# Barrier Membrane Coating of Hydrophilic Matrices: A Simplified Strategy to Attain Zero Order Drug Release

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## Abstract Summary

Extended release hydrophilic matrix tablets of glipizide were formulated using hypromellose as the rate limiting polymer. Application of barrier membrane (BM) coating, aqueous ethylcellulose dispersion (Surelease®) with a pore-former (Opadry®), resulted in an initial lag phase followed by zero order drug release. The findings of the study indicate that BM coating of hydrophilic matrices can offer a simplified and cost-effective formulation approach to attain zero order drug release kinetics.

## Introduction

In recent years, there has been increasing interest to develop solid dosage forms that offer zero order drug release kinetics, such as push-pull osmotic pumps (PPOP) and multilayered tablets, such as GEOMATRIX technology. These dosage forms have distinct advantages, such as, low patient-to-patient variability, accurate prediction of in vivo performance from in vitro dissolution profiles and minimal effects of physiological factors (variation in pH, motility and ionic strength within GI tract).[2,3] However, the use of such technologies often involves complex and costly processing and unit operations.

This study investigates the influence of a water insoluble BM coating on hydrophilic matrices as a simplified and cost-effective formulation approach to achieve zero order drug release profiles. Glipizide was used as a practically insoluble model drug.

## Experimental Methods

### *Formulation and Tablet Preparation*

The formulation of glipizide hydrophilic matrix tablets used in this study is shown in **Table 1**. A low viscosity grade of hypromellose, METHOCEL™ Premium K100LV CR, was used as the rate controlling polymer and lactose as a soluble filler assisting consistent drug release. The glipizide matrix formulation was sieved through a 30-mesh screen, followed by blending (10 minutes) in a twin shell V-blender. Magnesium stearate was added and blended (3 minutes). The final blend was compressed using a Piccola press (Riva, Aregntina), fitted with 7.1 mm diameter tooling (target tablet weight, 200mg). Tablets of sufficient mechanical strength [hardness (tensile strength) > 10 kP (3.1 MPa)] were produced and used for BM coating applications.

### *Application of BM Coating*

Glipizide matrix tablets were coated using a formulation containing Surelease, with Opadry system as a pore-former, weight ratio of 85:15 w/w. The coating dispersions were prepared in water at 10% w/w solids content. Tablets were then coated to 2-8% weight gain (WG), according to the recommended coating process parameters.[4]

### *Dissolution Studies*

In vitro dissolution studies of uncoated and coated glipizide matrix tablets were carried out using USP Apparatus II (paddles) at 50 rpm , with sinkers, in 900 ml of simulated intestinal fluid (SIF) without enzyme, pH 7.5. Drug release was determined spectrophotometrically at wavelength of 275 nm. Drug release data for all matrix tablets were compared using release rate and three point dissolution data ($t_{10\%}$, $t_{50\%}$, $t_{90\%}$, time required to dissolve 10, 50 or 90% of the drug).

*Table 1.* Composition of Extended Release Glipizide Matrix Tablets

| Ingredients | Concentration (%w/w) |
|---|---|
| **Glipizide** (Ria International LLC, USA) | 5.0 |
| **Hypromellose** (METHOCEL™ K100LV PR CR, Dow Chemical Company, USA) | 35.0 |
| **Lactose Monohydrate** (FastFlo®, Foremost, USA) | 59.0 |
| **Colloidal Silica** (CAB-O-Sil® M5P, Cabot Corp., USA) | 0.5 |
| **Magnesium Stearate** (Mallinckrodt, USA) | 0.5 |
| Total | 100 |

## Results and Discussion

**Figure 1** shows drug release profiles for uncoated glipizide matrices and BM coated matrices at various coating weight gains. Application of BM coating on glipizide matrices resulted in a lag phase, followed by linear release, indicative of zero order or near zero order kinetics.

*Figure 1.* Dissolution Profiles of Uncoated and BM Coated Glipizide Matrices at Various Weight Gains

