Barrier Membrane Coating of Hydrophilic Matrices: Influence of Tablet Shape and Geometry on Drug Release

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Abstract Summary

The objective of the study was to investigate the effect of various tablet shapes such as round, caplet, pentagon and flat-faced on the drug release profiles from uncoated and barrier membrane (BM) coated hydrophilic matrix tablets of hydrochlorothiazide (HCTZ), a very slightly soluble drug. The drug release from the matrix tablets of HCTZ was found to be similar for the tablets of different shapes because of the similarity of surface area/volume (SA/V) ratio. However, the application of a barrier membrane coating consisting of, Surelease® aqueous ethylcellulose dispersion and Opadry® complete film coating system as pore-former on these matrices did not result in similar release profiles despite similar SA/V ratios. The results were found to be attributed to the controlled rupture of the barrier membrane film around the belly band area of the tablet, which is governed by the tablet shape and geometry. The findings of this study indicated that barrier membrane coating of hydrophilic matrix tablets of different shapes offers an opportunity for drug release modulation and tailoring the drug release profile. Additionally there are advantages such as rebranding of existing products, and creating distinctive formulations. Barrier membrane coating may also protect against food effect as reported elsewhere.[1]

Introduction

Hypromellose (hydroxypropyl methylcellulose, HPMC) is the most widely used rate controlling polymer in hydrophilic matrices for oral ER drug delivery, providing robust formulations and simplified production.[2] Different tablet shapes are used for a variety of reasons such as brand identification, dose strength distinction and patient compliance. Selection of a specific shape may enhance the aesthetic appearance, mechanical strength for packaging and handling, and swallowability of the tablets. The shape and geometry of the matrix tablet is one of the critical parameters in determining the release rate from hydrophilic matrices.[3] It is reported that drug release from matrix tablets of equal mass at constant SA/V ratios were similar among different tablet shapes, irrespective of the drug solubility.[3]

The purpose of this study was to investigate the effect of barrier membrane coating on drug release rate of hydrophilic matrices of different shape and geometries of equivalent surface area to volume (SA/V) ratios. Hydrochlorothiazide (HCTZ), a very slightly soluble drug (solubility of ~ 0.7 mg/mL), at a dose level of 200 mg was used as a model drug.

Experimental Methods

Formulation and Tablet Preparation

Hydrochlorothiazide extended release tablets consisted of 50% w/w active (Hubei Maxpharm, China), 30% w/w HPMC (METHOCEL™ K100LV Premium CR, Dow Chemical Co., USA), 19% w/w lactose (FastFlo, Foremost, USA) and 0.5% w/w each of colloidal silicon dioxide (Cab-O-Sil M5P, Cabot Corp., USA) and magnesium stearate (Mallinckrodt, USA). The tablets of different shapes (round, caplet, pentagon and flat-faced) with constant SA/V ratio were compressed using instrumented rotary press (Piccola, Riva, Argentina) at a constant target weight of 400 mg. Tablets with sufficient mechanical strength [hardness ≥15kP (≥2.9 MPa)] were used for application of barrier membrane coating.

Application of Barrier Membrane Coating

HCTZ matrix tablets were coated with a BM coating consisting of a combination of Surelease® E-7-19010 and HPMC based Opadry® as a pore-former at ratio of 85:15. Prior to application, the coatings were dispersed at a 10% w/w solids level in water. Tablets were then coated to a 2% weight gain (WG). Standard coating processing parameters were used for application of BM coating (**Table 1**).

Drug Dissolution Studies

In vitro dissolution studies of the formulated HCTZ ER tablets were conducted using Apparatus II, 100 rpm with sinkers and 900 mL of dissolution media (pH 4.5 acetate buffer for 4 hrs followed by pH 6.8 phosphate buffer for 12 hrs) at 37 °C ± 0.5 °C. HCTZ release was determined spectrophotometrically at a wavelength of 272 nm.

Table 1. Coating Process Parameters Used for Application of BM Coating on Hydrophilic Matrix Tablets

Parameter	Value
Tablet charge (kg)	1
Inlet temperature (^{o}C)	55-57
Bed temperature (^{o}C)	45-48
Exhaust temperature (^{o}C)	47-49
Air Velocity (m^3/hr)	290
Spray rate (g/min)	6-8

