

# The Influence of Film Coating and Storage on Propranolol Hydrochloride Release from Polyethylene Oxide Extended Release Matrices

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## Abstract Summary

This study investigated the influence of film coating (Opadry® II high performance film coating system) and storage on in vitro release of a model drug, propranolol HCl, from polyethylene oxide (POLYOX™ water soluble resin) extended release (ER) matrices.

## Introduction

Polyethylene oxide (PEO) is prone to autoxidation, leading to chain cleavage and reduction of polymer viscosity on storage. High temperature accelerates PEO degradation. Several autoxidative mechanisms of PEO degradation have been mentioned in the literature.<sup>1-3</sup> Degradation can be limited by oxygen impediment (i.e. consolidation/ tableting), oxygen removal (application of an oxygen barrier film coat onto the final dosage form) and the use of antioxidants, i.e. BHT or vitamin E, and other methods.<sup>4</sup>

This study investigated the influence of a high performance, immediate release film coating system, Opadry® II, and storage on the release of the freely water-soluble (360 mg/mL)<sup>5</sup> drug, propranolol HCl from PEO ER matrices.

## Experimental Methods

All ingredients (**Table 1**) with the exception of lubricant were blended in a 1 L mixer (T2C, Turbula, Willi A. Bachofen, Switzerland) at 64 rpm for three minutes. Magnesium stearate was then added and blended for an additional one minute.

Table 1. Propranolol HCl PEO ER Matrix Formulation

Material	% w/w	mg/tab
Propranolol HCl (S.I.M.S., Italy)	30.0	159.9
PEO (POLYOX™ WSR Coagulant, Dow Chemical Company, USA)	20.0	106.6
Partially pre-gelatinized starch (Starch 1500®, Colorcon, USA)	49.5	263.8
Magnesium stearate (Peter Greven, Germany)	0.5	2.7
Total	100.0	533.0

POLYOX™ ER tablets were manufactured by direct compression using a 10-station rotary press (Piccola, Riva, Argentina), fitted with 10 mm diameter round normal concave tooling and operated at 20 rpm and 20 kN compression force.

Some of the manufactured matrices were coated with a high productivity, complete film-coating system (PVA-based Opadry® II, Colorcon) dispersed at 20% w/w in purified water. Tablets were coated to the target theoretical weight gain (WG) of 3% (2.6 mg/cm<sup>2</sup>) in a side-vented coating pan (Labcoat II, O'Hara, Canada) fitted with a 15" pan and using a 1.2 mm spraying gun (Schlick, Germany); with drive bar baffles and a 15 cm gun to bed distance. Coating process parameters are listed in **Table 2**.

Table 2. Coating Process Parameters

Process parameters	Values
Pan speed (rpm)	20
Inlet air temperature (°C)	65-69
Exhaust air temperature (°C)	48-53
Product temperature (°C)	42-45
Air volume (m <sup>3</sup> /hour)	250
Atomization (fan) air pressure (bar)	1.5
Spray rate (g/min)	4-10
Process time (min)	17

A stability study of the propranolol HCl matrix tablets was carried out at 40°C/75% RH as per ICH guidelines. Tablets were placed into 85 mL high-density polyethylene (HDPE) bottles (Drug Plastics and Glass Co., USA), 25 tablets per bottle, with and without a desiccant (3964, Süd-Chemie Ltd, UK) and foil-sealed.

The physical parameters of the uncoated and coated tablets such as weight, diameter, thickness and mechanical strength were analyzed over a period of six months.