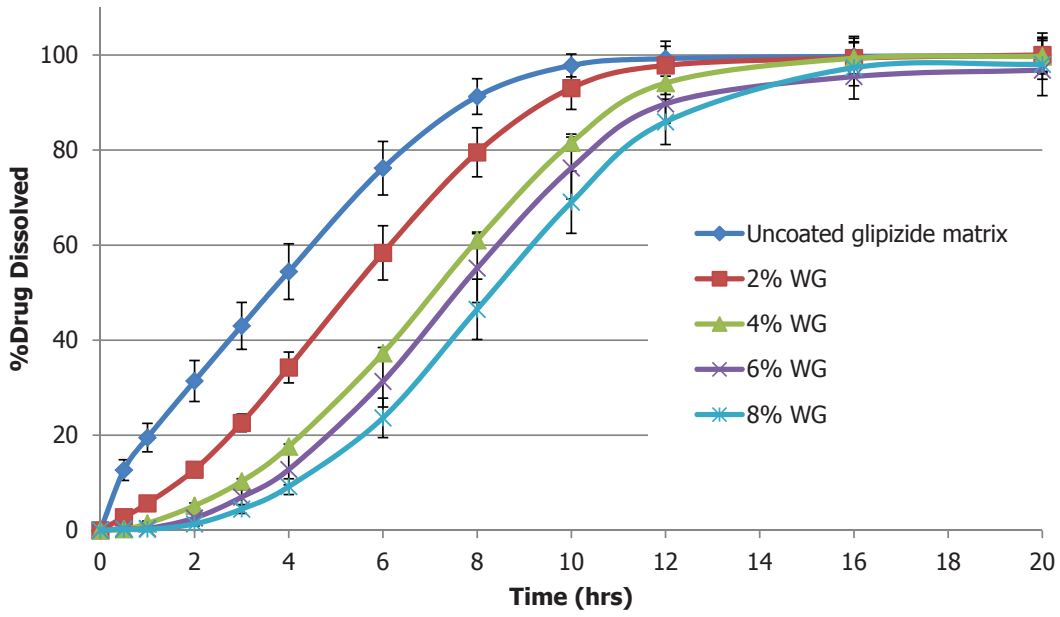

**Figure 2** shows drug release profiles from a BM coated glipizide matrix vs.PPOP formulation of glipizide. At 6%WG of insoluble barrier membrane coating of the matrix, the release profiles are similar ($f_2$ value = 65).

*Figure 2.* Comparison of glipizide release profiles from BM coated matrix and PPOP formulation

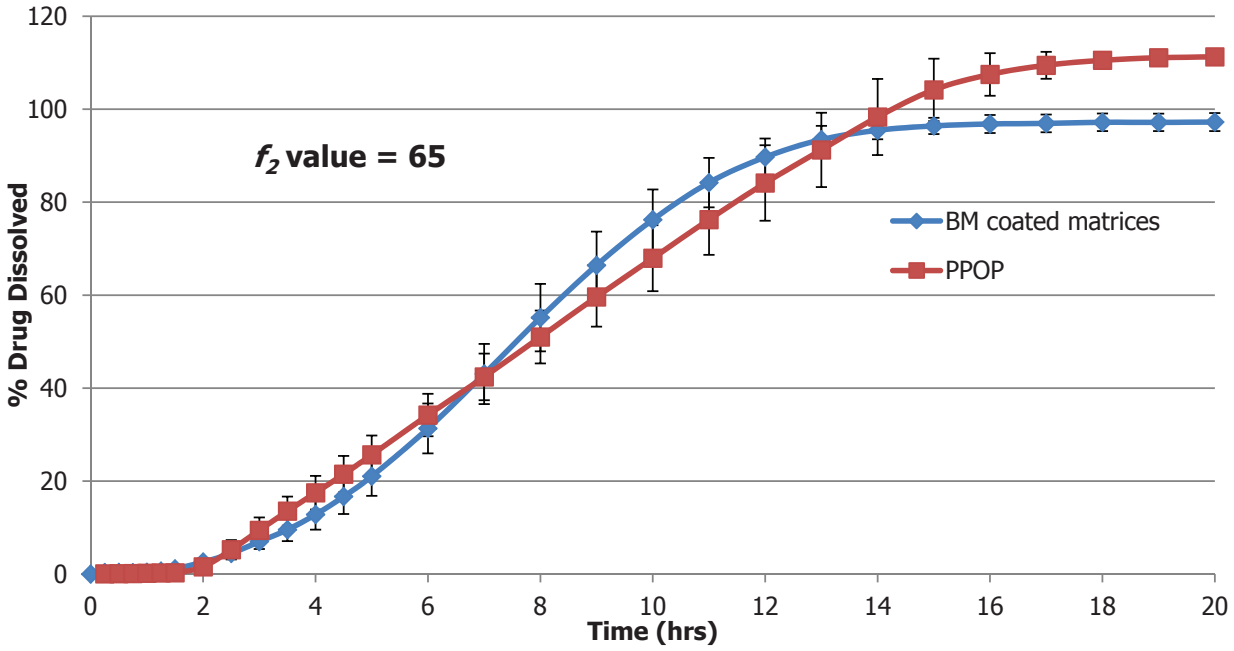


**Figure 3** shows a schematic representation of a possible mechanism involved in drug release from uncoated and BM coated matrices. It has been observed that the BM ruptures during dissolution testing, thereby exposing the surface area of the matrix to dissolution media over time, in a more controlled manner.

