	S
	40	11.1	0.2			
45	10	22.4	0.06			
	30	18.9	0.76	102.32	0.0000	S
	40	14.8	0.42			
60	10	27.8	6.72			
	30	22.2	3.99	18.29	0.0028	S
	40	18.4	0.21			
90	10	39.0	8.82			
	30	40.8	58.61	9.62	0.0134	S
	40	25.3	0.013			
180	10	83.2	11.29			
	30	60.8	138.97	21.52	0.0018	S
	40	45.1	3.10			
360	10	94.1	12.50			
	30	106.5	55.42	15.17	0.0045	S
	40	85.0	1.20			

[a] P = Probability of obtaining a value of the statistic test as extreme or more extreme than the actual sample value when the null hypothesis is true.

buffer pH 7.4 (71.5%) and the lowest percent drug release was in distilled water (48%). The percent drug release in 0.1 N HCl was 71.5% at 3 hr of testing dissolution. The solubility of theophylline in the three different dissolution media is similar. However, the data obtained may be due to the fact that in acid medium, the viscosity of the hydrated gel layer that surrounds each tablet was decreased and consequently the drug release was increased. The high release rate in phosphate buffer may be due to the solubility characteristics of Carrageenan, which can be affected by the presence of salts in the phosphate buffer, i.e., gel formation is decreased by increasing salt concentration. Fisher's *T*-test supported these data and showed significant difference in drug release in the three different dissolution media (Table 8).

Figure 8 depicts the effect of dissolution apparatus type on drug release from Carrageenan matrix. No significant differences in drug release were observed from tablets containing 40% polymer and lactose fast flo when different apparatus were used for testing dissolution. This indicates that a matrix formation occurs between the binary mixture of lactose fast flo and Carrageenan, at a polymer level of 40%. Fisher's *T*-test analysis showed no significant difference between formulations containing 40% polymer and lactose fast flo tested in different dissolution apparatus (Table 9).

The dissolution data was analyzed to determine the mechanism of drug release from Carrageenan matrices. Figures 9 and 10 show that the drug release from matrices containing 40% Carrageenan and lactose fast flo follows the Higuchi diffusion model up to 90 min (Fig. 9). After 90 min, a zero-order release was obtained, indicating that there was erosion and the erosion rate was constant (Fig. 10). This change in the kinetics of drug release is in accordance with the change in swelling of the tablets. A swelling test performed demonstrated that erosion

Table 4

Fisher's Least Significant Difference (LSD) for Lactose Fast Flo Formulations Containing Different Polymer Levels

Time (min)	Polymer % Comparison	Mean Difference	Fisher's LSD Limit	Results
15	10 vs. 30	16.97		S
	10 vs. 40	19.47	5.48	S
	30 vs. 40	2.50		NS
30	10 vs. 30	23.97		S
	10 vs. 40	26.17	1.87	S
	30 vs. 40	2.20		S
45	10 vs. 30	24.30		S
	10 vs. 40	28.33	5.64	S
	30 vs. 40	4.03		NS
60	10 vs. 30	35.00		S
	10 vs. 40	37.43	10.90	S
	30 vs. 40	2.43		NS
90	10 vs. 30	42.17		S
	10 vs. 40	48.80	1.90	S
	30 vs. 40	6.63		S
180	10 vs. 30	34.93		S
	10 vs. 40	46.10	4.50	S
	30 vs. 40	11.17		S
360	10 vs. 30	26.60		S
	10 vs. 40	33.30	7.15	S
	30 vs. 40	6.70		NS

