Performance Characteristics of Acryl-EZE®, Aqueous Acrylic Enteric System

Eudragit L100-55 is a copolymer of methacrylic acid and ethyl acrylate (1:1 ratio) which meets the USP definition for Methacrylic Acid Copolymer Type C. L100-55 is a re-dispersible powder produced by spray drying Eudragit L30-D. Aqueous film coating dispersions based on L100-55 are typically prepared by stepwise addition of an alkalizing agent, a detackifier, a plasticizer and optional colorants to the re-dispersed L 100-55. Film coatings prepared from such dispersions are resistant to gastric juice but readily dissolve at a pH above 5.5.

To increase convenience and production efficiency, a re-dispersible dry powder containing L100-55 and requisite additives was formulated. An aqueous dispersion was then prepared in one step by dispersing the fully formulated dry powder in water with the aid of a high shear mixer. The dispersion and film coating characteristics of the one-step system were then compared to those of a similar system prepared by the stepwise combination of excipients. Dispersion particle size, delayed-release aspirin dissolution, free-salicylic acid content, and enteric disintegration were measured.

Delayed Release Film Coating

All samples were prepared in an O'Hara Labcoat II side vented coating unit equipped with a 15" pan and VAU spraying nozzles. Tablets were coated to theoretical 8 and 10 percent weight gains from a dispersion containing 20% solids. The coating parameters were as follows:

Table 1. Coating Parameters

Parameter	15" Pan
Bed Temperature (ºC)	30
Inlet Temperature (ºC)	45
Outlet Temperature (ºC)	32
Atomization Pressure (psi/bar)	20/1.4
Pattern Air Pressure (psi/bar)	20/1.4
Pan Speed (rpm)	17
Pan Charge (kg)	2.5
Fluid Delivery Rate (g/min)	20
Drying Air Volume (cfm/cmh)	180/300
Coating Time (min): 2% Opadry® II Subcoat 10% Enteric Coat Total (minutes)	 15 60 75

Coating Dispersion Properties

Samples of Acryl-EZE were prepared by dispersing 20 parts of the powder into 80 parts of water using a high shear mixer and a pharmaceutically approved, anti-foaming agent. The multi-step system was prepared according to Rohm's Technical bulletin.[1]

Analytical Methodology

The following methods were employed for sample analysis:

- USP Delayed Release Aspirin Tablet Monograph

Dissolution <724> (Baskets, 100 rpm)

Acid Phase

- 0.1N HCl
- Not more than 10% dissolved after 120 minutes

Buffer Phase

- pH 6.8 phosphate buffer
- Not less than 80% dissolved after 90 minutes

Free Salicylic Acid Content

- Not more than 3.0%

Enteric Disintegration <701>

- Modified to include 50 tablets rather than 6 tablets
- 0.1N HCl for 1 hour
- Pass = no signs of cracking, peeling, bloating, or disintegration

Dispersion Particle Size Distribution

- Coulter LS Particle Size Analyzer
- Laser light scanning
- Fraunhofer optical model
- Medium – Deionized Water

RESULTS AND DISCUSSIONS

The dissolution performance of aspirin coated with either the Acryl-EZE or the multi-step system met the USP Delayed-Release Aspirin Tablet Monograph requirements.

Figure 1 shows no change in the dissolution profile of aspirin tablets coated with the Acryl-EZE system from the initial to the 3 month time pull. More interestingly, the profile of samples subjected to storage at one month open dish does not vary from that of samples stored in HDPE bottles.

Figure 1.

