Drug Development and Industrial Pharmacy, 26(6), 651–660 (2000)

RESEARCH PAPER

Comparative Study of Drug Release from Pellets Coated with HPMC or Surelease

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ABSTRACT

The release of metoclopramide hydrochloride (very water soluble cationic drug) and diclofenac sodium (sparingly soluble anionic drug) from pellets coated with hydroxypropylmethylcellulose (HPMC; water-soluble polymer) or ethylcellulose aqueous dispersion (Surelease; water-insoluble polymer) at different coating loads was investigated. The release rates of either drug decreased as the coating load of HPMC increased, but overall, the release was fast, and the majority of both drugs released in about 1 hr, even at the highest coating load. The drug release mechanism for either drug was not affected by the coating load of HPMC or by the type of drug used, and it was found to be mainly diffusion controlled. Diclofenac sodium released slightly more slowly than metoclopramide hydrochloride from HPMC-coated pellets. This was attributed to the lower water solubility of the former drug. The release rate of either drug decreased greatly as the coating load of Surelease increased. The release of both drugs was sustained over 12 hr as the coating load of Surelease increased, and only about 70% of either drug was released after this period at the highest coating load (20%). The mechanism of release of metoclopramide hydrochloride was independent of coating load, and it was predominantly diffusion controlled. However, the mechanism of diclofenac sodium release was dependent on the coating load of Surelease. At low coating loads, diffusion of drug was facilitated due to the presence of more pores at the surface of the coated pellets;

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therefore, the rate of dissolution of the drug particles was the rate-limiting step. However, at high coating loads, drug release was mainly diffusion controlled. Despite its lower water solubility, diclofenac sodium released slightly faster than metoclopramide hydrochloride from Surelease-coated pellets at equivalent coating loads.

Key Words: *Coating; HPMC; Pellets; Surelease; Sustained release.*

INTRODUCTION

Oral sustained- and controlled-release formulations are used to modify the release rates of active substances. Among sustained-release dosage forms, those based on multiparticulate systems have attracted much attention due to their various benefits (1). In addition to in vivo advantages such as reduction in the risk of dose dumping, reduced local irritation of irritant drugs and more predictable drug release profiles, multiparticulate systems are also suitable for a combination of incompatible drugs or when different release rates of a drug are needed from the same dosage form (2). The cores of multiple unit dosage forms generally consist of nonpareil seeds on which the drug layer is applied. The drug-loaded beads are then coated with suitable polymers to provide sustained release.

Ethylcellulose (3,4) and poly(methacrylic acid) (5) are the most common polymers used in the production of coated sustained-release pellets. As these polymers are water insoluble, they can be applied either from their organic solutions or in the form of an aqueous dispersion. Water-soluble polymers are often used in film coating to protect the dosage form from environmental influence and also to improve other properties such as appearance, ingestability, and taste (6). Aqueous films based on hydroxypropylmethylcellulose (HPMC) are the first choice for masking bitter taste, making tablets easy to swallow, imparting esthetic appearances, and identifying products (7). Low-viscosity grades of HPMC are commonly used in film coating. High-viscosity grades of HPMC are unsuitable for film coating because they need organic solvents to make sprayable dispersions (8). Aqueous solutions of high-viscosity grades of HPMC can be used, but only at very low concentrations to achieve sprayability. This results in long processing time (9). On the other hand, Chang et al. (10) reported that water-soluble polymers that yield solutions of low viscosity are not suitable for controlled drug release. However, these authors have not given empirical evidence of the unsuitability of low-viscosity polymers to control drug release.

Several studies have investigated the effect of parameters that influence the rate of drug release from coated pellets. The effects of drug solubility (5,11), coating equipment (12), process of coating (13,14), and core characteristics (3) have been demonstrated previously.

The present study was carried out to evaluate the influence of the drug type on the release behavior from pellets coated with water-soluble polymer (HPMC) or water-insoluble polymer (ethylcellulose aqueous dispersion) using metoclopramide hydrochloride as a highly water soluble cationic drug and diclofenac sodium as an anionic drug with lower solubility.

MATERIALS AND METHODS

Materials

Metoclopramide hydrochloride (metoclopramide HCl) was obtained from Wilfrid Smith Limited (Edgware, Middlesex, UK). Diclofenac sodium (diclofenac Na) was obtained from Industria Chimica Profarmaco (Milan, Italy). Nonpareil (sugar spheres composed of sucrose and starch), 20–25 mesh size (0.710–0.840 mm) were obtained from Forum Chemicals Limited (Redhill, Surrey, UK). HPMC E15 (Methocel E15, manufactured by Dow Chemical Co., Midland, MI), Surelease E-7-7050 (ethylcellulose aqueous dispersion), and triacetin were supplied by Colorcon (Orpington, Kent, UK). Talc was obtained from British Drug Houses (BDH) (Poole, Dorset, UK).