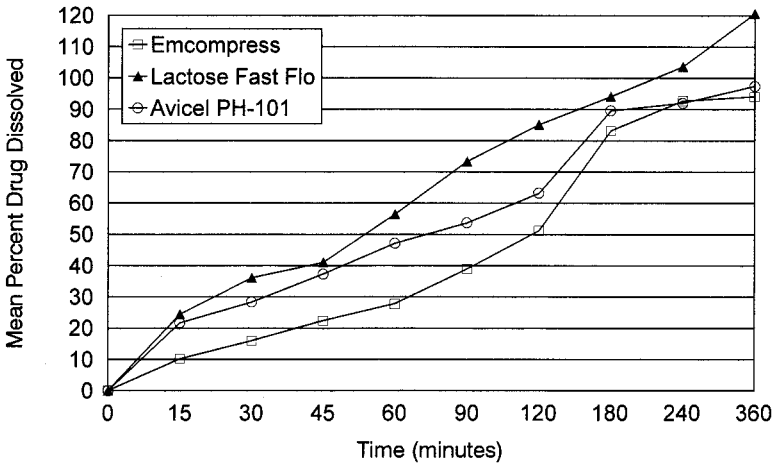

Figure 4. Effect of type of diluents on drug release from tablets containing 10% polymer.

of tablets started after 90 min of testing dissolution. The tablet thickness increased with time up to 90 min, after which the thickness started to decrease.

CONCLUSIONS

Theophylline matrices were successfully prepared by direct compression using Carrageenan polymer.

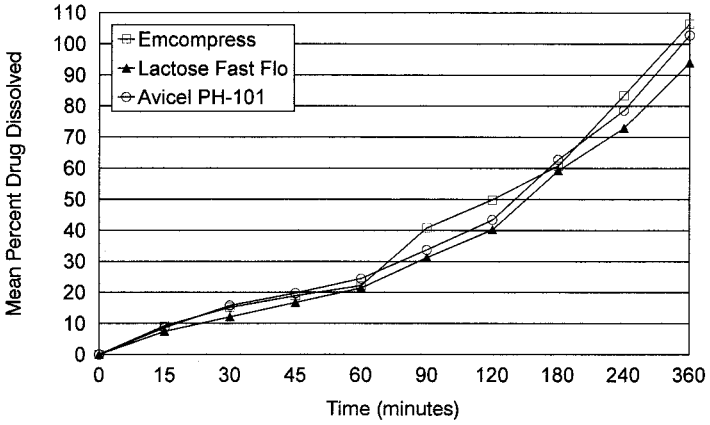

Figure 5. Effect of type of diluents on drug release from tablets containing 30% polymer.

Table 5

Analysis of Variance for Formulations Containing 10% Polymer and Different Diluents

Time (min)	Diluents	Mean Percent Drug Dissolved	Variance	*F* (Mean Square of Treatment/ Mean Square of Error)	*P*	Results
15	Emcompress	10.2	0.13			
	Lactose ff	24.4	22.0	7.88	0.0210	S
	Avicel	21.7	42.7			
30	Emcompress	16.0	0.39			
	Lactose ff	36.1	0.19	253.1	0.0000	S
	Avicel	28.3	3.04			
45	Emcompress	22.40	0.06			
	Lactose ff	41.0	22.53	32.95	0.0006	S
	Avicel	37.3	3.99			
60	Emcompress	27.8	6.72			
	Lactose ff	56.4	80.82	17.41	0.0032	S
	Avicel	47.1	23.05			
90	Emcompress	39.0	8.82			
	Lactose ff	73.3	0.37	143.41	0.0000	S
	Avicel	53.7	9.39			
180	Emcompress	83.2	11.3			
	Lactose ff	94.1	2.5	2.68	0.1471	NS
	Avicel	89.6	86.2			
360	Emcompress	94.1	12.5			
	Lactose ff	120.6	20.58	13.98	0.0055	S
	Avicel	97.5	101.37			

The drug release decreased as the polymer increased in the formula. The diluent type appears to control the drug release from matrices only at low polymer level. As the polymer level is increased, the polymer controls the drug release and the type of excipient used will have no significant effect on drug release. Optimum matrix formulations with desired drug release and physical properties were formulations

Table 6

Analysis of Variance for Formulations Containing 30% Polymer and Different Diluents

