Application of Opadry® II, complete film coating system, on metformin HCl extended release matrices containing POLYOX™ water soluble resin

APPLICATIONS DATA SUMMARY

- Film coating of tablets containing POLYOX™ WSR 303 water soluble resin, using high productivity Opadry® II, complete film coating system, (85 series) is described
- Compacts of POLYOX™ only and metformin ER matrices were effectively coated
- Typical Opadry II coating conditions with a product bed temperature of around 42-45°C were found to be suitable
- Coating of POLYOX™ matrices was shown to have no significant effect on drug dissolution (*f2* value of 91)

INTRODUCTION

The film coating process is frequently performed in the pharmaceutical industry to serve a variety of purposes. It has found applications in taste masking; protection of the active ingredients from degradation by environmental factors, as well as gastrointestinal fluids and enzymes; improvement of the handling properties of tablets; and modification of the drug release from tablets and multiparticulate systems [1].

Polyethylene oxide (PEO) polymers, available commercially under the trade name of POLYOX™ water soluble resins (WSR), are novel materials with unique properties. They have found a number of uses in pharmaceutical applications such as extended release (ER) matrices[2, 3], osmotic pumps[4-7], mucosal bio-adhesives[8-10], hot melt extrusion[11-13] and gastro-retentive dosage forms[14-17]. PEO polymers are nonionic, highly swelling, thermoplastic and soluble in water, and selected organic solvents.
Tablets containing POLYOX™ are potentially challenging to coat due to the high hydrophilicity and swelling properties of the polymer.

The purpose of this work was to investigate the behavior of tablets containing PEO during coating trials in a perforated coating pan. Tablets containing only POLYOX™ were used as a control in order to investigate a potential effect of coating on matrices, independent of a drug and other excipients.

MATERIALS AND METHODS

Manufacture of Compacts Containing POLYOX™

Compacts containing 100% POLYOX™ WSR-303 LEO NF (Colorcon, UK), with a target weight of 350 mg, were manufactured by direct compression on an instrumented 10 station rotary tablet press (Piccola, Riva, Argentina); fitted with round flat-faced 10 mm tooling; at 20 rpm and 20 kN compression force.

Formulation and Manufacture of ER POLYOX™ Matrices

Table 1 shows details of the ER matrix formulations used in the study.

Table 1. ER Matrix Formulations

Material	Supplier	% w/w	mg/tablet
Metformin HCl	AMRI, India	50.0	500
PEO (POLYOX™ WSR 303 LEO)	Colorcon, USA	30.0	300
Microcrystalline cellulose (Microcel® 102)	Blanver, Brazil	19.0	190
Fumed silica (Aerosil® 200)	Evonik, Germany	0.5	5
Magnesium stearate	Peter Greven, UK	0.5	1
Total		100.0	1000

All powders were passed through a 500 µm sieve (35 mesh). All ingredients, except for magnesium stearate, were blended in a V-cone mixer (GlobePharma, India) for 10 minutes. Magnesium stearate was then added and the formulation mixed for an additional 2 minutes.

Tablets with a target weight of 1000 mg were manufactured by direct compression on an instrumented 10 station rotary tablet press (Piccola, Riva, Argentina); fitted with caplet 7x18 mm tooling; at 20 rpm and 20 kN compression force.

Coating Trials

PEO compacts and metformin HCl ER matrix caplets were coated to the target weight gain (WG) in a side-vented machine (Labcoat II, 15", 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.

POLYOX™ compacts were coated with Opadry II (85F23861, Colorcon, UK) aqueous suspension up to approximately 3% WG. In order to obtain an optimum machine load of 1 kg, 20 g of PEO compacts were mixed with 980 g of placebo tablets.

Metformin HCl caplets were coated with Opadry II (85G18490, Colorcon, UK) aqueous suspension up to approximately 4% WG. A 1 kg coating batch was composed of 500 g of metformin HCl tablets and 500 g of placebo tablets.

The coating dispersions were prepared and continuously mixed throughout the coating process using a propeller mixer (IKA Labortechnik, Germany).

Coating process parameters are listed in Table 2 and Table 3 for PEO compacts and metformin HCl caplets, respectively.