Preparation of Drug-Loaded Pellets

Metoclopramide hydrochloride was applied on batches of 4500 g of nonpareil seeds using Accela-Cota 10 (Manesty, Liverpool, UK). A solution of HPMC E15 in water was prepared by dispersing the 40 g of HPMC powder in 300 ml of preheated water (80°C–90°C) and then diluting it with an additional 300 ml of cold water and allowing it to stand for 2 hr. Metoclopramide hydrochloride (200 g) was separately dissolved in 400 ml of water and then mixed with the HPMC E15 solution. The talc (60 g), which was dispersed in 100 ml of water, was then added and stirred before and during the application of the drug layer.

Table 1

Conditions Used in Drug Layering

Conditions	Metoclopramide HCl	Diclofenac Na
Inlet air temperature (°C)	60–63	60–63
Spray rate (g/min)	15	18
Atomizing air pressure (psi)	40	40

To prepare the diclofenac sodium suspension for drug layering, 200 g of diclofenac sodium (<90 mm) was dispersed in 500 ml of water. The dispersion of drug was passed through a 105-μm sieve with the aid of an additional 100 ml of water to disperse any large aggregates of the drug. A solution containing 40 g of HPMC E15 was prepared as above and then was added to the drug suspension and stirred before and during the application of the fixing liquid to the pellets. The conditions used for metoclopramide hydrochloride or diclofenac sodium layering are shown in Table 1.

Coating of Drug-Loaded Pellets with HPMC E15 or Surelease

For coating, 4500 g quantities of drug-loaded pellets were used. The drug-loaded pellets contained 3.98% ± 0.03% w/w and 3.93 ± 0.08% w/w metoclopramide hydrochloride and diclofenac sodium, respectively. These pellets were coated with HPMC E15 to different thicknesses. Samples of 50 g of pellets were removed from the coating pan when the coating had reached 4%, 8%, 12%, 16%, or 20% by weight. The composition of the coating suspension is shown in Table 2. A solution containing HPMC E15 prepared as described in preparation of drug-loaded pellets. Talc (antiadherent) and triacetin (plasticizer) were also added. The suspension was then stored for 24 hr before use to ensure uniform and full solvation of the polymer. The final suspensions were agitated continuously throughout the coating processes.

Table 2

Composition of Coating Fluid for HPMC E15

Ingredient	% w/w
HPMC E15	3.76
Triacetin	0.94
Talc	1.39
Water	93.91

Surelease was diluted to a 15% w/w dispersion, based on the manufacturer's recommendation, by adding distilled water while stirring with a paddle stirrer at a low shear rate for 15 min. Quantities (4500 g) of pellets loaded with metoclopramide hydrochloride or diclofenac sodium with the drug loads of 3.98% ± 0.03% w/w and 3.93% ± 0.08% w/w, respectively, were coated with Surelease to different thicknesses. Samples of 50 g of pellets were removed from the coating pan when the coating had reached 4%, 8%, 12%, 16%, or 20% by weight.

The final suspensions were agitated continuously throughout the coating process. All the coating processes were performed using an Accela-Cota 10 (Manesty, Liverpool, UK) under the coating conditions shown in Table 3.

Assay of Drug Content

Quantities (400 mg) of each batch of coated beads were weighed accurately, ground to a fine powder using a pestle and mortar, dispersed in 1000 ml of water, and allowed to stand for 1 hr. Aliquots of the solutions were filtered and assayed spectrophotometrically for metoclopramide hydrochloride and diclofenac sodium at 309 nm and 275 nm, respectively.

Dissolution Studies

The dissolution behavior of the pellets was measured using a Pharmatest tester (GMbH, Heinburg, Germany) (USP apparatus I) in line with a Hewlett Packard HP8452A diode array spectrophotometer. The release profiles of beads containing 15 mg of drug in 900 ml of distilled water at a rotating speed of 50 ± 0.5 rpm and 37°C ± 0.5°C were determined. The means of six determinations were used to calculate the drug release for each formulation. For pellets coated with HPMC E15, the pellets were put in small bags (with major dimensions of 2 cm × 3 cm) made from metal gauze (25 mm) to prevent the pellets from coming out of the baskets during the dis-

Table 3

Process Conditions Used in Coating Operations

Condition	HPMC E15	Surelease
Inlet air temperture (°C)	72–74	60–62
Outlet air temperature (°C)	56–58	51–53
Spray rate (g/min)	21	16
Atomizing air pressure (psi)	40	40

solution tests. These metal bags were placed inside the dissolution baskets.