Time (min)	Diluents	Mean Percent Drug Dissolved	Variance	*F* (Mean Square of Treatment/ Mean Square of Error)	*P*	Results
15	Emcompress	9.2	0.6433			
	Lactose ff	7.4	0.31	4.19	0.0727	NS
	Avicel	8.6	0.91			
30	Emcompress	15.2	1.7			
	Lactose ff	12.1	0.0933	2.64	0.1503	NS
	Avicel	15.8	11.47			
45	Emcompress	18.9	0.7633			
	Lactose ff	16.7	0.04	18.53	0.0027	S
	Avicel	19.8	0.4033			
60	Emcompress	22.2	3.99			
	Lactose ff	21.4	0.0533	0.56	0.5979	NS
	Avicel	24.5	36.81			
90	Emcompress	40.8	58.6133			
	Lactose ff	31.2	0.5033	3.53	0.0972	NS
	Avicel	33.7	4.2033			
180	Emcompress	60.8	139.0			
	Lactose ff	59.2	8.8033	0.14	0.8680	NS
	Avicel	62.8	62.063			
360	Emcompress	106.5	55.4233			
	Lactose ff	94.0	1.8033	6.36	0.0329	S
	Avicel	102.8	0.9733			

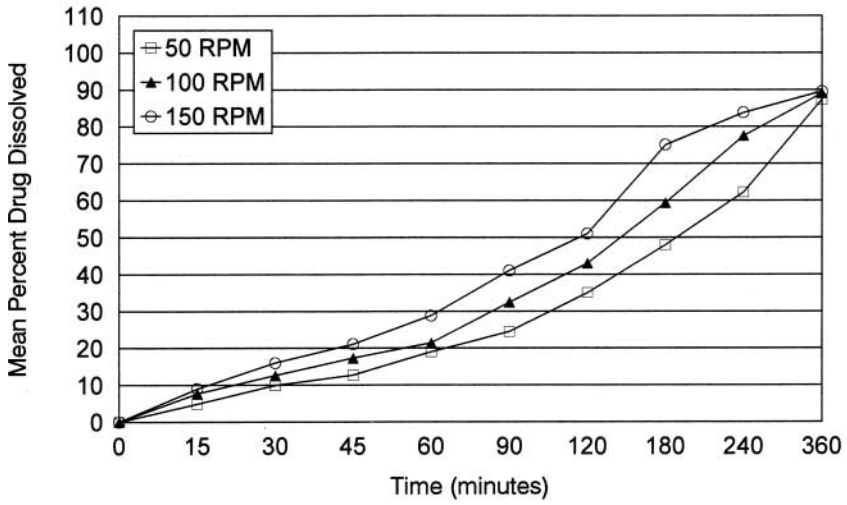

Figure 6. Effect of rotational speed of the basket on drug release from tablets containing 40% polymer and lactose fast flo.

Table 7

Fisher's Least Significant Difference (LSD) for Formulation Containing Lactose Fast Flo and 40% Polymer Tested at Different Rotational Speeds

Time (min)	Rotational Speeds (rpm)	Mean Difference	Fisher's LSD Limit	Results
15	50 vs. 100	−2.8		S
	50 vs. 150	−4.13	1.15	S
	100 vs. 150	−1.33		S
30	50 vs. 100	−2.67		S
	50 vs. 150	−6.07	2.43	S
	100 vs. 150	−3.4		S
45	50 vs. 100	−4.63		S
	50 vs. 150	−8.4	2.24	S
	100 vs. 150	−3.77		S
60	50 vs. 100	−2.43		S
	50 vs. 150	−9.83	4.42	S
	100 vs. 150	−7.4		S
90	50 vs. 100	−7.87		S
	50 vs. 150	−16.5	3.08	S
	100 vs. 150	−8.63		S
180	50 vs. 100	−8.0		S
	50 vs. 150	−15.93	7.47	S
	100 vs. 150	−7.93		S
360	50 vs. 100	−1.63		NS
	50 vs. 150	−2.13	7.13	NS
	100 vs. 150	−0.5		NS

