Investigation of the Effect of Tablet Geometry and Film Coating on Drug Release from Hypromellose Matrices at Constant Surface Area to Volume Ratio Using Two Model Drugs

ABSTRACT SUMMARY

Different tablet shapes were used to evaluate the effect of geometry on the release of model drugs, with varying aqueous solubility and dose, from hydrophilic matrices at constant tablet surface area/volume ratios. Results showed no significant difference in release for each drug regardless of tablet shape or presence of film coating.

INTRODUCTION

Hypromellose (hydroxypropyl methylcellulose [HPMC]) has been widely used in the formulation of hydrophilic matrices for oral extended release (ER) drug delivery. Drug release from HPMC matrix tablets may be affected by several variables, such as tablet shape, size and surface area.[1] Once a hydrophilic matrix tablet is developed and the release profile is established with a certain tablet shape, there is reluctance to modify the product geometry. This is particularly true for drugs at the extremes of dose or solubility, for which the drug release is mainly controlled via diffusion or erosion. A previous study examined the release of highly water-soluble drugs from HPMC matrices and demonstrated that when surface area to volume ratio (SA/V) is held constant, the drug release profiles are similar regardless of the tablet shape (round or oval).[2]

The objective of this study was to evaluate the effect of various tablet shapes on drug release from HPMC matrices, using two model drugs, metformin HCl, as a freely soluble drug, used at a high dose (50% w/w), and indapamide as a practically insoluble drug, used at a low dose (0.75% w/w). The mechanism of release is expected to be primarily diffusion-controlled for metformin HCl and erosion-controlled for indapamide. In addition to round and caplet shapes, tablets with dumbbell and pentagon geometries were also evaluated. These shapes could potentially be used to enhance a products brand. For all formulations, SA/V was held constant. In addition, the effect of film coating on drug release from selected tablet shapes was also evaluated.

EXPERIMENTAL METHODS

The composition of extended release matrix formulations for metformin HCl and indapamide is shown (Table 1). All matrices were prepared using direct compression method (batch size = 2 kg). For metformin HCl matrices, microcrystalline cellulose (MCC) and fumed silica were passed through an ASTM mesh # 35 sieve (500 µm). All ingredients, except magnesium stearate, were mixed in a twin shell blender (Patterson Kelley, USA) for 5 minutes. Magnesium stearate was then added to the blender and mixed for another minute.[3] In case of indapamide matrices, drug and half of the lactose were blended in a high shear granulator (VG-25, Glatt Air Techniques, USA) for 5 minutes at an impeller speed of 200 rpm and a chopper speed of 500 rpm. The remaining lactose (sieved with fumed silica through an ASTM mesh # 35 sieve) was added to the bowl and mixed for 5 minutes. HPMC was then added and blended for an additional 5 minutes. Finally, magnesium stearate was added and the formulation was mixed for one minute at an impeller speed of 400 rpm.[4]

Table 1. Extended Release Matrix Formulations of Metformin HCl and Indapamide

Ingredients	**Amount per Tablet (mg)**	
***Metformin** HCl* (Wanbury, India)	500.0	-
Indapamide (Jinan Shandong, China)	-	1.5
Microcrystalline cellulose (Emcocel 90M, JRS Pharma, Germany)	190.0	-
Lactose (Fast Flo, Foremost, USA)	-	119.1
HPMC (METHOCEL K15M Prem CR, IFF., USA)	-	77.4
HPMC (METHOCEL K100M Prem CR, IFF., USA)	300.0	-
Fumed silica (Aerosil 200, Evonik, Germany)	5.0	1.0
Magnesium stearate (Mallinckrodt, USA)	5.0	1.0
Total (mg)	1000.0	200.0

Tablets were manufactured using an instrumented 10-station rotary press (Piccola, Riva, Argentina), operated at 20 rpm. For each drug, 3 tablet shapes were evaluated; standard concave round, caplet and dumbbell for metformin HCl, and standard concave round, caplet and pentagon for indapamide. The resulting tablets were evaluated for physical properties, including weight variation, hardness, and dimensions (Multicheck, Erweka, Germany), friability (Vanderkamp Friabilator, VanKel Industries, USA), and SA/V values (using the tooling specifications and relevant mathematical equations). To evaluate the effect of film coating on drug release, the dumbbell and pentagon shaped tablets were selected and coated with Opadry® II, high performance film coating system, 85F18422 white (Colorcon, USA) in a fully perforated coating pan (Compu-Lab, Thomas Engineering, USA) to a 4% w/w weight gain. Drug release was measured in a USP compliant dissolution bath (VanKel VK7000, Varian Inc. USA) using methods reported previously.[3-4]

RESULTS AND DISCUSSION

Physical properties for the tablets are shown (Table 2). Both tablet formulations exhibited low friability values (≤0.59%).