*Figure 3.* Schematic Representation of Drug Release from Uncoated & BM Coated Matrices

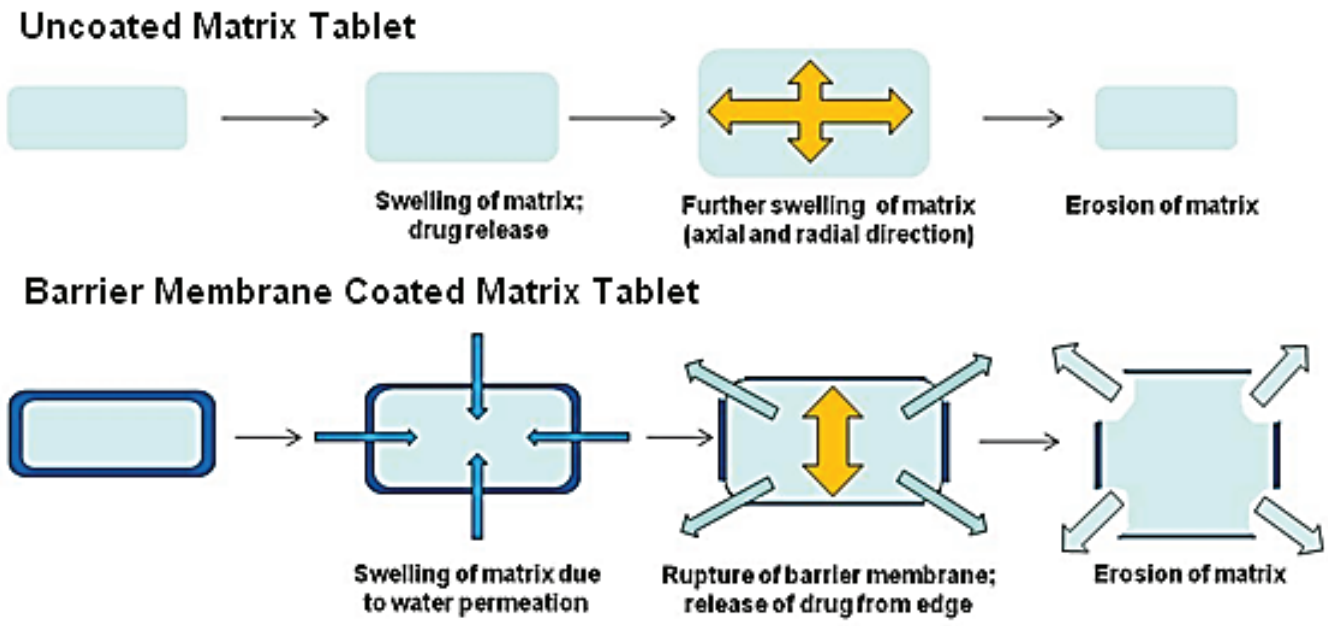

**Table 2** displays the calculated values for release rate and the three-point dissolution data. For the uncoated matrices, the drug release data (10-90%) presented a suitable fit to the Power Law model.[5] Values of n=0.6893 indicated that erosion was the primary mechanism of drug release from uncoated matrices.

For BM coated matrices, the drug release rate was calculated using the linear section of dissolution profiles in the range of 5-85%. The drug release from BM coated matrices provided suitable fit to zero order kinetics. Increasing the coating weight gain from 2 to 8% resulted in longer lag time, indicated by increasing $t_{10\%}$ values (from 1.6 to 4.1hrs) (**Figure 2** and **Table 2**). The declining trend of release rate (from 10.4 to 8.9 hrs) suggests a slower release from BM coated matrices at elevated weight gains.

*Table 2.* Comparison of Drug Release Rate from Uncoated & Barrier Membrane Coated Matrices

| Formulation | Equation | $R^2$ | Release Rate (%/h) | $t_{10\%}$ (hr) | $t_{50\%}$ (hr) | $t_{90\%}$ (hr) |
|---|---|---|---|---|---|---|
| Uncoated matrices | Power law | 0.9926 | 20.2 | 0.4 | 3.6 | 7.8 |
| 2% WG | Linear | 0.9924 | 10.4 | 1.6 | 5.2 | 9.0 |
| 4%WG | Linear | 0.9912 | 9.9 | 3.0 | 7.1 | 11.0 |
| 6%WG | Linear | 0.9906 | 9.3 | 3.6 | 7.8 | 12.3 |
| 8%WG | Linear | 0.9826 | 8.9 | 4.1 | 8.3 | 13 |

## Conclusions

The application of a BM coating of Surelease and Opadry on hydrophilic matrices of glipizide resulted in a lag phase, followed by zero order drug release kinetics, similar to osmotic technology. Such a formulation strategy may provide options for the development of dosage forms where zero order release of drug is desired.

## References


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