



# Investigation of the Influence of Polyethylene Oxide in a Compression-Coated, Controlled-Release Tablet Containing a Water-Soluble Active

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# ***Investigation of the Influence of Polyethylene Oxide in a Compression-Coated, Controlled-Release Tablet Containing a Water-Soluble Active***

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## **Introduction**

Numerous approaches have been evaluated for providing controlled-release drug delivery, including hydrophilic matrix tablets and osmotic pump systems. Although not as popular, compression-coated systems have also been shown to be effective.

Pillay and Fassihi developed a composite disk-compressed drug delivery system that provided up-curving and constant drug delivery. The electrolyte-induced compositional heterogeneity within the polymeric matrix of hypromellose (HPMC) or polyethylene oxide (PEO) was found to be a critical component.<sup>1</sup>

Pollock and Balwinski examined the effect of the particle size of the polymeric film former on the functionality of a compression coating. As the particle size of the polymer decreased, the release rate slowed and the lag times increased.<sup>2</sup>

The objective of this study was to modify the release of a water-soluble drug utilizing polyethylene oxide (PEO) in a compression-coated, controlled-release tablet.

## **Experimental Procedures**

### ***Materials***

The following materials were used as received: diphenhydramine HCl (Spectrum Chemical, Gardena, CA); tramadol HCl (a gift from Ashbourne Pharmaceuticals, Vorthampton, GB); POLYOX™ Coag (Union Carbide, a subsidiary of the Dow Chemical Company, Bound Brook, NJ); ETHOCEL\* Standard 10 FP Premium (The Dow Chemical Company, Midland, MI)

### ***Tablet Preparation***

Three different core tablets were used: 100% tramadol HCl; 90% tramadol HCl/10% ETHOCEL Std 10 FP Prem; and 90% diphenhydramine HCl/10% ETHOCEL Std 10 FP Prem.

The core tablets were formed on an automated Carver (model C) press with 0.25-inch concave tooling and an applied compression force of 2000 lb. The pump speed and dwell times were 15% maximum and 5 s, respectively.

The compression-coated tablets were prepared by placing 50% of the POLYOX Coag (200, 300, or 400 mg) in a 0.5-inch die containing the bottom concave punch.

A core tablet was manually centered and the remaining 50% of the polymer was applied on top. The applied compression force was held at 3000 lb.

### ***Drug Dissolution***

Dissolution testing of tablets was performed using a Distek dissolution system. The USP Apparatus 1 with sinkers was used with an agitation rate of 50 rpm.

Dissolution profiles of tablets containing tramadol HCl were generated in 0.1N HCl and deionized water. Deionized water was the medium used for the diphenhydramine HCl tablets.

All tablets were introduced into 900 mL of 37.0 ± 0.5°C media; profiles were generated with detection at 230 nm for diphenhydramine HCl and 274 nm for the tramadol HCl tablets. Six tablets were used for the dissolution measurements.

### ***Tablet Swelling***

The initial weight, thickness, and diameter of the tablets were measured. The tablets were then placed on a wire screen and submerged in deionized water.

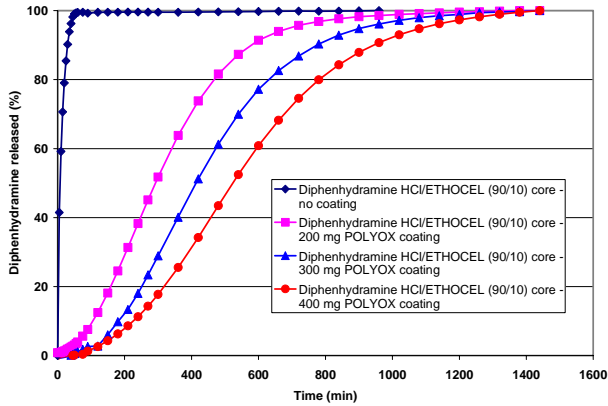
The measurements were repeated at the following time intervals: 20 min, 40 min, 1 h, 2 h, 3 h, 6 h, and 24 h. An average of three runs was reported.

## **Results and Discussion**

For both actives, the presence of the compression coating provided an initial lag as well as significantly extending the drug release. As the POLYOX coating was doubled in weight on the core tablets containing ETHOCEL, the release of the diphenhydramine HCl was found to decrease from 66% to 25% after 6 h (Figure 1).

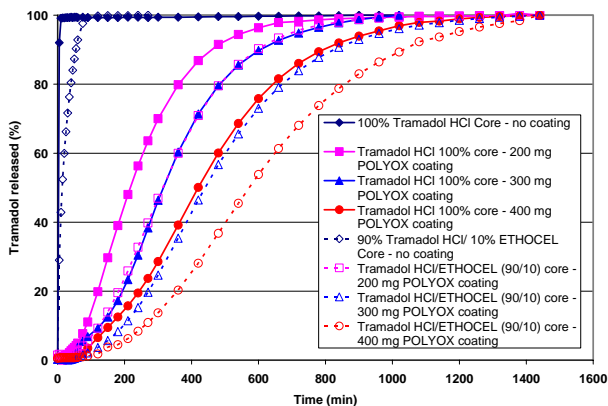
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**Figure 1. POLYOX compression-coated diphenhydramine HCl/ETHOCEL tablets (medium: deionized water).**



A similar effect from doubling the coating layer was also observed for tramadol HCl, with a decrease in drug release from 62% to 21% after 6 h in 0.1N HCl (Figure 2). For tramadol HCl alone (no ETHOCEL in the core), the release was approximately twice as fast for the tablet containing the 200 mg coating versus the 400 mg coating. The drug release profiles were found to be similar in both media (deionized water and 0.1N HCl).