Release Kinetics for Coated Pellets

To determine drug release rates, dissolution data were fitted to various models (zero-order, square-root, and first-order kinetic models, Eqs. 1–3, respectively) using statistical software (Minitab, standard release 9.1).

$$Q = 100 - K_1 t \quad (1)$$

$$Q = K_2 t^{1/2} + C \quad (2)$$

$$Q = 100e^{K3t} \quad (3)$$

where Q is the percentage of drug released at time t; K_1, K_2, and K_3 are zero-order, root time, and first-order release rate constants, respectively. Regression analyses were used to obtain the release constants K and correlation coefficients r for each model. The correlation coefficients for the best statistical fit were used as the principal criteria to evaluate the models. The equation with the highest correlation coefficient was judged to be the most appropriate model for each system. The lag time for Surelease-coated pellets was also calculated from the X intercept when the amount of drug released was zero.

To evaluate the mechanism of drug release, the release data were also analyzed using Eq. 4 (15):

$$Q = K_4(t - t_0)^n \quad (4)$$

where Q is the fraction of drug released, K is the release constant, t_0 is the lag time, and n is the release exponent indicating the mechanism of drug release. The data were fitted to Eq. 4 using a computer program to calculate the optimum values for n, K, and t_0 using a nonlinear least-squares fitting method (15). The understanding of the release mechanism is possible by fitting the release data to these equations and comparing the value of n to the semiempirical values for various geometries reported by Ritger and Peppas (16). For comparative purposes, release data between 15% and 60% were used for modeling drug release. This range also corresponded to the limits of applicability of Eqs. 1 and 2.

Scanning Electron Microscopy

The surface and cross section of the pellets were examined under a scanning electron microscope (SEM) (model Jeol JSM-T200, Tokyo, Japan). The coated pellets were mounted onto stubs using double-sided adhesive tape. The samples were vacuum coated with gold in an argon atmosphere, and then they were examined at 25 kV accelerating voltage. The cross sections of pellets were prepared using a razor blade.

RESULTS AND DISCUSSION

Drug Release from Pellets Coated with HPMC E15

The release profiles of metoclopramide hydrochloride and diclofenac sodium from pellets coated with HPMC E15 are shown in Figs. 1 and 2, respectively. All the pellets disintegrated during the dissolution test, and no gel like structure remained, indicating complete erosion of the membrane and pellets had taken place, even at the 20% w/w coating load. As the coating load increased, the drug release decreased. This is similar to the work reported by Wan et al. (17), who demonstrated that the release of chlorpheniramine maleate from pellets decreased as the coating load of HPMC increased.

The reduction in release rate with increasing coating load may be attributed to the increased diffusional path length with increase in the thickness of the coat (Fig. 3). On the other hand, HPMC hydrates and forms a gel when in contact with water. As the coat thickness increases, the resulting gel could become thicker; therefore, its resistance to penetration by water and to erosion increases.

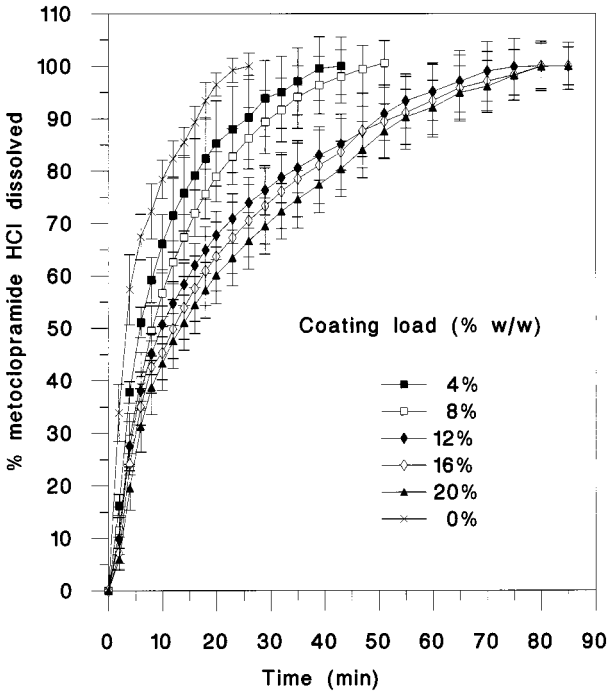


Figure 1. Effect of coating load on the release of metoclopramide HCl from pellets coated with HPMC E15.