For POLYOX™ compacts, two sets of conditions were used; “standard” and “non-standard” (high spray rate). An additional experiment heating PEO compacts in the coating pan to 55-70ºC without spraying was also conducted.

Table 2. Coating Process Parameters for PEO Compacts

Parameter	Opadry II (85F23861)	
	Standard conditions	Non-standard conditions
Batch size (kg)	1	1
Pan speed (rpm)	20	20
Inlet air temperature (ºC)	65-72	70
Exhaust air temperature (ºC)	50-53	52-58
Product temperature (ºC)	42-45	38-40
Fluidizing airflow (m^3/hour)	250	250
Atomization/fan air pressure (bar)	1.5	1.5
Spray rate (g/min)	4-10	24
Process duration (min)	21	14

Table 3. Coating Process Parameters for Metformin HCl ER Matrices

Parameter	Opadry II (85G18490)
Batch size (kg)	1
Pan speed (rpm)	20
Inlet air temperature (ºC)	65-69
Exhaust air temperature (ºC)	48-53
Product temperature (ºC)	42-45
Fluidizing airflow (m^3/hour)	250
Atomization/fan air pressure (bar)	1.5
Spray rate (g/min)	10-21
Process duration (min)	17

Testing of PEO Compacts and ER Matrices

Compact mechanical strength was determined both before and after the coating process. Breaking force values were obtained using a hardness tester (AT4, Dr Schleuniger-Pharmatron, Germany). Friability was determined using a friabilator (Copley, UK); at 25 rpm and 4 minutes running test time.

Drug Dissolution Testing

Drug release from metformin HCl PEO matrices was measured in an AT7 (Sotax, UK) dissolution bath at 100 rpm using USP Apparatus II (paddles) and 2.38 mm (8-mesh) stationary quadrangular baskets (QBs)[4] from Quality Lab Accessories (USA). The baskets were positioned within the dissolution vessel perpendicular to the shaft and 3 cm above the paddle. Previous work has validated the use of quadrangle baskets.[5]

The dissolution medium was 1000 mL of purified water at 37.0 ± 0.5ºC. Samples were analyzed with a dual beam spectrophotometer (Perkin Elmer, USA); using 0.1 mm quartz cells at a wavelength of 233 nm. Purified water was used as a reference. Measurements at each time point were performed in triplicate, and the mean and standard deviation (SD) values were calculated.

The dissolution results generated were compared using the *f2* factor. [6, 7] An *f2* value between 50 and 100 indicates that the two dissolution profiles are similar.

RESULTS AND DISCUSSION

Coated PEO Compacts

Tablet mechanical strength increased from 21.3 ± 0.5 kp for uncoated compacts to more than 30.0 kp for coated tablets. Friability decreased from 0.02% for uncoated compacts to less than 0.01% for coated tablets.

For PEO compacts coated with Opadry II a rougher surface was obtained when non-standard coating conditions (low product temperature of 38-40^{o}C, fast spray rate of 24 g/min for the first 3 minutes) were used (Figure 1b), compared to standard coating conditions (Figure 1a).

A slight difference in tablet thickness was recorded for compacts coated using standard and non-standard conditions (Figure 2).

At the experimental temperatures above the melting point of PEO (65^{o}C) the compacts became more rubber-like and could easily be deformed by the application of finger-pressure (Figure 3).

Figure 1. PEO Compacts Coated with Opadry II: (a) 10 g/min spray rate, 45°C product temp; (b) 24 g/min spray rate, 38ºC product temp (X10)

(a) (b)

