Preparation of an Enteric Dosage Form with a Water-Dispersible Acrylic Film Coating Formulation

OBJECTIVES

- To evaluate a fully formulated, water-dispersible, acrylic-based film coating system for enteric applications
- To monitor the stability of the acrylic coating formulation and the finished dosage form

METHODOLOGY

Dispersion preparation aqueous enteric film-coating dispersions were prepared by adding 20 parts of a dry powder formulation (Acryl-EZE®, aqueous acrylic enteric system, 93O92038) to 80 parts water, with a pharmaceutically approved anti-foaming agent, and stirring with a suitable mixer for 20 minutes. The resultant dispersions were then passed through a 60-mesh (250 micron) sieve prior to initiating the coating trials.

Sub and Enteric Film Coating 325mg Acetylsalicylic acid (ASA) tablets were aqueous film-coated in a 30 inch O'Hara Labcoat II side-vented coating pan according to the following parameters.

Table 1.

Parameters	Sub-Coat	Enteric Layer
Surface Bed Temperature (ºC)	42	30
Inlet Temperature (ºC)	62	46
Outlet Temperature (ºC)	44	32
Atomization Pressure (psi/bar)	45/3	45/3
Pattern Air Pressure (psi/bar)	40/2.8	40/2.8
Pan Speed (rpm)	7	8
Pan Charge (kg)	40	40
Fluid Delivery Rate (g/min)	140	115-120
Drying air volume (cfm/m^3/hr)	550/935	550/935

Note: In all cases the sub-coat was a 2% weight gain of Opadry® II, high performance film coating system, Y-30-18037.

Stability Samples

Tablets

ASA tablets were sampled at 8% theoretical weight gain of applied enteric coating for packaging. Samples were packaged and heat-sealed in 150cc HDPE bottles supplied from Drug Plastics. Inside each bottle were placed 2 cotton balls and 1 desiccant cartridge (Carbon/Silica) supplied from Sud-Chemie, unless otherwise indicated. These samples were then placed in stability chambers at 25°C/60% RH, and 40°C/75% RH conditions.

Dry powder formulations

Formulations were prepared via dry powder blending in a twin-shell mixing unit. Pigmentation was achieved by addition of titanium dioxide and yellow iron oxide colorants during the mixing process. Stability samples were packaged in double polyethylene bag liners with a desiccant sachet between the two layers of lining. These samples were then placed in stability chambers at 25°C/60% RH, and 40°C/75% RH conditions.

Analytical Methodology

The following methods were employed for sample analysis:

USP Delayed Release ASA Tablet Monograph

Dissolution <724>

Baskets, 100 rpm

Acid Phase	Buffer phase
- 0.1N HCL	- pH 6.8 phosphate buffer
- Not more than 10% dissolved after 120 minutes	- Not less than 80% dissolved after 90 minutes

Free Salicylic Acid Content - Not more than 3.0%

ASA Assay -95-105%

Dispersion Particle Size Distribution

- Coulter LS Particle Size Analyzer
- Laser light scanning
- Fraunhofer optical model
- Medium - deionized water

Dispersion Color

- Colorcon internal method

Dispersion pH

- Colorcon internal method

RESULTS

Enteric Coated Tablet Stability Results

Free Salicylic Acid Content

Figure 1 is a comparison of free salicylic acid contents for samples packaged without a desiccant cartridge from the initial to the 3 month 40/75 stability time pull. For reference purposes a sample with a desiccant cartridge (D) was also analyzed at 3 month 40/75 to highlight the effect of moisture protection in the final package.

As the data indicates, for this particular ASA core, the enteric coated tablets packaged with or without a desiccant cartridge meet the USP specification for free salicylic acid content at 3 months 40/75 stability conditions.

