Production-Scale Process and Performance Comparison of Two Fully Formulated Aqueous Enteric Coating Systems

OBJECTIVES

The addition of required plasticizers, detackifiers, and neutralization agents to traditional aqueous enteric coating systems, involves complex and time consuming mixing of multiple components. Two fully formulated, aqueous, delayed release coating systems, Sureteric®, aqueous enteric coating system, (polyvinyl acetate phthalate based, Colorcon) and Acryl-EZE®, aqueous acrylic enteric system, (methacrylic acid copolymer based, Colorcon) were evaluated for coating performance and product stability. The necessity of a sub-coat was also studied.

MATERIALS AND EQUIPMENT

The aspirin (ASA) 81 mg tablets (170 mg total weight), contained 40-mesh aspirin crystals (Aspirin 1040, Rhodia, Cranbury, NJ); partially pregelatinized corn starch (Starch 1500®, partially pregelatinized maize starch, Colorcon, West Point, PA, USA); microcrystalline cellulose (Emcocel 50M, Penwest, Patterson, NY, USA) and stearic acid N.F. (Purified vegetable grade powder, Oleotec Ltd., London, England). The enteric coating materials were polyvinyl acetate phthalate (PVAP) based Sureteric, and methacrylic acid copolymer based pigmented Acryl-EZE. The sub-coat material was Opadry® II, high performance film coating system, all by Colorcon, (West Point, PA, USA). An antifoaming agent (30% simethicone emulsion USP, Dow Chemical Co., Midland, MI, USA) was used in the preparation of the acrylic-based system. An Accelacota 150 (Manesty, Liverpool, England) was used to apply the coatings. A model ZT54 disintegration tester (Erweka, Milford, CT, USA) was used for acid uptake testing. A VK7010 dissolution apparatus I (VanKel, Cary, NC, USA) with a UV spectrophotometer (Varian, Palo Alto, CA, USA) was used for drug release testing. An HPLC (Alliance 2690, Waters Corp., Milford, MA, USA) was used for free salicylic acid determinations.

The packaging materials used for stability testing of the coated tablets were 85cc foil sealable HDPE bottles (Drug Plastics and Glass Co., Boyertown, PA, USA) and desiccant packs (3964, Süd-Chemie Performance Packaging, Belen, NM, USA).

METHODS

The coating dispersions were prepared by adding the dry aqueous enteric formulations directly into a mixing tank filled with deionized water (ambient ~ 25 ºC) under vigorous mixing conditions. Each of the dispersions was screened through a 250micron sieve prior to coating.

Table 1. Preparation of Coating Dispersions

Component	Sureteric		Acryl-EZE	
	%	Weight (kg)	%	Weight (kg)
Coating Solids	15.00	13.00	20.00	13.00
Deionized Water	85.00	73.67	80.00	52.00
Total	100.00	86.67	100.00	65.00*

**65.0 grams of antifoam emulsion was added to the water prior to the acrylic powder*

The tablet coating was carried out in the 48" side-vented pan equipped with four spray guns. The coating dispersions were delivered to the spray guns through individual tubes fed from a peristaltic pump. The pan load of ASA 81mg tablets was 130 kg.

Table 2. Coating Trials

Trial	Coating System	Dispersion Concentration (% w/w)	Sub-coat Applied % w.g.	Enteric Sampling Theor. % w.g.
1	Sureteric	15%	2.0%	5,6,7,8,9 and 10
2	Sureteric	15%	None	5,6,7,8,9 and 10
3	Acryl-EZE	20%	2.0%	5,6,7,8,9 and 10
4	Acryl-EZE	20%	None	5,6,7,8,9 and 10

The tablet samples were tested according to USP 24 requirements for delayed release aspirin initially and at 3 months storage at 40 °C/75% RH. Tablets were also tested for acid uptake according to the BP method.