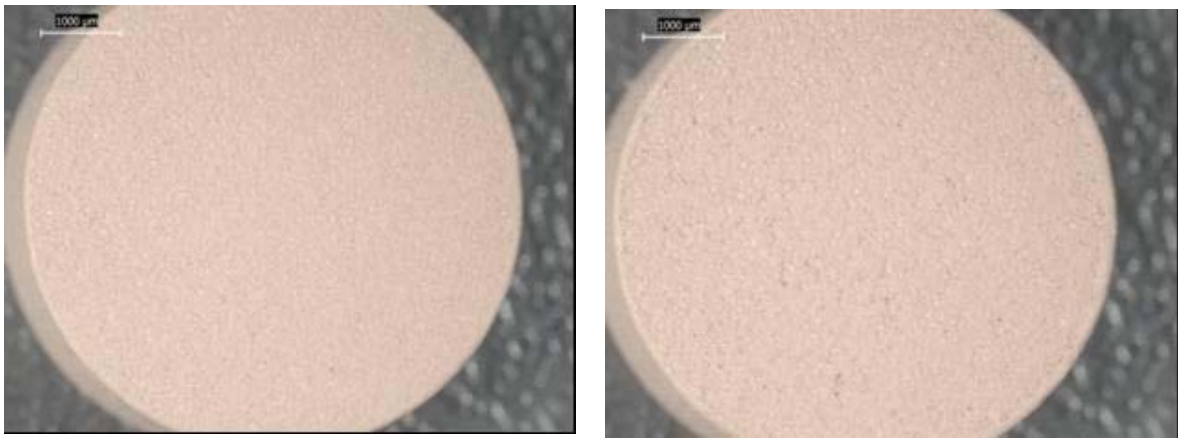


Figure 2. Thickness of PEO Compacts as a Function of Coating Conditions

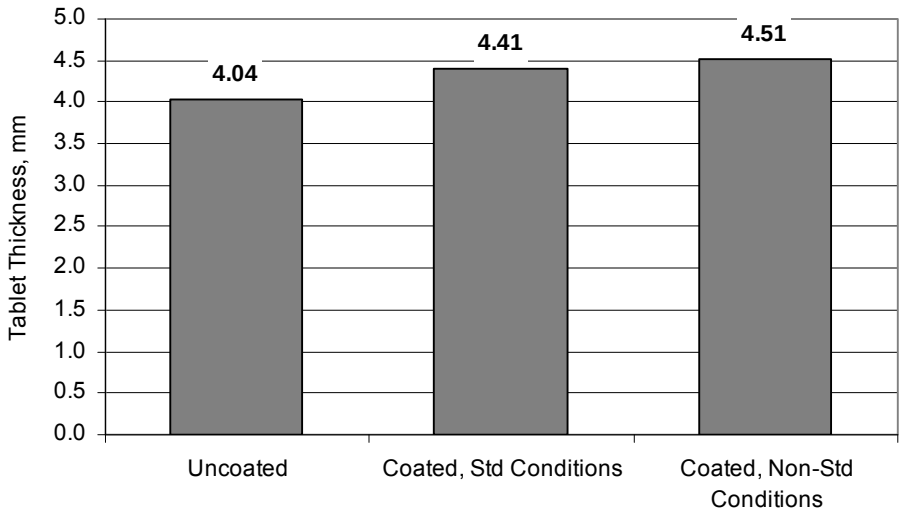
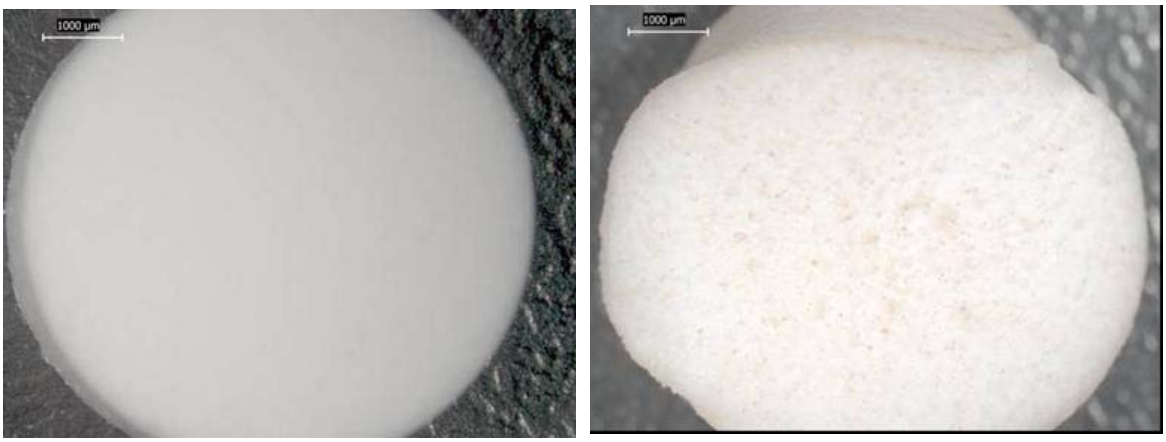