Figure. 1

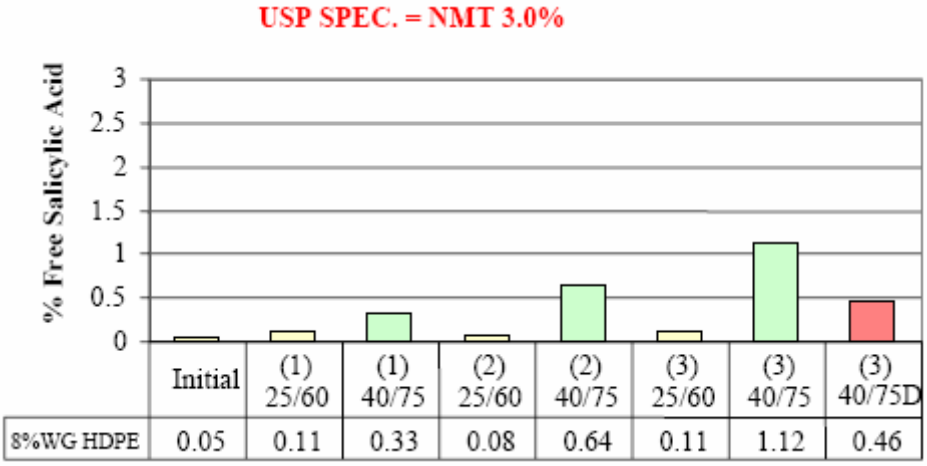
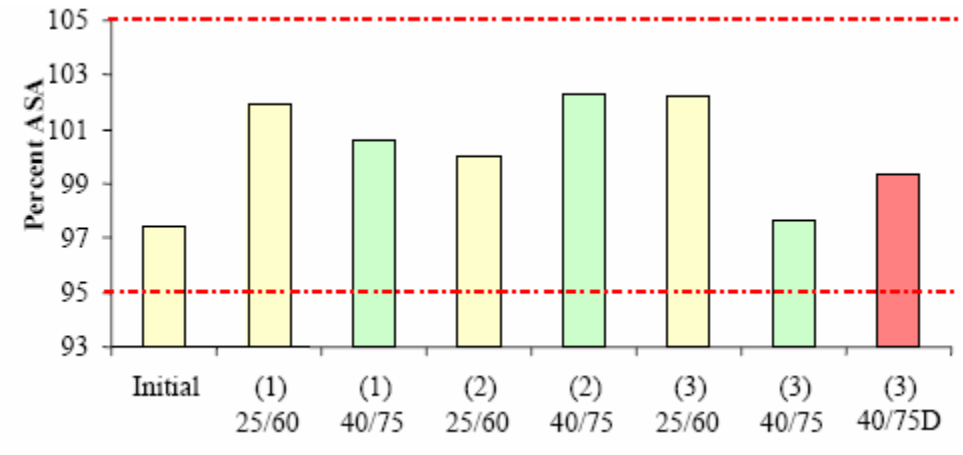


Figure 2 profiles ASA content versus stability storage interval and condition. For reference purposes a sample with a desiccant cartridge (D) was also analyzed at 3 month 40/75. Samples from each time pull meet the USP criteria of 95 105 ASA content.

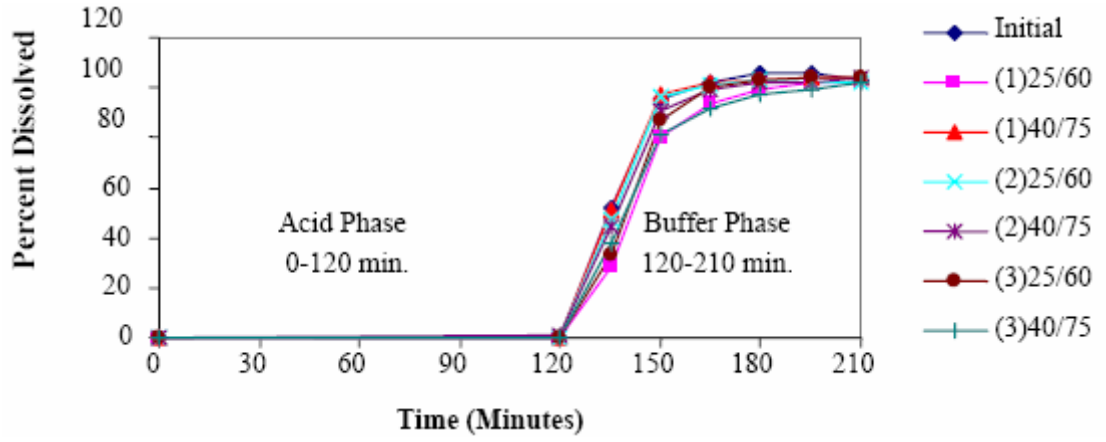
Figure 2.



Delayed Release ASA Tablet Dissolution

Figure 3 represents dissolution plots for enteric coated ASA tablets from time zero to 3 months 40 °C/75% RH. The USP acceptance criteria are met for all samples at each time interval and condition. Exceptional gastric protection is demonstrated in addition to reproducible release in the buffer phase.

Figure 3.