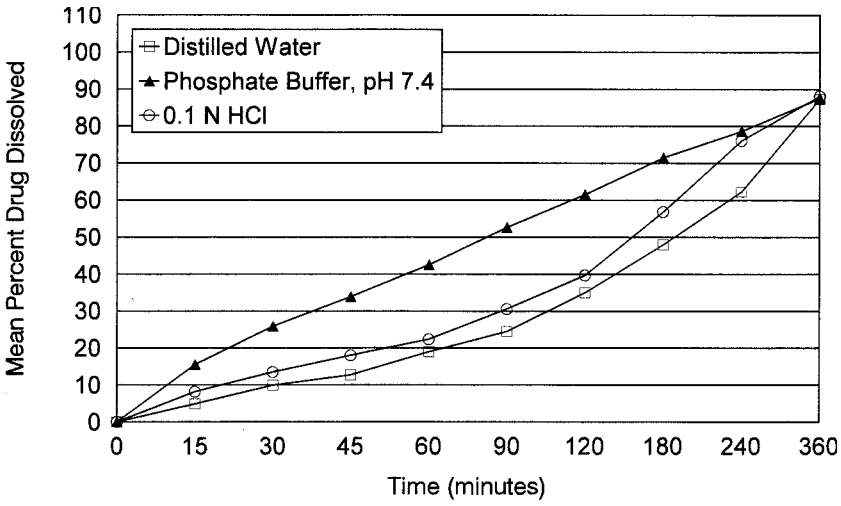

Figure 7. Effect of dissolution medium on drug release from tablets containing 40% polymer and lactose fast flo.

Table 8

Fisher's Least Significant Difference (LSD) for Formulation Containing Lactose Fast Flo and 40% Polymer Tested in Different Dissolution Media

Time (min)	Dissolution Medium[a]	Mean Difference	Fisher's LSD Limit	Results
15	Buffer–HCl	7.27		S
	Buffer–Water	10.57	0.981	S
	HCl–Water	3.30		S
30	Buffer–HCl	12.43		S
	Buffer–Water	16.00	2.89	S
	HCl–Water	3.57		S
45	Buffer–HCl	15.9		S
	Buffer–Water	21.23	3.45	S
	HCl–Water	5.33		S
60	Buffer–HCl	20.07		S
	Buffer–Water	23.47	3.79	S
	HCl–Water	3.4		NS
90	Buffer–HCl	22.00		S
	Buffer–Water	28.10	3.49	S
	HCl–Water	6.10		S
180	Buffer–HCl	14.67		S
	Buffer–Water	23.53	5.17	S
	HCl–Water	8.87		S
360	Buffer–HCl	−0.90		NS
	Buffer–Water	0.17	4.49	NS
	HCl–Water	1.07		NS

[a]HCl = 0.1 N HCl; Buffer = phosphate buffer (pH 7.4); water = distilled water.

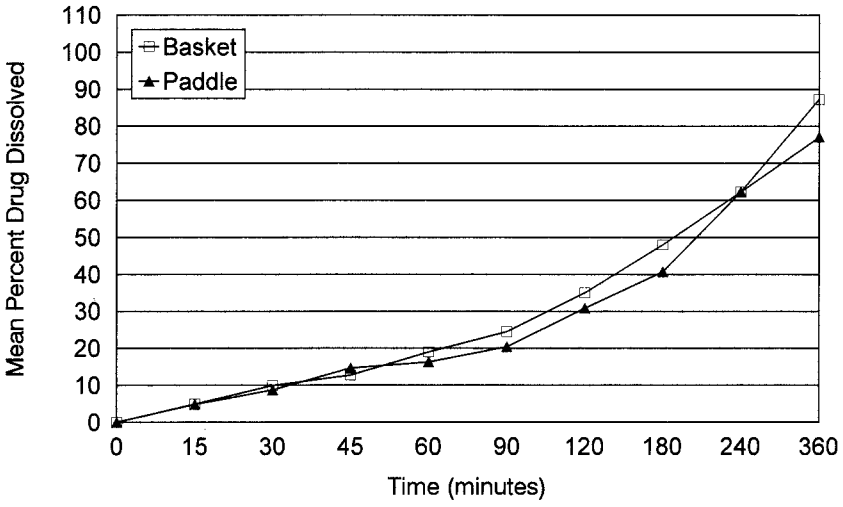

Figure 8. Effect of type of dissolution apparatus on drug release from tablets containing 40% polymer and lactose fast flo.