Figure 3. PEO Compacts: (a) uncoated and (b) tumbled in a coating pan for 10 min at 70ºC (X10)



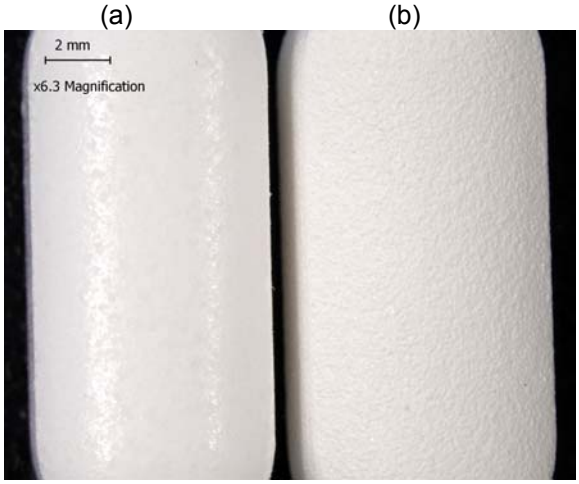
Coated Metformin HCl ER Matrices

Tablet mechanical strength increased from 20.0 ± 0.5 kp for uncoated tablets to more than 30.0 kp for coated metformin HCl matrices. Friability decreased from 0.03% for uncoated matrices to less than 0.01% for coated tablets.

No problems were observed during the coating process. Appearance of the coating was good; however, some surface roughness was observed at a lower spray rate of 5-15 g/min. This issue was minimized at a higher spray rate of 10-21 g/min. Figure 4 shows the appearance of uncoated and coated metformin HCl matrices.

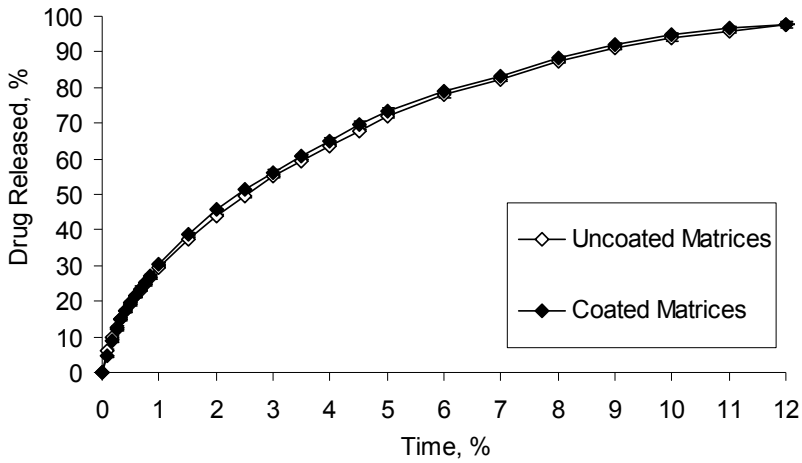
Figure 4. Appearance of (a) Uncoated and (b) Opadry II Coated Metformin HCl PEO Matrix (X6.3)

(a) (b)



Drug release from PEO matrices was not significantly affected by the coating applied (Figure 5). A calculated *f2* value of 91 indicates that the two dissolution profiles are similar.

Figure 4. Metformin HCl Release from Uncoated and Opadry II Coated POLYOX™ ER Matrices (n = 3)



CONCLUSIONS

- Appearance of coated POLYOX™ compacts and metformin HCl ER POLYOX™ matrices was good.
- The application of film coating resulted in a significant increase in tablet breaking force values and in a decrease in tablet friability.
- Product bed temperatures above 55°C are not recommended due to the low melting point of POLYOX™ (~65°C).
- For POLYOX™ containing tablets, typical Opadry® II coating conditions with a product bed temperature of around 42-45°C was found to be acceptable.
- Drug release from PEO matrices was not significantly affected by the coating applied.

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