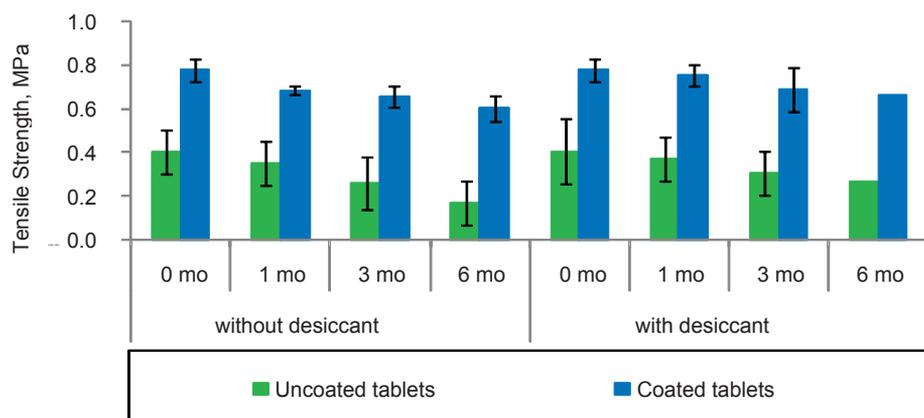
In vitro drug release was determined in a USP compliant dissolution bath (AT7 Smart, Sotax, Switzerland) using Apparatus II (paddles, with sinkers) operated at 100 rpm. The dissolution medium was purified water (900 mL) at 37.0 ± 0.5°C. Samples were analyzed using 5 mm quartz cells in a UV-Vis spectrophotometer (Lambda 25, PerkinElmer, USA) at a wavelength of 319 nm. The obtained profiles were compared to the drug release of a relevant sample using the  $f_2$  factor. An  $f_2$  value between 50 and 100 indicated that the two dissolution profiles were similar.<sup>6,7</sup>

## Results and Discussion

All tablets exhibited good appearance, showing no visual defects. The mechanical strength increased from 4.4 ± 0.2 kp (0.4 MPa) for uncoated to 8.8 ± 0.1 kp (0.8 MPa) for film coated matrices.

On storage, the breaking force decreased to a greater extent for uncoated (from 4.4 to 2.0 kp) compared to the coated matrices (from 8.8 to 7.8 kp). Better mechanical strength values were obtained after six months with addition of the desiccant, i.e. 3.1 kp (0.3 MPa) for uncoated and 8.1 kp (0.7 MPa) for coated tablets.

Figure 1. Effect of Storage on Tablet Mechanical Strength (0-6 months, ± desiccant)



Similar to the previously reported findings,<sup>8</sup> no effect of Opadry® II film coating on drug release from PEO ER matrices ( $f_2 = 83$ ) was recorded initially (**Figure 2**).

The results indicated that propranolol HCl ER PEO matrices were stable on storage at accelerated conditions (**Figures 3, 4**). **Figure 3** shows that only a slight increase ( $f_2 = 66$ ) in drug release from uncoated tablets was recorded after six months. Even better results were obtained for coated tablets (**Figure 4**) with propranolol HCl dissolution rate remaining unchanged on storage ( $f_2 = 83$ ).

The desiccant addition had no effect on drug release (**Figures 3, 4**).

Figure 2. Effect of Opadry® II Film Coating on Drug Release from PEO Tablets (initial)

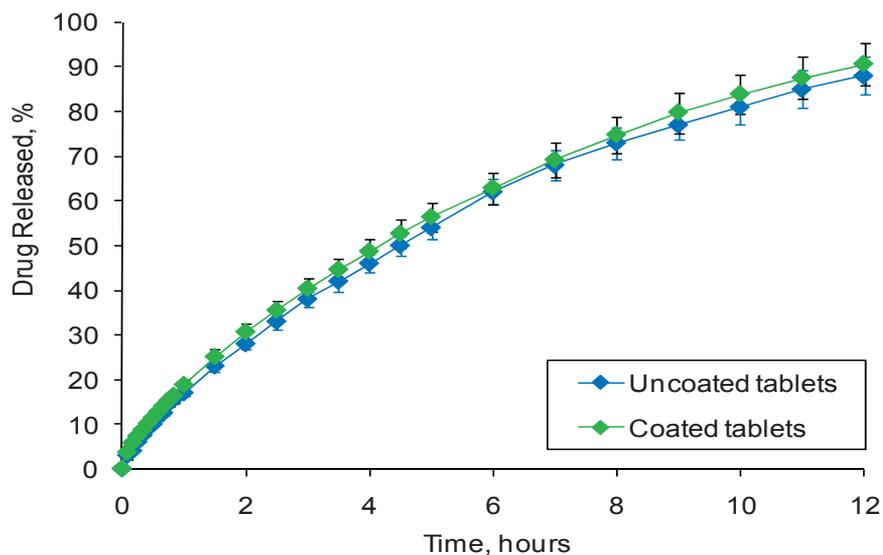


Figure 3. Effect of Storage on Drug Release from Uncoated PEO Tablets (0-6 months, ± desiccant)