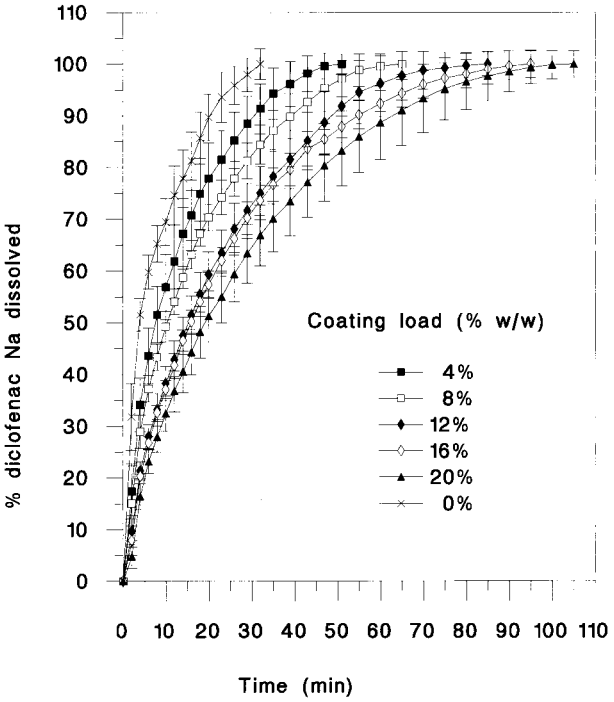
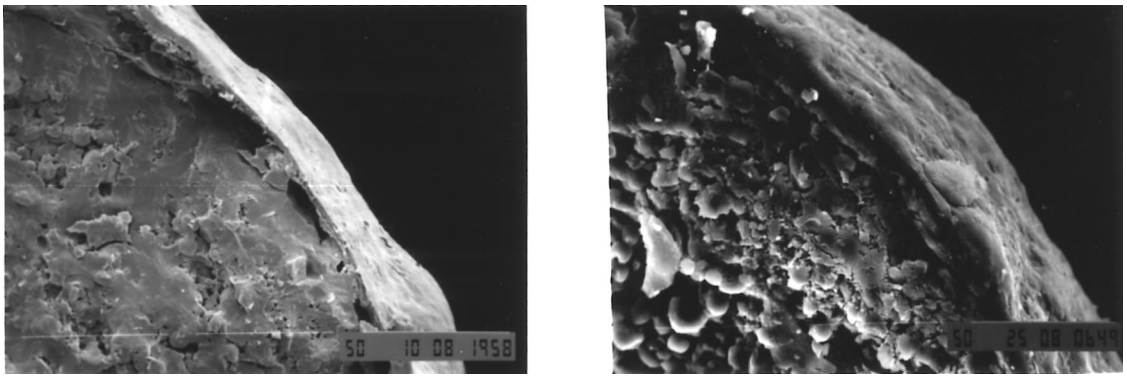


Figure 2. Effect of coating load on the release of diclofenac sodium from pellets coated with HPMC E15.

This would lead to a decrease in the release rate of the drug out of the gelled coat.

Tables 4 and 5 summarize the rate constants and the correlation coefficients for different kinetic models of the release for metoclopramide hydrochloride and diclofenac sodium coated with HPMC E15, respectively. The correlation coefficients for the best statistical line revealed that, at all coating loads, square-root kinetics were probably the most applicable to the release data for either drug. The increase in the coating load was accompanied by a decrease in the release rate. For example, the root time release rate of metoclopramide hydrochloride was halved as the coating load increased from 4% to 20% w/w. Although increasing the coating load of HPMC decreased the release rates of both drugs, the majority of both drugs (>90%) was released within approximately 1 hr, even at the highest coating load (20% w/w), indicating that the release was not controlled by applying an HPMC membrane. Comparison of the release rates for metoclopramide hydrochloride and diclofenac sodium indicates that diclofenac sodium was released slower than metoclopramide hydrochloride at equivalent coating loads. As the molecular weights of both drugs are similar, but slightly higher for metoclopramide hydrochloride (354.3) than diclofenac sodium (318.13), then the faster release of metoclopramide hydrochloride may be ascribed to its higher water solubility (>2.6 g in 1 ml water at 37°C compared to 30 ± 0.3 mg in 1 ml water for diclofenac sodium at this temperature).