RESULTS

Table 3. Delayed Release Coating Dispersion Preparation Time (minutes)

Mixing Step	Sureteric	Acryl-EZE
Antifoam addition (min) Enteric powder addition (min) Mixing prior to coating (min) Filtration through screen (min)	-5.0 30.0 5.0	0.50 5.0 20.0 5.0
Total dispersion preparation time (min)	40.0	30.5

Table 4. Coating Process Time (hours)

Sureteric		Acryl-EZE	
No Sub-coat	With Sub-coat	No Sub-coat	With Sub-coat
3.5	3.9	2.9	3.64

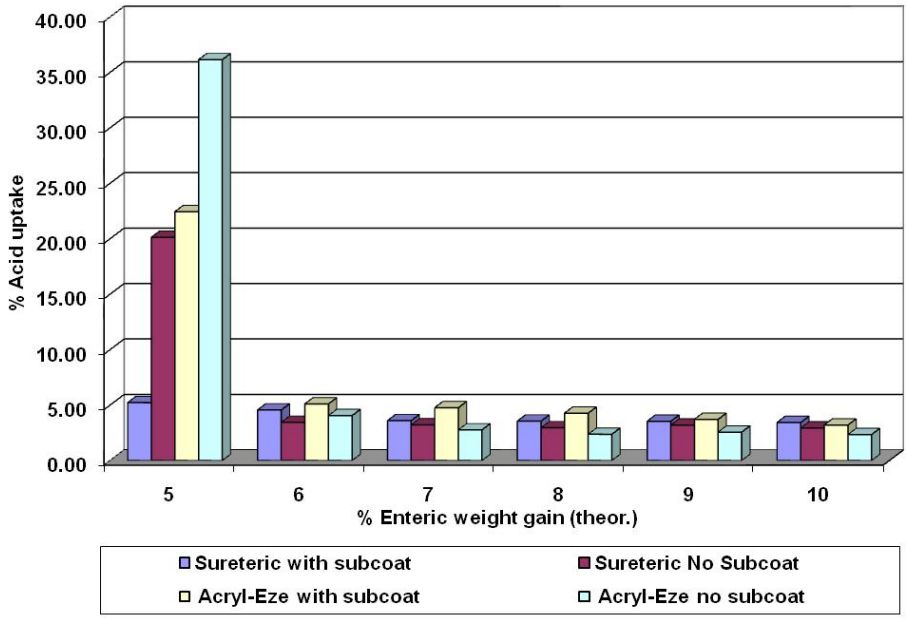
Figure 1. Coated Tablet Appearance

Sureteric Coated

Acryl-EZE Coated

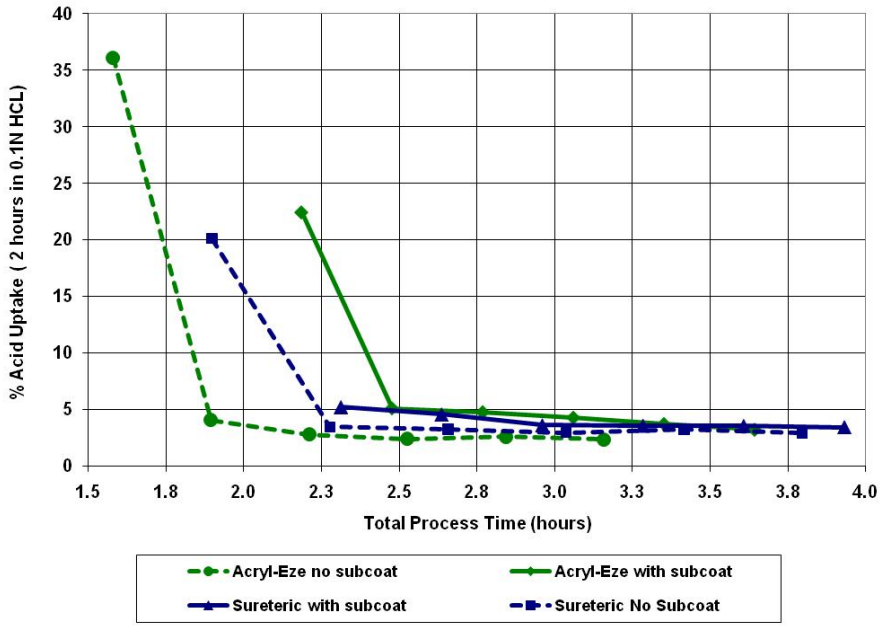
The coating process for both systems was free of any problems. The coated tablets had no obvious defects or signs of sticking or tackiness.

Figure 2. Acid Uptaking Testing



The acid uptake method provides an accurate measure of acid resistance of the coating and acid uptake values of less than 5% would suggest that the tablets would readily pass the acid phase of the delayed release dissolution testing. Samples taken at weight gains of 6% and above all had acid uptake values of 5% or less. At 6% weight gain and higher, the differences in acid uptake between the PVAP and the acrylic-based systems did not exceed 0.63%.