Table 2. Physical Properties of Matrices (n=10)

(A) Metformin HCl ER Matrix Tablets

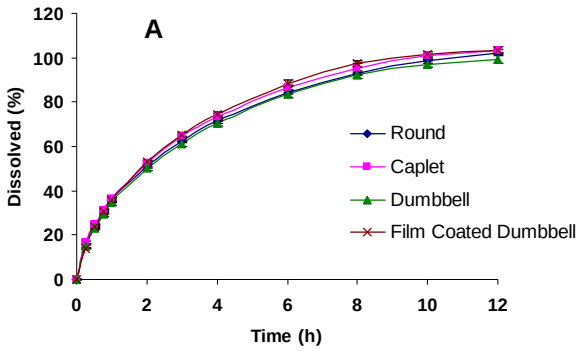
Tablet shape	Weight (mg)	Thickness (mm)	Diameter (mm)	SA/V	Hardness (kp)
Round	1010 ± 6	6.34	14.30	15.54	14.9 ± 0.5
Caplet	1008 ± 7	6.70	19.07	15.52	16.5 ± 0.7
Dumbbell	1001 ± 8	7.25	19.00	15.68	16.1 ± 0.9

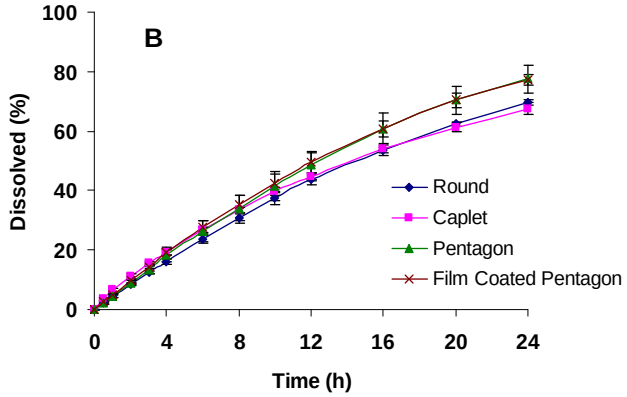
(B) Indapamide ER Matrix Tablets

Tablet shape	Weight (mg)	Thickness (mm)	Diameter (mm)	SA/V	Hardness (kp)
Round	206 ± 1	4.77	7.12	24.73	12.5 ± 0.5
Caplet	203 ± 1	3.83	9.40	26.84	10.0 ± 0.2
Pentagon	200 ± 1	4.14	7.94	26.44	12.7 ± 1.0

Drug release profiles for each tablet shape are shown (Figure 1). The similarity factors (f_2) were calculated[5] for different geometries utilizing the round shape as the reference. The f_2 values for metformin HCl tablets were 88.2 (caplet) and 92.4 (dumbbell). For indapamide matrices, the f_2 values were calculated as 78.4 (caplet) and 64.0 (pentagon). Thus, the drug release profiles were considered similar ($f_2 > 50$)[5], indicating that changing tablet geometry did not influence the drug release profile when SA/V is held constant. This is more evident with metformin HCl matrices, where the drug release mechanism is mainly controlled by diffusion. As shown (Figure 1) film coating of matrices with Opadry II 85F did not alter the drug release profiles. The f_2 values for coated tablets were >75.0, considering the uncoated tablets as reference. This is in agreement with the findings by Levina et al on traditional tablet shapes.[6]

Figure 1. Drug Release Profiles for Matrices (n=6) (A) Metformin HCl Matrices (B) Indapamide Matrices. The photorealistic images shown are merely illustrative of the tablet shape





CONCLUSION:

For METHOCEL hydrophilic matrices, surface area to volume ratio (SA/V) is an important parameter in controlling drug release. This is true regardless of the drug solubility, dose, and mechanism of drug release. Coating of matrices with Opadry II did not alter the drug release profile. The results indicate an opportunity for manipulation of matrix design (shape and coating), which could enhance product branding.

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