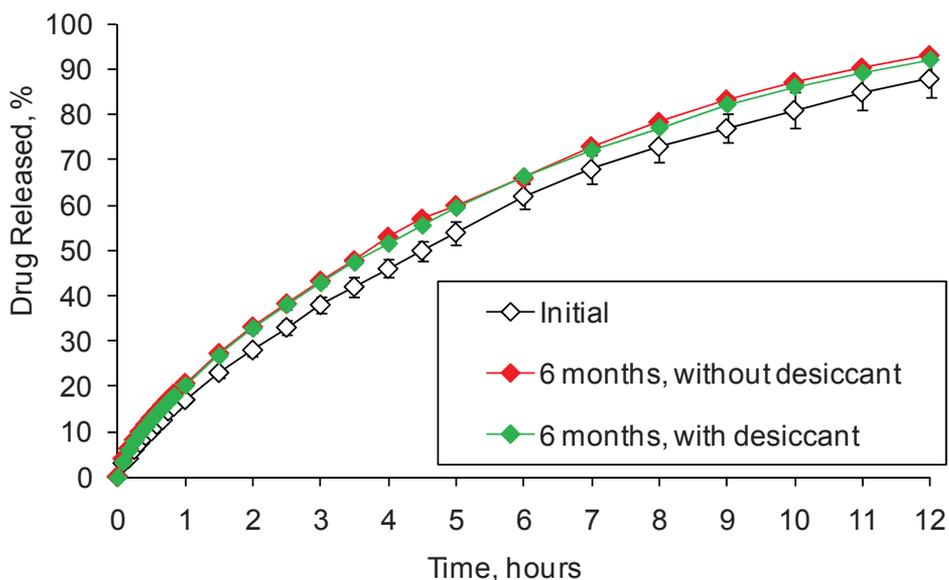
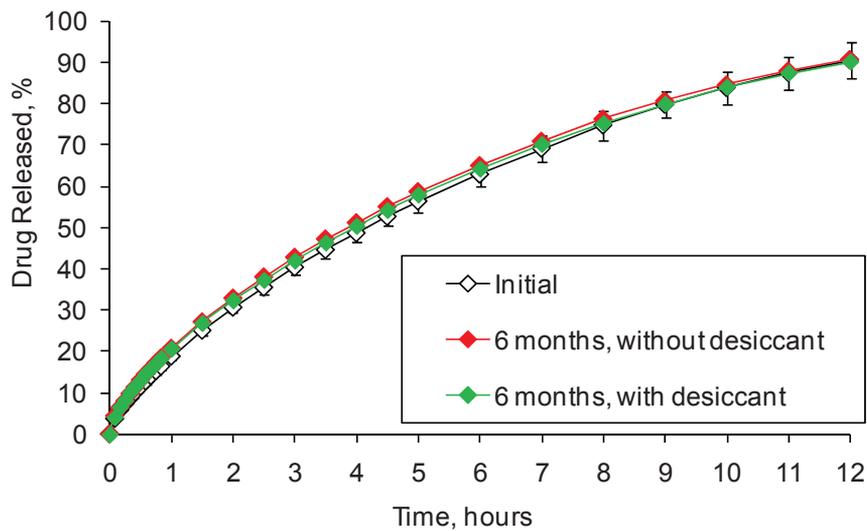


Figure 4. Effect of Storage on Drug Release from Coated PEO Tablets (0-6 months, ± desiccant)



## Conclusions

Robust POLYOX™ ER matrices containing model drug propranolol HCl were produced, the mechanical strength of which was significantly improved by the application of 3% WG of an Opadry II® film coating.

Drug release from POLYOX™ ER tablets was unaffected by the film coating application.

The addition of a desiccant to the packaging resulted in tablets with higher mechanical strength values on storage at 40°C/75% RH.

Stable drug release profiles were produced for all tested matrices stored at accelerated conditions for six months. Slightly better stability results were obtained for coated tablets probably due to the PVA-based Opadry II® film acting as a moisture and oxygen barrier.

## References

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