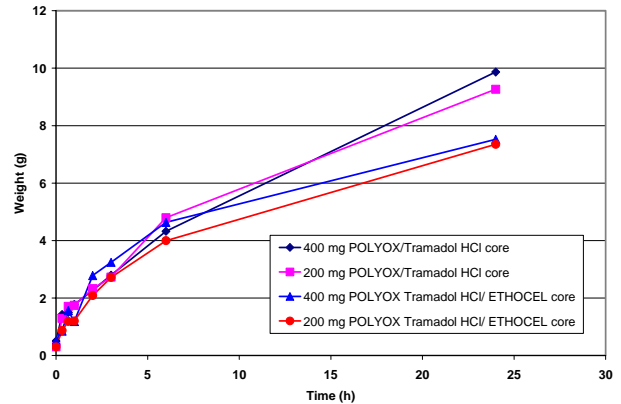
**Figure 2. POLYOX compression-coated tramadol HCl and tramadol HCl/ETHOCEL tablets (medium: 0.1N HCl).**



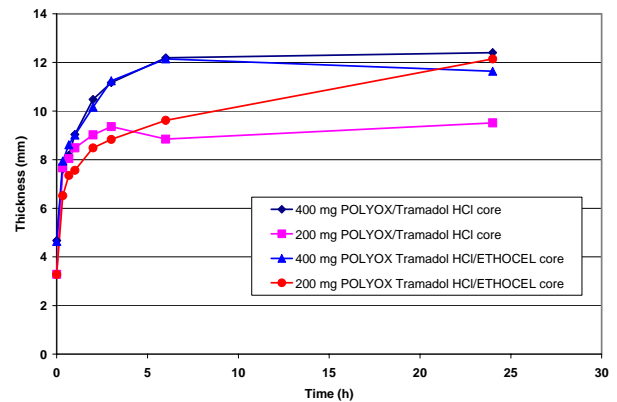
The tablets containing only tramadol HCl in the core were found to have the largest weight gain over a 24-h period compared to the tablets that contained the drug and ETHOCEL (Figure 3).

After several hours of being submerged in water, the tablets containing the 400 mg POLYOX coating were found to swell more than those with 50% less polymer coating (Figure 4). All tablets were found to swell significantly (Figure 5). The presence of ETHOCEL in the core did not typically impact the swelling characteristics of the tablets.

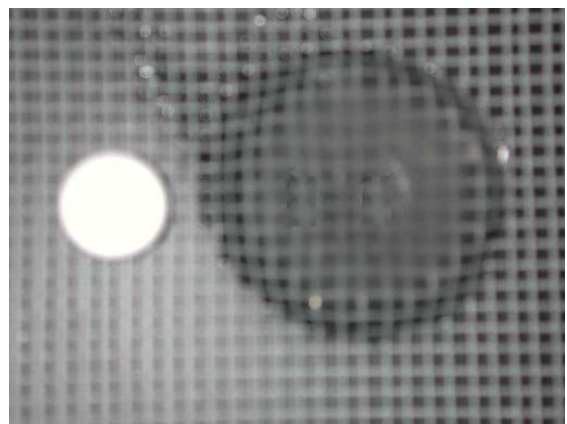
**Figure 3. Weight gain of tablets with tramadol HCl (in water).**



**Figure 4. Swelling test (tablet thickness in water).**



**Figure 5. Comparison between the tablet before and after being exposed to water for 24 hours. The tablet contained a core of tramadol HCl with 200 mg of POLYOX coating.**



## Conclusions

POLYOX Coag was found to work well for compression coating due to its good flow properties and fast hydration rates.

Increasing the POLYOX content in the compression coating layer resulted in an extended diffusional path for the media to reach the drug-containing core. As a result of this effect, an increased lag time was observed in the drug release profiles for both tramadol HCl and diphenhydramine HCl tablets. Over time, the swelling front eventually reaches the surface of the core tablet.

By adding ETHOCEL STD 10 Premium FP to the core of the tablets, less coating material was needed to achieve the same release profile, and additional flexibility in modifying the release of the water-soluble actives was demonstrated.

## Acknowledgments

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## References

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2. D. Pollock and K. Balwinski, "Influence of the Particle Size on the Inert Polymer in a Compression Controlled Release Tablet," *Proc. 26th International Symposium on Controlled Release of Bioactive Materials*, 1999.

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