Table 6 shows the values of K, n, and t_0 for the release data that corresponded to 15–60% of drug released from pellets coated with HPMC E15 for metoclopramide hydrochloride and diclofenac sodium. According to Ritger and Peppas (16), the value of n around 0.5 represents predominantly a diffusion-controlled release mechanism. Coating load had no apparent effect on the value of n and, consequently, the release mechanism for either drug. The mean value of n was 0.46 ± 0.04 for metoclopramide hydrochloride. The corresponding value for diclofenac sodium was 0.50 ± 0.05. These values indicate that diffusion of drug through the hydrated polymeric gel was probably the predominant mechanism controlling the release



(a) (b)

Figure 3. Micrographs of cross sections of metoclopramide HCl pellets coated with HPMC E15: (a) 4% w/w coating load; (b) 20% w/w coating load (magnification ×350).

Table 4

Values of Release Constants K *and Correlation Coefficients* r *Obtained from Data Corresponding to 15–60% Release of Metoclopramide HCl from Pellets Coated with HPMC E15*

Model[a]	4%	8%	12%	16%	20%
Zero order					
K_1	6.4 ± 1.2	5.1 ± 0.8	3.8 ± 0.3	2.9 ± 0.3	2.1 ± 0.3
r	.977	.980	.957	.949	.956
P<	.1	.01	.01	.001	.001
Square root					
K_2	29.1 ± 3.9	25.3 ± 2.8	19.3 ± 0.8	18.1 ± 1.4	14.6 ± 1.2
r	.993	.997	.986	.982	.987
P<	.01	.001	.001	.001	.001
First order					
K_3	0.113 ± 0.021	0.087 ± 0.011	0.057 ± 0.007	0.048 ± 0.005	0.034 ± 0.005
r	.992	.995	.983	.979	.983
P<	.01	.001	.001	.001	.001

* The units of rate constants are as follows: K_1, %min^{-1}; K_2, %min$^{-1/2}$; K_3, min^{-1}; *P* is the degree of significance.

rate of both drugs. The similar values of *n* for each drug indicated that drug solubility may have little effect on the mechanism of drug release from HPMC-coated pellets.

Drug Release from Pellets Coated with Surelease

The effect of coating load on the release of metoclopramide hydrochloride and diclofenac sodium from pellets coated with Surelease is shown in Figs. 4 and 5, respectively. Uncoated metoclopramide hydrochloride or diclofenac sodium pellets disintegrated rapidly in the dissolution medium and released their drug content in less than 5 min. The drug release decreased dramatically as the Surelease coating loads increased. For instance, at higher coating loads, such as 20% coating, only about 7% of metoclopramide hydrochloride was released in 2 hr, whereas those pellets coated to weight increases of 10% and 4% released 51% and 97% of drug, respectively, in 2 hr. For diclofenac sodium, increasing the coating load from 12% to 20% decreased the amount of drug released from 40% to 8% after 2 hr. In addition, as the level of coating increased, the release profiles showed a biphasic pattern in which there was a phase that showed

Table 5

Values of Release Constants K *and Correlation Coefficients* r *Obtained from Data Corresponding to 15–60% Release of Diclofenac Sodium from Pellets Coated with HPMC E15*

Model[a]	4%	8%	12%	16%	20%
Zero order					
K_1	4.4 ± 1.2	3.6 ± 0.4	2.7 ± 0.3	2.1 ± 0.1	2.0 ± 0.3
r	.976	.979	.986	.982	.979
P<	.001	.001	.001	.001	.001
Square root					
K_2	21.9 ± 4.4	19.2 ± 2.1	17.0 ± 0.4	14.6 ± 0.5	14.4 ± 1.4
r	.994	.997	.999	.998	.998
P<	.001	.001	.001	.001	.001
First order					
K_3	0.078 ± 0.021	0.062 ± 0.005	0.046 ± 0.005	0.037 ± 0.016	0.034 ± 0.004
r	.992	.995	.998	.996	.996
P<	.001	.001	.001	.001	.001

[a] See Table 4.

