A Comparison of Delayed Release Film Coating Systems for Pharmaceutical Dosage Forms

ABSTRACT SUMMARY

The comparative performance of four commercially available delayed release film coating systems for pharmaceutical dosage forms is reported. The film coating systems varied widely in particle size and aqueous dispersion viscosity, which impacted coating process productivity, final coated product appearance and coated product performance. While all film coatings were resistant to 0.1N HCl, only tablets coated with Acryl-EZE® 93A, aqueous acrylic enteric system, remained intact in pH 4.5 sodium acetate buffer for two hours.

INTRODUCTION

Delayed release (DR) film coated products are some of the most complex dosage forms to develop. Challenges arise not only in designing a film coating that possesses good mechanical properties to ensure coating integrity, but the applied coating must also prevent drug release and ingress of gastric fluids under specified pH, and pH conditions influenced by fed state and concurrent medicine use, e.g., proton pump inhibitors (PPI)[1]. Rapid release of the drug in the higher pH regions of the small intestine is also required. The objective of this work was to evaluate and compare the dispersion properties, film properties and enteric performance at varying pH conditions, of four aqueous, white-pigmented, DR film coating systems.

EXPERIMENTAL METHODS

The four film coating systems evaluated were: Acryl-EZE® 93A (Colorcon), Instacoat EN Super-II enteric film coating system (IC) (Ideal Cures PVT, Ltd.), Colorcoat EC4W, coating system (EC4W) (Corel Pharma Chem), and Advantia Performance coating system (AP) (International Specialty Products, Inc. [ISP]), based on methacrylic acid ethyl acrylate copolymer. 93A comprises methacrylic acid copolymer Type C NF/EP/JPE. IC and AP comprise methacrylic acid - ethylacrylate copolymer 1:1 (Type B) Ph.Eur. (non-compendial in the US and Japan), and EC4W comprises a methacrylic acid copolymer of unconfirmed compendial status. Products were examined for dispersion properties (particle size, pH, and viscosity), film coating performance and enteric disintegration testing (liquid uptake in 0.1N HCl) and sodium acetate buffer (pH4.5) and disintegration in phosphate buffer (pH 6.8). Mechanical film properties such as tensile strength, Young's modulus, tablet adhesion and moisture vapor transmission rate (MVTR) were also examined.

Dispersion Properties

The film coating powders were mixed in purified water at low shear using the solids concentration and mixing time recommended in the respective manufacturer's guidelines.[2,3,4,5] The solids used for 93A, AP and IC were 20% w/w; EC4W was hydrated at 13% w/w. Additionally, all systems contained polymer, pigment and plasticizer, with the exception of 93A, where plasticizer choice is at the formulator's discretion. For purposes of this study, PEG 8000 was used as the plasticizer for 93A at 10% w/w with respect to polymer level. Particle size (Coulter LS230), viscosity (Brookfield DVII, RVA spindle set, spindle 1, 50 rpm, 20% torque), and pH (Beckman 240 pH/Temperature SN4183) were determined.

Coated Tablet Properties

For each formulation evaluated, 900 g of standard concave placebo tablets were seal-coated to theoretical weight gain (WG_T) of 3% using Opadry®, complete film coating system, [HPMC-based], at 10% solids, then followed with the enteric formulations coated to 8% and 10% WG_T in an O'Hara Labcoat I (12 inch) fully perforated pan. The enteric coating dispersions were prepared as described above, screened (250µm, 60 mesh), and mixed continuously during coating. The coating parameters for each formulation are listed in **Table 1**.

Table 1. Coating Parameters

Product Name	Opadry 03K	Acryl-EZE 93A	Instacoat EN-Super II	Advantia Performance	Colorcoat EC4W
Solids (%)	10	20	20	20	13
WG_T (%)	3	8, 10	8, 10	8, 10	8, 10
Spray Rate (g/min)	8	10	8 - 9	10	5 - 6
Atomizing Air (psi)	15	15	22	20	15
Pattern Air (psi)	20	20	20	20	20
Air volume (cfm)	130	130	130	130	130
Inlet Air Temp (ºC)	70 - 72	37 - 40	56	50	44 - 46
Product Temp (ºC)	43 - 44	30	31 - 33	34	35
Pan Speed (rpm)	20	20	20	20	20
Coat Time (min)	34	45	50 - 57	45	115 - 138

Liquid uptake (n = 6) was measured after 2 hours in 0.1N HCl and in sodium acetate buffer (pH 4.5), the expected pH in a growing population of PPI-treated patients. Following the 0.1N HCl acid phase, the disintegration time (DT, n = 6) in phosphate buffer (pH 6.8) was recorded according to USP 32, NF 27 <701> Disintegration of Delayed Release Enteric-coated Tablets.[6]

Evaluation of Cast Films

Tensile strength, modulus of elasticity, and adhesion testing were determined using an Instron Mini 44 Materials Analyzer (n=10). Moisture vapor transmission rate (MVTR) was measured on a VTI WPA 100 Water Permeability Analyzer (n=2).

Tensile strength, modulus of elasticity, and adhesion testing were determined using an Instron Mini 44 Materials Analyzer (n=10). Moisture vapor transmission rate (MVTR) was measured on a VTI WPA 100 Water Permeability Analyzer (n=2).

Films were cast from the previously described coating solutions (de-aerated for several hours prior to casting) on Teflon-coated glass plates using a Gardner Casting Knife, (Silver Spring, MD, USA) to a targeted dry film thickness of 150µm ± 10%. Cast films were dried in a convection oven at 50°C for 120 minutes. Films were equilibrated at room temperature (23ºC/50% RH) for 48 hours prior to testing. Non-waxy and waxy flat face tablets, coated to 10% WG_T were used for adhesion testing of all systems.