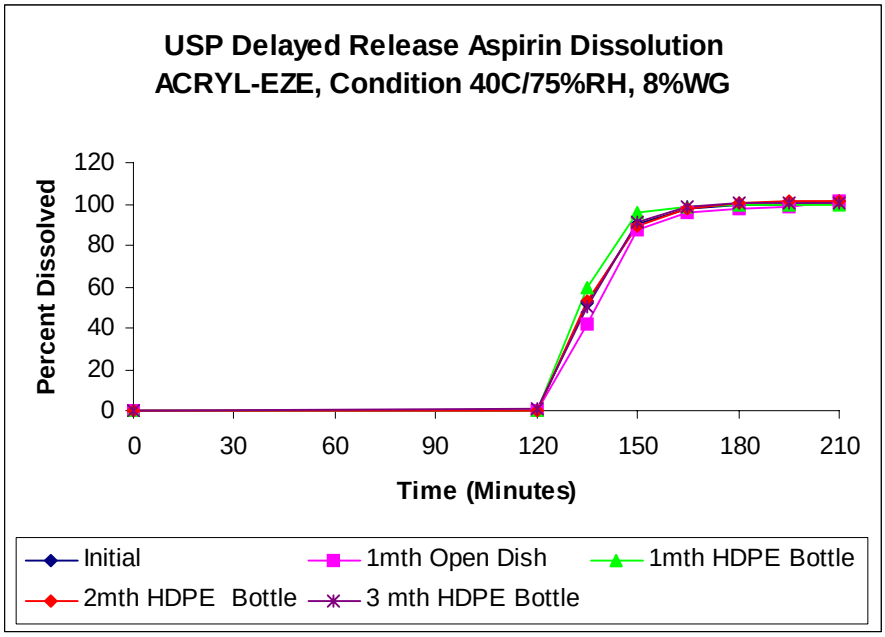
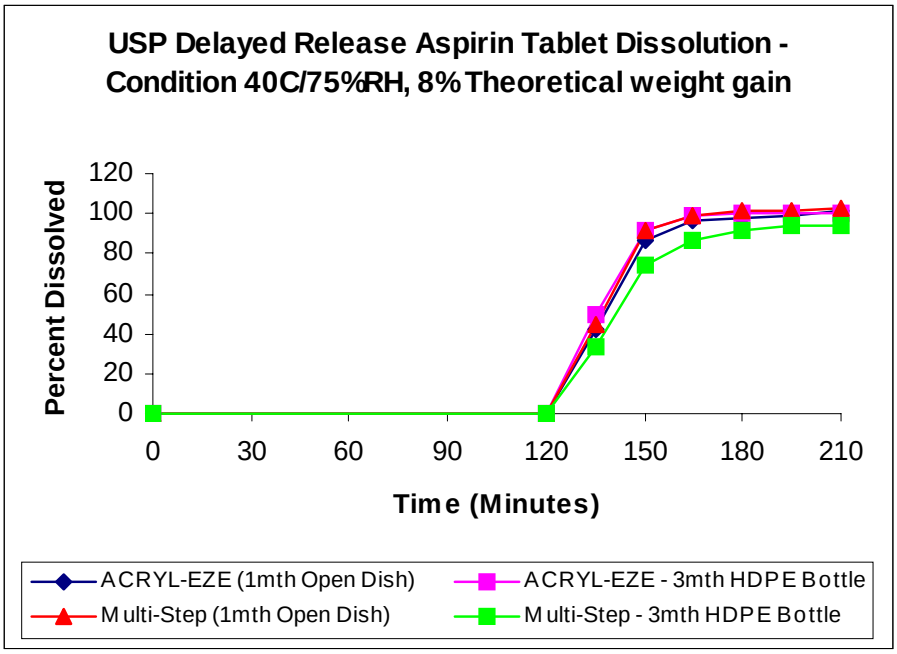


Figure 2 is a comparison of the drug release profiles for the Acryl-EZE and the multi-step enteric film coating system. As is shown, there is no significant difference in the aspirin release profile between the two systems. This confirms that although the preparation of the coating dispersion is significantly different for the two systems, the end result is not.

Figure 2.



Note: Time 0 to 120 minutes = ACID PHASE

Time 120 to 210 minutes = BUFFER PHASE

The free salicylic acid content of the enteric-coated aspirin was also investigated to compare the relative permeability of the film coatings to the atmosphere. The results indicated that the film quality of the Acryl-EZE is equivalent to that of the multi-step system at 3 month 40°C/75% relative humidity in HDPE bottles with desiccant and cotton.