Table 6

Values of K_4, t_0, *and* n *Based on Equation 4 Calculated in the Range 15–60% Metoclopramide HCl or Diclofenac Sodium Release from Pellets Coated with HPMC E15*

Coating Load	Metoclopramide HCl			Diclofenac Na		
	K_4[a]	t_0[a]	n	K_4[a]	t_0	n
4%	26.30	1.67	0.44	23.30	1.51	0.42
8%	18.00	1.57	0.54	18.50	1.35	0.45
12%	20.70	1.83	0.42	11.17	1.25	0.55
16%	18.90	1.90	0.42	12.00	1.53	0.53
20%	15.80	1.88	0.47	10.30	1.74	0.55

[a] The units of K_4 are $\%min^{-n}$, and t_0 is in minutes.

a low slope followed by a phase with a steep slope. The change in release pattern was achieved after a longer period (commonly known as the *lag time*) as the coating load increased. It is evident from the results that the coating load had a major effect on the ultimate rate of drug release and the duration of the lag times. All the pellets remained intact during the dissolution test, indicating that the Surelease membrane controlled the drug release. These results are in agreement with the findings of Ghebre-Sellassie et al. (18) and Porter (3), who showed that the release of drug (diphenhydramine hydrochloride or chlorpheniramine maleate) from pellets coated with Surelease was related to the weight of coating material deposited on the pellets. The dependency of the release of drugs on the thickness of ethylcellulose membranes has been reported by many authors (19–22).

Generally, in dosage forms that have a water-insoluble polymer as the rate-controlling membrane, since diffusion through the membrane controls the overall release rate of the drug, the membrane properties and geometry,

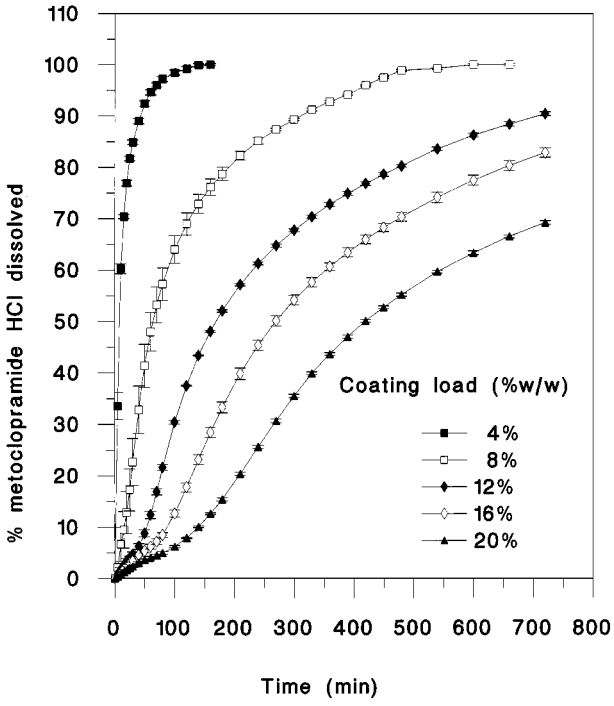


Figure 4. Effect of coating load on the release of metoclopramide HCl from Surelease-coated pellets.

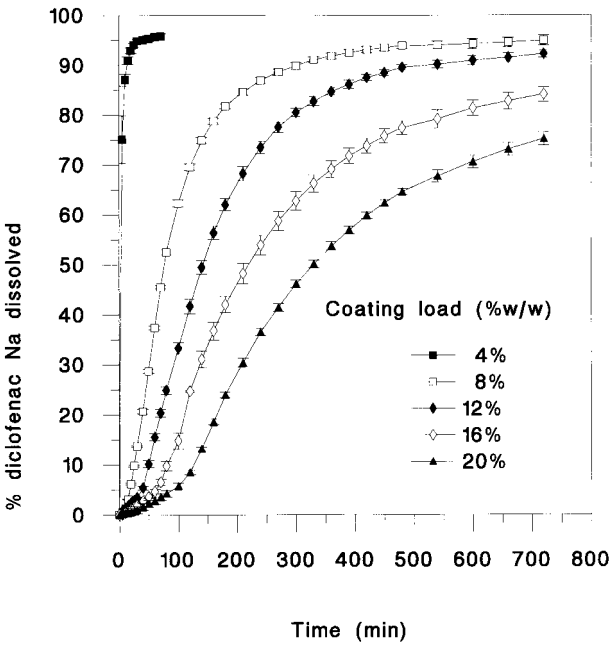
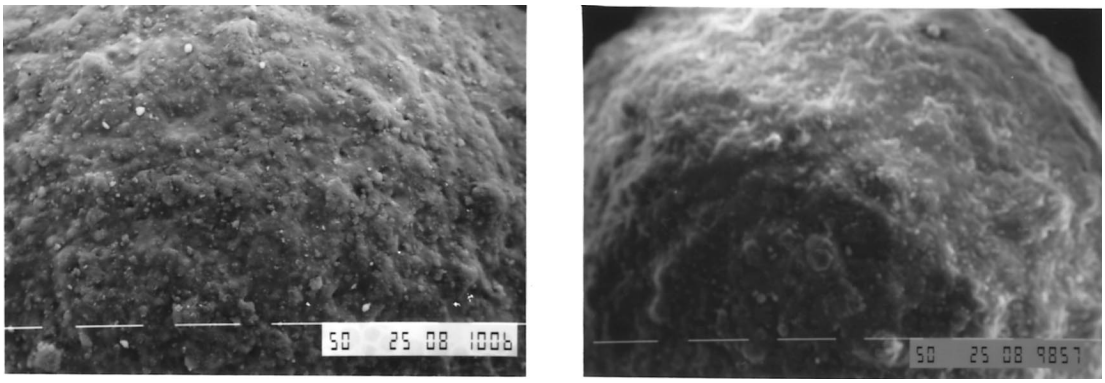