RESULTS AND DISCUSSION

Dispersion Properties

The pH of the four DR systems was similar, but viscosity and particle size were very different. Colorcoat viscosity was 600% higher than the lowest viscosity product, Advantia Performance, at nearly two-thirds the solids. Particle size of the four systems from highest to lowest was: Instacoat EN Super II >> Colorcoat EC4W > Acryl-EZE > Advantia Performance. See **Table 2**.

Table 2. Dispersion Results

Dispersion Parameter (screened 250µm)	Product Name			
	Acryl-EZE 93A	Instacoat EN-Super II	Advantia Performance	Colorcoat EC4W
Solids (%)	20	20	20	13
Particle size (D_{50} / D_{90})	7.2 / 26.7	90.4 / 187	3.8 / 10.2	18.1 / 50
Viscosity (cP)	10	29	4	24
pH	5.3	5	5.4	5.8

Film Coating Performance

EC4W was significantly tackier than the other systems and required higher product temperatures and slower fluid delivery rates (FDR) during coating. Final coated tablet appearance of EC4W was rough, with dark scuff marks on the tablet surface from coating pan abrasion. Although alterations in coating parameters were not required for IC dispersion, the coated tablet appearance of IC was also rough and less white than the other systems. AP and 93A coated tablets were white and smooth with a satin finish.

Liquid Uptake and Disintegration

All four enteric systems had low liquid uptake (<5%) after two hours in 0.1N HCl. However, 93A was the only system to remain intact and pass uptake testing (<10%) after two hours in intermediate pH 4.5 sodium acetate buffer. All enteric systems disintegrated in pH 6.8 buffer in under 15 minutes. See **Table 3** for liquid uptake and DT results.

Table 3. Liquid Uptake and Disintegration Results

DR Formula	WG(%)	Liquid Uptake(%) 0.1N HCl	Liquid Uptake(%) pH 4.5 buffer	DT(min) pH 6.8 buffer
Acryl-EZE 93A	8	4.2	5.4	7
	10	3.8	5.1	8
Advantia Performance	8	4.4	Disintegrated	7
	10	4.3	Disintegrated	10
Instacoat EN Super II	8	4.3	Disintegrated	5
	10	3.8	Disintegrated	5
Colorcoat EC4W	8	3.6	Bloated/Failed	11
	10	3.2	Bloated/Failed	12

Mechanical Properties of Cast DR Films

Of the four systems, only two could be evaluated for mechanical properties. Films of IC and EC4W were too brittle to obtain measurements. AP had greater tensile strength than 93A, however, flexibility of 93A, as measured by Young's modulus, was superior to AP. MVTR of AP and 93A was equivalent. EC4W and 93A films had the lowest adhesion to waxy substrates, but all four adhered well to non-waxy substrates. Mechanical film property results are listed in **Table 4**.

Table 4. Mechanical Film properties

DR Formula	Tensile Strength MPa (SD)	Modulus of Elasticity MPa (SD)	MVTR g H2O/day / 100 sq in. (SD)	Adhesion kPa (SD)	
				Waxy	Non-Waxy
Acryl-EZE 93A	10.7 (4.7)	1091 (709)	1.17 (0.31)	100 (17)	181 (25)
Instacoat EN Super-II	Film was too brittle to test			171 (15)	202 (28)
Advantia Performance	21.7 (4.9)	2202 (488)	1.50 (0.18)	244 (78)	183 (62)
Colorcoat EC4W	Film was too brittle to test			72 (20)	247 (68)

CONCLUSIONS

Overall, differences were evident among the film coating dispersions and coating process parameters of the four systems, impacting the final coated tablet appearance. The large dispersion particle size and high viscosity of Instacoat and Colorcoat formulations, respectively, heavily influenced coated tablet quality and performance. Only Acryl-EZE 93A coated tablets remained intact with <10% liquid uptake in pH 4.5 sodium acetate buffer for two hours. Sustained resistance at intermediate pH is considered important to maintain efficacy in fed states, and gastric protection in patients treated with PPI or other enteric coated products.

Reprint of poster presented at Controlled Release Society Meeting, 2010.

Authors: Rita Steffenino, Tom Farrell, and Ali R. Rajabi-Siahboomi

REFERENCES

1. Missaghi, S., Young, C., Fegely, K. and Rajabi-Siahboomi, A.R., Delayed release film coating applications on oral solid dosage forms of proton pump inhibitors: case studies, Drug Del. Ind. Pharm, 2010, 36 (2) 180-189
2. Colorcon. Acryl-EZE Product Information Sheet website. Accessed January 2010. http://www.colorcon.com/resources/lit/Products.
3. Ideal Cures Pvt, Ltd. Instacoat EN Super II Product Information Sheet website. Accessed January 2010. http://www.idealcures.co.in/instacoat_en_super_II.htm
4. Corel Pharma Chem. Colorcoat FC and EC Product Information Sheet website. Accessed January 2010. http://www.corelpharmachem.com/pdf/colorcoat.pdf
5. International Specialty Products (ISP). Advantia Performance Product Guide. Accessed January 2010. http://online1.ispcorp.com/Brochures/Pharma/PHAR_C1020_PRF_07.pdf
6. USP 32/NF 27. <701> Disintegration of Delayed Release Dosage Forms.

For more information, contact your Colorcon representative or call:

North America	Europe/Middle East/Africa	Asia Pacific	Latin America
+1-215-699-7733	**+44-(0)-1322-293000**	**+65-6438-0318**	**+54-11-5556-7700**

You can also visit our website at **www.colorcon.com**

ads_comp_dr_fc_ver1_04.2011