Application of Barrier Membrane Coating to Reduce the Weight of Metformin HCl Extended Release Tablets

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Introduction

Hyprophilic matrices are among the most widely used technologies for oral extended release (ER) drug delivery systems, providing robust formulations and straightforward tablet production. For a high dose, high solubility drug, a high polymer concentration is often required to achieve ER; this results in large-sized tablets, which may affect patient acceptability and compliance. For example, metformin hydrochloride (HCl) ER formulation with high dose (1000 mg), results in the finished tablet weight being significantly higher (1500 mg). Reducing the size of the tablets results in improved patient compliance, cost reduction and more efficient manufacturing. However, reducing tablet size for ER formulations, while achieving similar drug release profiles and, maintaining flow and compressibility of the formulation, may be challenging. The purpose of this work was to investigate the application of a barrier membrane coating approach to support the reduction of the weight and size for metformin HCl ER tablets.

Methods

Metformin HCl (1000 mg) ER hydrophilic matrices were manufactured according to the formulation in Table 1, using high shear wet granulation (HSWG). The lubricated blend was compressed on a single rotary tablet press (Rimek, Mini Press II) fitted with 19 x 9 mm plain, oval standard concave tablet tooling at a target weight of 1290 mg. The tablets were then coated with a barrier membrane (BM) consisting of Surelease®, ethylcellulose dispersion type B NF and Opadry®, complete film coating system (Table 1) at 3 to 8% theoretical weight gain (Table 1) using a perforated pan auto-coater (Lab Coat, O'Hara[4]).

Dissolution testing

Dissolution testing of metformin HCl ER tablets was carried out in 900 mL phosphate buffer pH 6.8 at 37°C temperature, in a USP I (basket) apparatus at a stirring speed of 100 rpm. Drug release was analysed spectrophotometrically at 250 nm. The dissolution test results were compared with USP 40 monograph test #5 specification (Table 2) for compliance[2].

Swelling and erosion testing

Testing for swelling (% weight gain of wet samples) and erosion (% mass loss of dried sample) was conducted in 900 mL phosphate buffer pH 6.8 at 37°C using USP II apparatus with stirring speed at 100 rpm. Tablets with different coating weight gains were placed in individual vessels, then withdrawn at specific time intervals. Excess water was blotted, weighed, and then oven fried at 60°C until constant weight was obtained. Values for swelling and erosion were calculated using the following equations[3].

$$\textbf{Swelling (\% Weight Gain)} = \frac{[\text{Wet Weight} - \text{Original Weight}]}{\text{Original Weight}} \times 100$$

$$\textbf{Erosion (\% Mass Loss)} = \frac{[\text{Original Weight} - \text{Remaining Dry Weight}]}{\text{Original Weight}} \times 100$$

Title 1. Composition of Metformin HCl ER Tablets

Ingredients	% w/w
Hydrophillic matrix core tablet	
Intra-granular	
Metformin HCl	77.53
METHOCEL™ K200M Premium	6.47
METHOCEL™ K4M Premium	6.47
PVP K30	2.53
Purified Water*	Q.S.
Extra-granular	
Microcrystalline Cellulose [100 µm]	6.50
Magnesium stearate	0.50
Core Tablet Weight	100.00
Barrier Membrane (BM) Coating**	
Surelease E-7-19040	7.5
Opadry 03B59002	2.5
Purified water* to make 10% w/w solid content	Q.S.

Note: *Does not remain in the final product, **Barrier membrane consisted of Surelease : Opadry; 75:25 ratio on dry basis

Table 2. Dissolution Test #5 Specification for Metformin HCl ER Tablets

Time (h)	Dissolution Test Specifications (%)
2	NMT30
8	60-85
16	NLT 90

Results

Reduced size ER metformin HCl (1000 mg dose) ER tablets, with final weight ~1300 mg were developed. A burst release was seen with the uncoated core tablets of metformin HCl, whilst the BM coated tablets showed good ER profiles, which was similar to earlier work[4-6]. As the weight gain of BM coating increased, then dissolution, tablet swelling, and erosion were significantly reduced compared to uncoated tablets. Figure 1 shows dissolution profiles of BM coated metformin HCl ER tablets at different weight gains. Tablets with a 5-6% weight gain (w/w) complied with USP monograph test #5 dissolution specifications (Table 3). Figure 2 shows that rapid swelling of the uncoated tablets as compared to BM coated tablets. Tablets with increasing weight gains of BM coating swelled slowly; however, BM coating weight gains above 6%, did not change the swelling characteristics (Figure 3a). Similar trends were observed in the erosion of the tablets at various time points, and Figure 3b shows the erosion behaviour of the uncoated and BM coated matrices. The BM coated hydrophilic matrices[5]. The coating was retained around the tablet face and belly band through the sixth hour of study.