Figure 5. Effect of coating load on the release of diclofenac sodium from Surelease-coated pellets.



(a) (b)

Figure 6. Micrographs of metoclopramide HCl pellets coated with Surelease: (a) 8% coating load; (b) 20% coating load (magnification ×150).

Table 7

Values of Release Constants K, *Correlation Coefficients* r, *and Lag Time* t_0 *Obtained from Data Corresponding to 15–60% Release of Metoclopramide HCl from Pellets Coated with Surelease*

Model[a]	8%	12%	16%	20%
Zero order				
K_1	0.71 ± 0.04	0.28 ± 0.01	0.19 ± <0.01	0.12 ± <0.01
r	.983	.978	.988	.985
$P<$	.001	.001	.001	.001
t_{01}	2.0 ± 3.2	−2.3 ± 3.3	12.9 ± 5.1	32.9 ± 3.4
Square root				
K_2	9.8 ± 0.2	6.5 ± 0.1	5.5 ± 0.1	4.5 ± 0.1
r	.995	.993	.996	.996
$P<$	.001	.001	.001	.001
t_{02}	9.5 ± 3.0	30.3 ± 1.6	56.4 ± 2.6	92.9 ± 1.8
First order				
K_3	0.0117 ± 0.0007	0.0046 ± 0.0001	0.0032 ± 0.0001	0.0020 ± 0.0000
r	.996	.995	.998	.998
$P<$	.001	.001	.001	.001
t_{03}	6.8 ± 3.6	23.3 ± 1.9	54.5 ± 0.83	90.1 ± 1.1

[a] The units of rate constants are as follows: K_1, $\%min^{-1}$; K_2, $\%min^{-1/2}$; K_3, min^{-1}; the units of t_{01}, t_{02}, and t_{03} are minutes. P is the degree of significance.

such as membrane porosity, internal structure (tortuosity), and membrane thickness, may be critical factors in determining the release rate of the drug (23). During film application, the pellets are continuously layered with additional coating material; the film formed is therefore composed of overlapping segments (24). As more layers of film are applied, the holes from overlapping films are gradually blocked. Hence, this reduces the dissolution rate; therefore, the higher the coating level is, the longer the lag time and the lower the apparent drug dissolution rate. Scanning electron micrographs of coated pellets with 8% and 20% coating levels are shown in Fig. 6. The presence and distribution of the pores are more apparent on the surface of pellets with a low coating load (8%) than those with the higher coating level (20%). These pores may act as points of entry for dissolution fluid into the pellets and as points of exit for the release of dissolved drug into the dissolution medium. On the other hand, the coating layer was thicker as the load increased. Therefore, the diffusion path length for the dissolution

Table 8

Values of Release Constants K, *Correlation Coefficients* r, *and Lag Time* t_0 *Obtained from Data Corresponding to 15–60% Release of Diclofenac Sodium from Pellets Coated with Surelease*