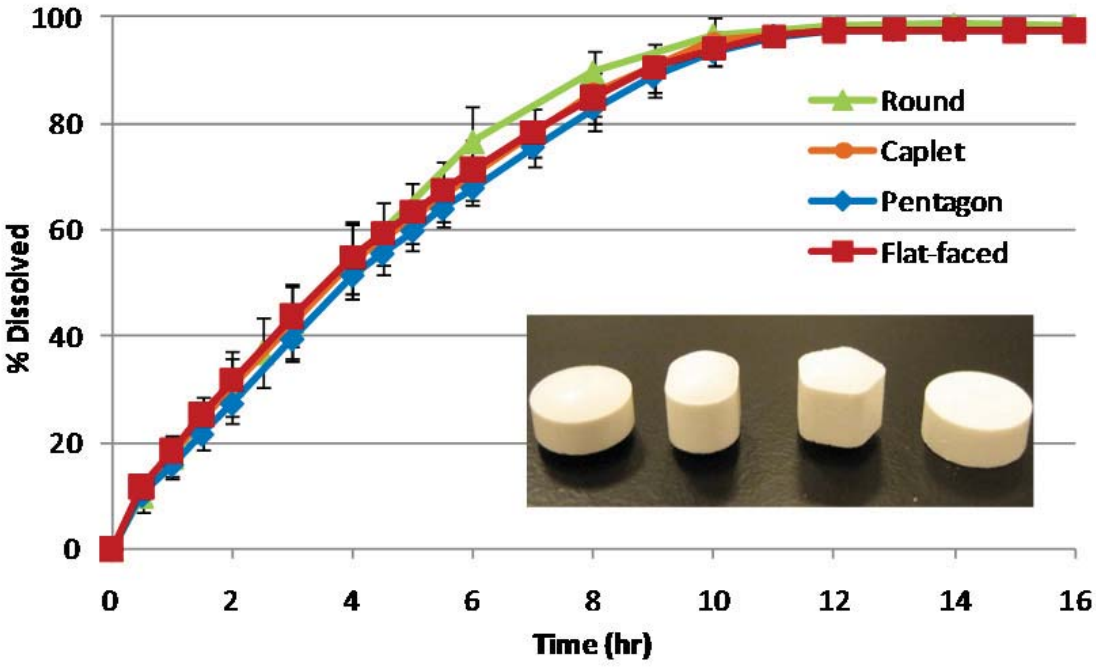
Results and Discussion

The physical properties of HCTZ hydrophilic matrix tablets of different tablet shapes are listed in **Table 2**. All the tablet formulations exhibited equivalent SA/V ratios and acceptable mechanical properties for coating application. The drug release profiles for uncoated HCTZ matrix tablets of different shapes are shown in **Figure 1**. Results indicated similar drug release profiles for different shapes and geometries as evident by similarity factor, f_2 values (74.1 for caplet, 64.7 for pentagon and 74.2 for flat-faced shape considering round tablet as a reference) when a constant SA/V ratio was maintained.

Table 2. Physical Properties of Different Shapes of Tablets

Shape	Thickness (mm)	Hardness (kp [MPa])	SA/V mm^2/mm^3	f_2 Value (BM coated)
Round	5.11 ± 0.02	17.0 ± 0.7 [3.9]	0.821	Ref.
Caplet	6.62 ± 0.01	17.8 ± 1.2 [2.9]	0.780	45.1
Pentagon	7.19 ± 0.04	18.1 ± 1.5 [3.2]	0.780	32.7
Flat-faced	3.73 ± 0.02	16.2 ± 0.8 [4.5]	0.936	51.8

Figure 1. Dissolution Profile of HCTZ 200 mg Uncoated ER Tablets



Drug release from BM coated matrices of different shapes and geometries is shown in **Figure 2**. Results indicated that application of a BM coating with a pore-former on hydrophilic matrix tablets of different geometries with constant SA/V ratio resulted in variable drug release rates (see f_2 values in **Table 2**). BM coated, round tablets produced the slowest release rate; whereas, the pentagon shape resulted in the fastest release profile. The results were attributed to the rupture of the barrier membrane film around the belly band area of the tablet, which is in fact governed by the tablet shape and geometry (**Figure 3**). As seen in **Figure 3**, the pentagon shape has the maximum edge area amongst the selected tablet shapes, which may result in weaker coverage of the BM coating film at those edges. The rupture of the film at those edges during the dissolution led to the faster drug release rate compared to other shapes. On the other hand, minimal belly band area for the round shape resulted in slower release rate. One could also explain the observed results with the amount of barrier membrane film retained over the tablet surface during dissolution, which was higher for round and flat-faced tablets than pentagon and caplet shaped tablets.

Figure 2. Dissolution Profile of HCTZ 200 mg ER Tablets Coated with BM Coating Consisting of Surelease® and Opadry® at 85:15 Ratio and 2% WG.