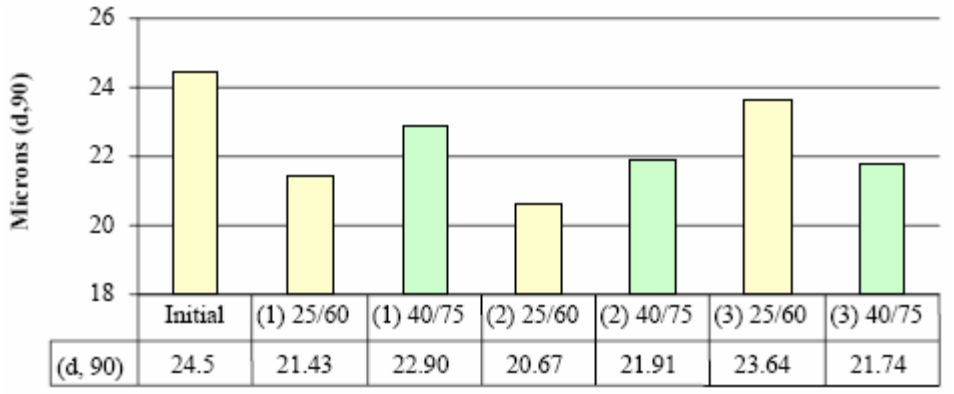


Dry Powder Formulation Stability Results

Dispersion Particle Size Distribution

At each stability interval and condition, samples of the dry powder formulation were removed from a stability chamber. These samples were then re-dispersed for coating application. After the recommended dispersion preparation time, an aliquot was removed for particle size analysis. Figure 4 represents the particle size in microns that 90.

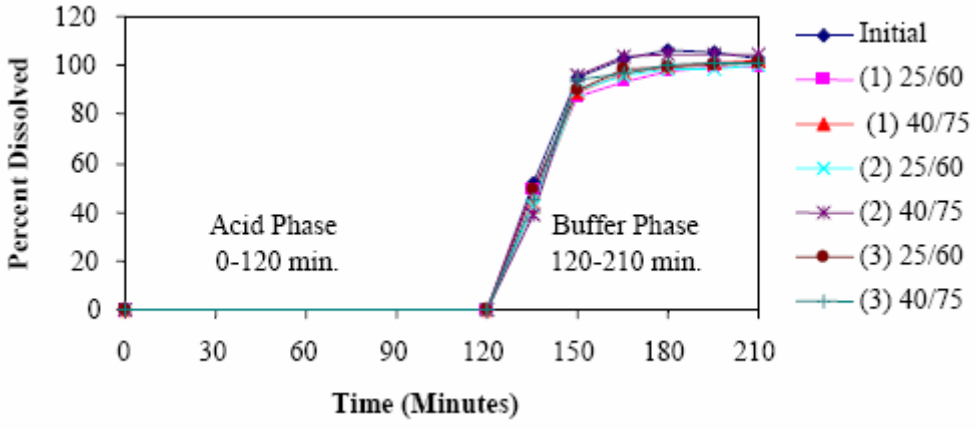
Figure 4.



Delayed Release ASA Tablet Dissolution - Re-coats

As mentioned previously, dry powder samples were pulled at each stability interval and condition to be re-coated onto ASA tablets. This method is employed to verify that the characteristics of the final film coat a re not compromised due to powder instability (Figure 5).

Figure 5.



Dispersion pH and Color Stability

Small aliquots of the dispersions prepared for the re-coating of the dry powder formulations at a given stability interval and condition were measured for pH.

Dry powder methacrylic acid/ethyl acrylate polymers are aided in dispersion by the presence of a neutralizing agent. The amount included in the Acryl-EZE formula is intended to achieve a pH of approximately 5.

Due to this relationship, the pH of the dispersion and any changes over time were monitored to ensure the reproducibility of the end product. Table 1 displays the pH versus time interval and stability condition. Table 1 also displays the relationship between color change in the dry powder formulation and stability interval and condition relative to the initial time point. The color change is represented as the total color difference (DE). As is expected a larger color change is observed at 40 °C/75% RH conditions, yet still within the specification of not more than 2 DE units.

Table 1.

	pH	DE
Initial	5.6	N/A
(1) 25/60	5.6	0.35
(1) 40/75	5.5	0.65
(2) 25/60	5.6	0.25
(2) 40/75	5.5	0.83
(3) 25/60	5.2	0.11
(3) 40/75	5.6	0.63

CONCLUSIONS

A fully formulated, water-dispersible, acrylic based film coating system has been successfully employed to film coat ASA tablets for enteric protection. The acrylic coating formulation and the enteric coated ASA tablets are stable under room temperature and accelerated stability conditions.

Reprint of poster presented at AAPS – Oct 2001. Authors: Kurt Fegely, Jason Pollock, Alaine Zumpino, George Reyes.

REFERENCES

1. Eudragit L100-55 Technical Application Pamphlet (Info LD-13/e)

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