Model[a]	8%	12%	16%	20%
Zero order				
K_1	0.73 ± 0.01	0.40 ± 0.01	0.24 ± 0.01	0.16 ± <0.01
r	.996	.997	.985	.985
$P<$	.001	.001	.001	.001
t_{01}	10.5 ± 0.2	19.9 ± 1.5	18.3 ± 5.1	25.1 ± 4.3
Square root				
K_2	10.9 ± 0.1	8.3 ± 0.1	6.4 ± 0.1	5.3 ± 0.1
r	.997	.998	.996	.995
$P<$	.001	.001	.001	.001
t_{02}	18.0 ± 0.1	34.8 ± 0.8	50.7 ± 2.7	78.5 ± 2.1
First order				
K_3	0.0119 ± 0.0002	0.0067 ± 0.0002	0.0039 ± 0.0002	0.0028 ± 0.0001
r	.996	.999	.999	.998
$P<$	.001	.001	.001	.001
t_{03}	18.9 ± 0.7	36.1 ± 1.0	51.3 ± 2.3	78.3 ± 2.3

[a] See Table 7.

medium to enter the core and the dissolved drug to come out through the core could be increased. This would account for the much lower release rates for pellets with higher coating levels.

Tables 7 and 8 show the release constants K and lag times t_0 of the fits of release data to different kinetic models. Due to insufficient data points for release of either drug from pellets with a 4% coating load of Surelease, it was not possible to perform regression analysis for these pellets; therefore, no results are reported for 4% coating load. The correlation coefficients r for the best statistical fit revealed that, for both drugs, first-order kinetics are probably most applicable to model all the release data. A dramatic decrease in the release rate of either drug with increasing the coating load of Surelease can be observed. For instance, the first-order release rate of metoclopramide hydrochloride was more than five times faster at the 8% coating load than the 20% load. The calculated lag times also increased as the coating load increased irrespective of the kinetic model used.

Table 9 shows the values of K, n, and t_0 obtained from Eq. 4. The mean value of n was 0.60 ± 0.03 for pellets loaded with metoclopramide hydrochloride, indicating that diffusion is the predominant mechanism controlling drug release. It was also observed that the coating load had no apparent effect on the mechanism of release of metoclopramide hydrochloride as the values of n were similar for all coating loads.

Table 9

Values of K_4, t_0, *and n Based on Equation 4 Calculated in the Range 15–60% Metoclopramide HCl or Diclofenac Sodium Release from Surelease-Coated Pellets*

Coating Load	Metoclopramide HCl			Diclofenac Na		
	K_4[a]	t_0[a]	n	K_4[a]	t_0	n
8%	4.74	15.40	0.60	0.71	12.40	1.02
12%	3.72	52.00	0.54	1.59	39.40	0.73
16%	1.95	81.40	0.62	4.36	88.50	0.50
20%	1.48	133.00	0.62	2.62	123.00	0.55

[a] See Table 6.

It seems that the diclofenac sodium release mechanism was dependent on the coating load of Surelease. The higher values of *n* were obtained for 8% and 12% coating loads. At these coating loads, due to the ease of diffusion through the numerous pores, diffusion of drug has not been a major rate-limiting step in the release process; therefore, the rate of dissolution of the drug particles mostly controlled the release mechanism. While at high coating loads fewer pores are available for release, the diffusion of drug has been a slow process controlling the release mechanism.

A comparison of the release profiles for metoclopramide hydrochloride and diclofenac sodium coated with Surelease revealed that, despite its lower solubility, diclofenac sodium showed faster release rates than metoclopramide hydrochloride at equivalent coating loads (Tables 7 and 8). However, it has been claimed that the aqueous solubility of the drug plays an important role in the release rate of the drug from coated pellets (4,18). Highly water soluble drugs generally release faster than poorly water soluble compounds. The slower release of metoclopramide hydrochloride from Surelease-coated pellets may be due to possible interactions between the drug and the coating suspension.

CONCLUSIONS

Overall, the drug release from pellets coated with HPMC E15 (up to 20% w/w) was fast and was completed within 1 hr. It was found that the release of both metoclopramide hydrochloride and diclofenac sodium decreased as the coating load of HPMC increased. However, diclofenac sodium released slightly slower than metoclopramide hydrochloride at equivalent coating loads of HPMC. The mechanism of drug release was unaffected by the solubility of the drugs and also coating the load of the polymer, and diffusion was the main mechanism controlling the release rate of drug.

The release of either drug from Surelease-coated pellets was sustained over a period of 12 hr. The coating load had a great effect on the release rate of drugs from Surelease-coated pellets. Despite its lower solubility, diclofenac sodium was released faster than metoclopramide hydrochloride at equivalent coating loads of Surelease. The mechanism controlling the release rate of water-soluble metoclopramide hydrochloride at all coating loads was predominantly diffusion. However, the mechanism controlling the release of diclofenac sodium from Surelease-coated pellets was dependent on the coating load.

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