Table 9

Fisher's Least Significant Difference (LSD) for Lactose Fast Flo Formulation Containing 40% Polymer and Tested in Different Dissolution Apparatus

Time (min)	Dissolution Testing Method	Mean Difference	Fisher's LSD Limit	Results
15	Paddle–Basket	0.0667	1.160	NS
30	Paddle–Basket	1.23	3.443	NS
45	Paddle–Basket	−1.967	4.719	NS
60	Paddle–Basket	2.733	6.269	NS
90	Paddle–Basket	4.10	9.942	NS
180	Paddle–Basket	7.267	16.136	NS
360	Paddle–Basket	10.267	23.038	NS

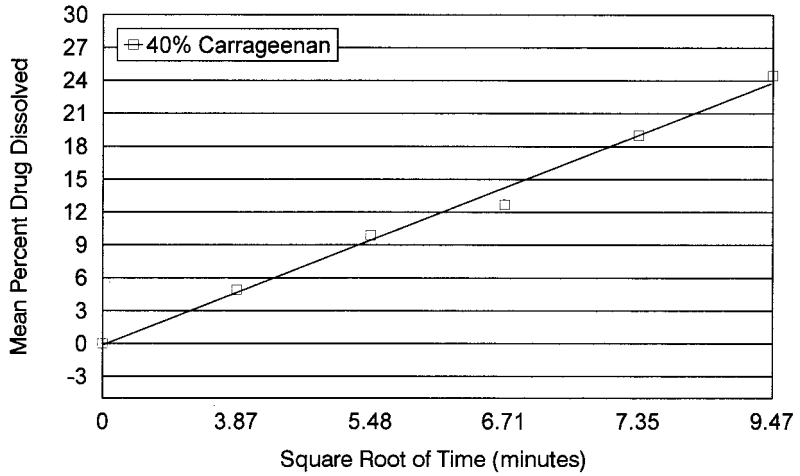

Figure 9. Square root of time plot for tablets containing 40% polymer and lactose fast flo.

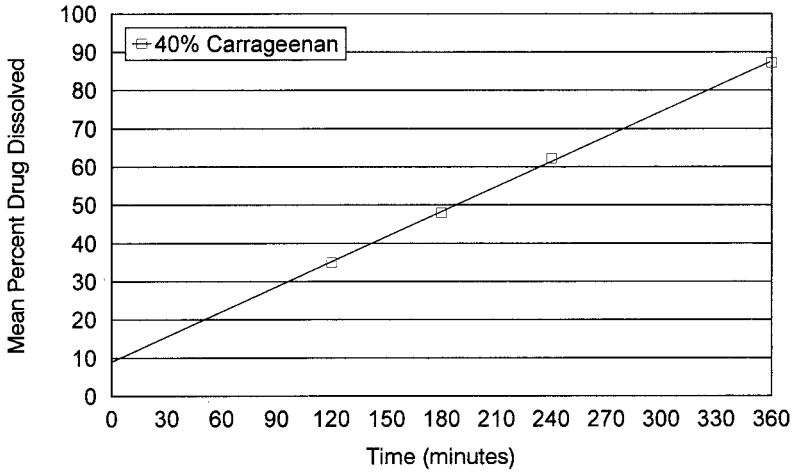

Figure 10. Zero-order release for tablets containing 40% polymer and lactose fast flo.

containing 40% Carrageenan and lactose fast flo or Emcompress as excipient.

Testing dissolution in 0.1 N HCl or phosphate buffer pH 7.4 appears to affect the integrity of the Carrageenan gel layer and consequently the drug release was higher than in distilled water. Also, increasing the rotational speed of the dissolution apparatus interrupts and decreases the thickness of the gel layer.

The mechanism of drug release from Carrageenan matrices appears to follow the diffusion model up to 90 min and after 90 min it follows the zero-order release model.

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