Table 2

Sample ID	Free Salicylic Acid Content at 3 Months
Acryl-EZE	0.21%
Multi-Step	0.17%

The integrity of the film coatings was not only quantified by dissolution but also by disintegration in 0.1N HCL at 8 and 10 percent theoretical coating weight gains. For these sample sets, 50 tablets were analyzed for resistance in the gastric phase according to USP Method <701>. The results are expressed as the percentage of tablets which did not show signs of cracking, peeling, bloating, or disintegration after 1 hour in the acid phase at 8 and 10 percent weight gains. All samples were packaged in HDPE bottles, unless otherwise indicated.

Table 2 indicates that there is not a significant change in the enteric protection of the Acryl-EZE system from the initial to the three month time pull at 40°C/75% relative humidity conditions.

Table 3.

Acryl-EZE	Initial	1 mth Open Dish	1 mth HDPE	2 mth HDPE	3 mth HDPE
8% WG	98	98	90	98	100
10% WG	100	100	100	100	100

Table 3 is a comparison of the enteric protection provided by Acryl-EZE versus the multi-step enteric film coating system. Results show that there is not a significant performance difference in the enteric protection provided by either.

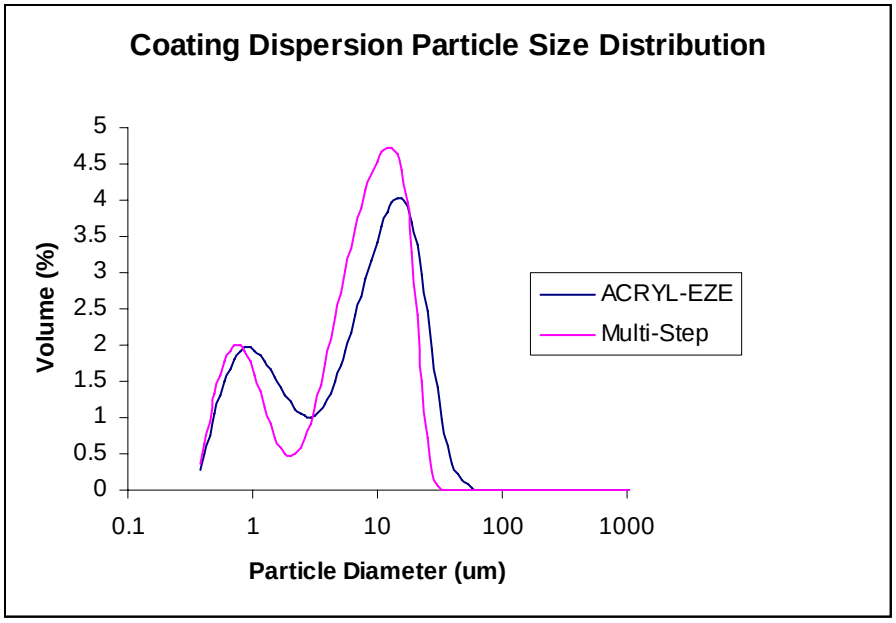
Table 4. Passing Percentage – DT 0.1 N HCL.

Sample ID	Initial	1 mth 40/75	3 mth 40/75
Acryl-EZE	98/100	90/100	98/100
Multi-step	96/98	100/100	92/98

In addition, Acryl-EZE and multi-step coating dispersion(s) were analyzed for particle-size distribution to verify the consistency of the dispersion, and any effect high shear mixing may have on the dispersion characteristics of the one-step system. The data indicated that 90 percent of the particles by volume are less than 23.64 microns for the Acryl-EZE system, and less than 18.10 microns for the multi-step system, for a 22 kilogram total dispersion batch weight.

Figure 3 indicates that changing the number of steps required to prepare the aqueous enteric coating dispersion does not significantly influence the particle size or coating performance of the dispersion.

Figure 3.



CONCLUSIONS

This study indicated that Acryl-EZE can be successfully applied to a pharmaceutical active ingredient, thus eliminating several steps and time from the manufacturing process. The Acryl-EZE coating system performance was equivalent to a similar multi- step system in a variety of performance tests indicating that Acryl-EZE is a viable substitute for the multi-step system. Future work will focus on coating scale-up and stability of Acryl-EZE versus the multi-step system.

REFERENCES

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

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