Figure 1. Metformin HCl Release Profiles from Hydrophilic Matrix Tablets

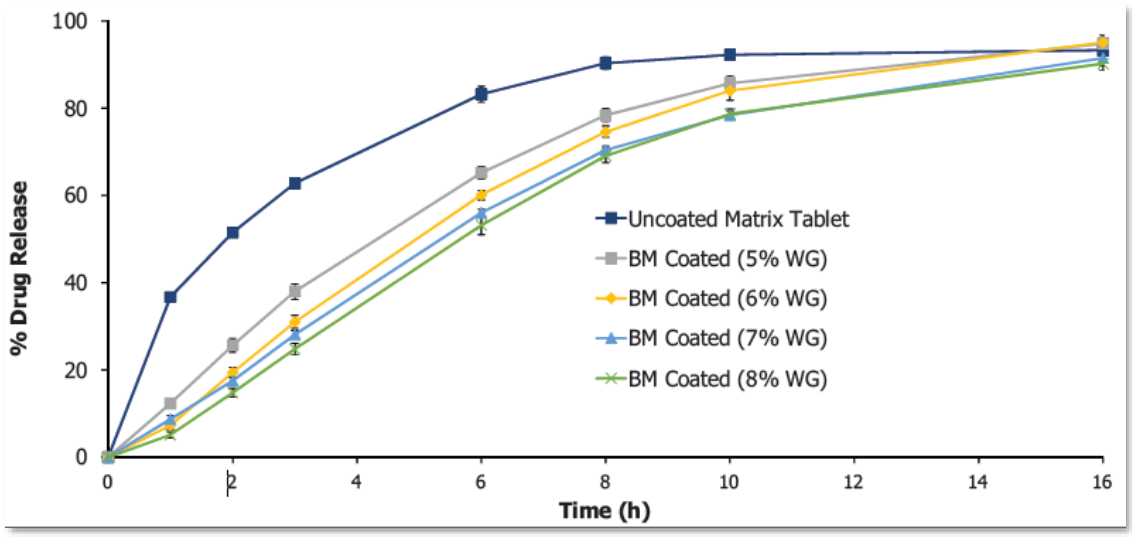


Table 3. Application of BM Coating to Comply with Dissolution Test #5 Specification for Metformin HCl ER Tablet Monograph[2]

Formulation	Barrier Membrane Weight Gain (%)	Core Tab Weight (mg)	Compiled to Test #5 for Metformin HCl ER Tablets
Uncoated Matrix Tablet	0	1290	No
BM Coated Tablet	5	1345	Yes
BM Coated Tablet	6	1367	Yes
BM Coated Tablet	7	1380	Yes
BM Coated Tablet	8	1393	Yes

Figure 2. Swelling and Erosion of Uncoated and BM Coated Tablets of Metformin HCl ER, 1000 mg.

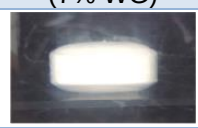
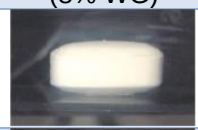
	Uncoated Matrix Tablet	Barrier Membrane Coated Matrix Tablets			
		(5% WG)	(6% WG)	(7% WG)	(8% WG)
Initial					
30 min					
2 hours					
6 hours					

Figure 3a. Swelling (%WG)

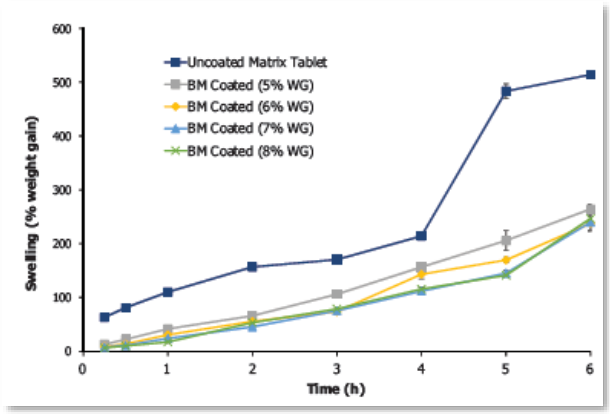
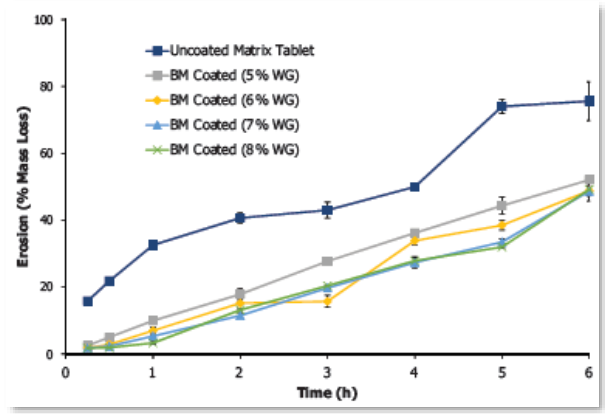


Figure 3b. Erosion (% Mass Loss)



Conclusions

Reducing total tablet weight of metformin HCl ER 1000 mg tablets was possible using a matrix core coated with a water insoluble BM coating. Matrices coated with 5-8% weight gain with BM coating complied with dissolution test #5 specifications of USP 40 monograph on metformin HCl ER tablets (1000 mg dose).

References

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