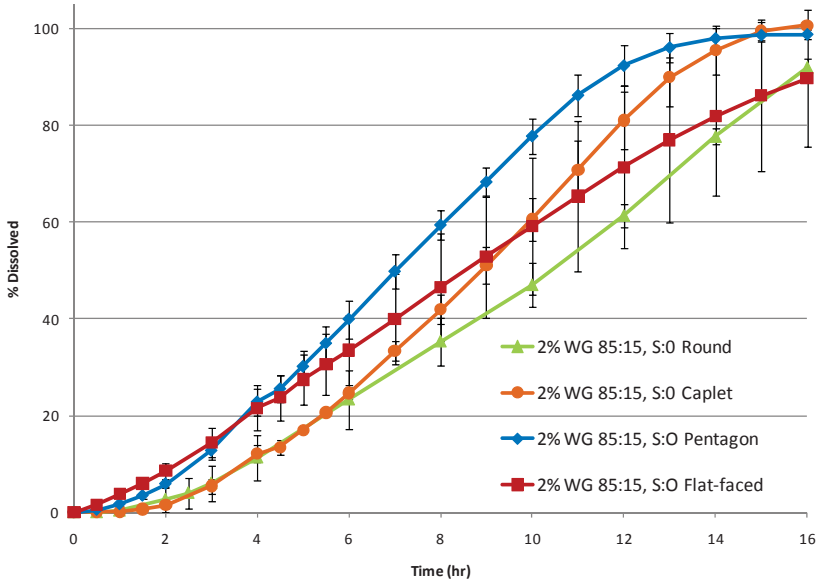
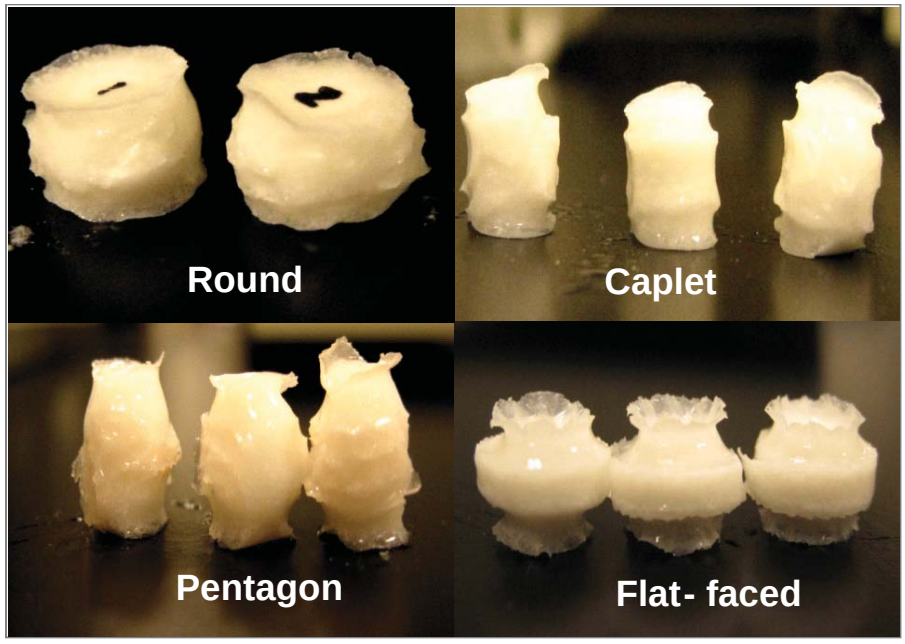


Figure 3. Coating Rupture Pattern of HCTZ 200 mg ER Tablets Coated with BM Coating After 4 hr Exposure to Dissolution Media.



Conclusions

The study results indicated that barrier membrane coating of hydrophilic matrix tablets resulted in zero oder drug release. Barrier membrane coating of different shaped hydrophilic matrix tablets offers an opportunity for drug release modulation and tailoring the drug release profile in addition to advantages such as rebranding of existing products, and creating distinctive formulations.

References

1. Ayrus JW, Coated Platform-Generating Tablets, US Patent 6733784B1
2. Tiwari SB and Rajabi-Siahboomi AR. Extended-Release Oral Drug Delivery Technologies: Monolithic Matrix Systems. In: Jain KK, ed. *Drug Delivery Systems, Methods Mol Biol*. Vol. 437, Humana Press: Totowa, NJ; 2008:217-243.
3. Shahrzad M. et al. Investigation of the Influence of Tablet Shape,Geometry & Film Coating on Drug Release From Hypromellose Extended-Release Matrices, *Drug Del. Tech*., Mar 2010,Vol:10, 2-8.