Figure 3. Process Time vs. Enteric Protection



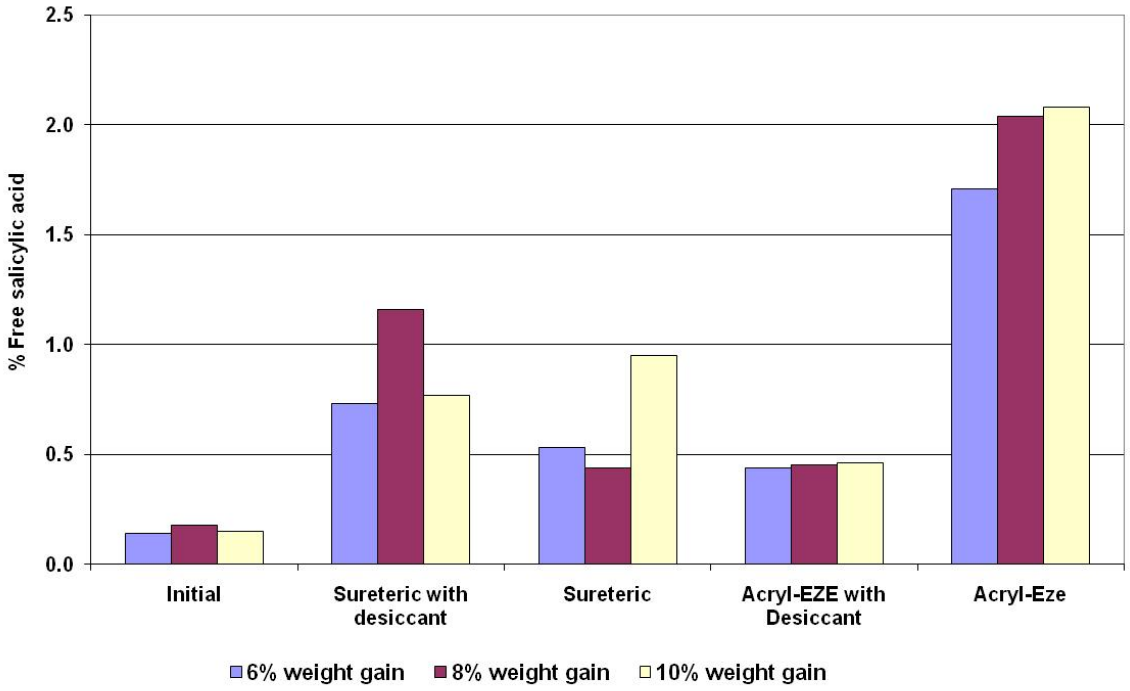
The coating time needed to reach an acceptable level of enteric performance was less than 1.9 hours for the acrylic system and less than 2.3 hours for the PVAP based system.

Table 5. Dissolution Results With or Without Sub-coat

Sureteric Coated Aspirin 81mg Tablets			**Acryl-EZE Coated Aspirin 81 mg Tablets**		
Theoretical Weight Gain (%)	% Released in 0.1N HCl after 2 hours	t80% in Phosphate Buffer (pH = 6.8)	Theoretical Weight Gain (%)	% Released in 0.7N HCl after 2 hours	t80% in Phosphate Buffer (pH = 6.8)
6	0.0	< 30 minutes	6	0.0	< 30 minutes
7	0.0	< 30 minutes	7	0.0	< 30 minutes
8	0.0	< 30 minutes	8	0.0	< 30 minutes
9	0.0	< 30 minutes	9	0.0	< 30 minutes
10	0.0	< 30 minutes	10	0.0	< 30 minutes

Stability Results

Figure 4. Free Salicylic Acid Stability



The tablet samples coated with either delayed release system and without a sub-coat, passed the requirements for less than 3% free salicylic acid. For the samples packaged without desiccant packages, the acrylic-based system had slightly higher free salicylic acid values.

All samples coated to a 6% weight gain or higher with either delayed release system also passed the USP requirements for dissolution at 3 months storage in accelerated conditions.

CONCLUSIONS

Optimum levels of delayed release coating for the ASA 81mg tablet were determined. Both coating systems were comparable in process and delayed release performance. These systems were dispersed in one step in a minimum amount of time. Each system provided acceptable enteric protection to the ASA tablets at low weight gains, and the Acryl-EZE system offers the additional advantage of being fully pigmented. Both systems also provided for good stability under adverse storage conditions in this moisture sensitive application.

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