Preparation of Robust, Enteric Coated Dosage Forms Utilizing Acryl-EZE® and Aluminum Lake-Based Pigments

OBJECTIVES

To prepare a one-step, aluminium lake-pigmented, delayed release coating formulation (Acryl-EZE®, aqueous acrylic enteric system) that provides suitable protection of dosage forms from acidic media, and reproducible drug release over time.

To overcome performance difficulties observed between acetylsalicylic acid (ASA) and lake-pigmented acrylic film layers.

METHODOLOGY

Acryl-EZE Formulations

Ready-to-disperse, dry particulate, pigmented, enteric coating formulations were prepared utilizing various natural and synthetic pigments. Table 1 summarizes the type of pigment utilized, the vendor, and the quantity present in the coating formulation (%w/w).

Table 1.

Pigment Type	Vendor	Pigment Load (%w/w)
Yellow Iron Oxide	BASF	3%
Riboflavin	Roche Vitamins	6%
FD&C Yellow #6 Dye	Noveon	1%
FD&C Yellow #6 Lake	Colorcon	6%
Aluminum Hydrate	Colorcon	4%

Dispersion Preparation

Aqueous enteric film coating dispersions were prepared by adding 20 parts of the pigmented coating formulations to 80 parts distilled water (ambient ~ 25°C), followed by low shear mixing for 25 minutes. The resultant dispersions were then passed through a 60-mesh (250-micron) sieve prior to initiating the film coating trials.

Enteric Film Coating Trials

Tablet coating trials were conducted in a 24-inch side-vented coating pan on 325mg ASA, 200mg ibuprofen, 500mg acetaminophen, and 50 mg diclofenac sodium. The coating parameters were as described in Table 2. All tablets were enteric coated to a theoretical 8% weight gain (wgt).

All samples were packaged in HDPE bottles with a desiccant or “open dish” and placed in a 40ºC/75%RH stability chamber.

Table 2.

Parameters	Subcoat	Enteric Layer
Surface Bed Temperature (C)	45	30
Inlet Temperature (C)	64	55
Outlet Temperature (C)	45	33
Atomization Pressure (psi/bar)	35/2.4	35/2.4
Pattern Air Pressure (psi/bar)	35/2.4	35/2.4
Pan Speed (rpm)	12	12
Pan Charge (kg)	15	15
Fluid Delivery Rate (g/min)	40	60
Drying Air Volume (cfm/m^3/hr)	250/425	250/425

Note: The subcoat in all cases was Opadry® II, high performance film coating system, formulation number 85G28725 at a 2% theoretical weight gain.

Analytical Methodology

Samples from each study were analyzed at pre-determined intervals according to the USP dissolution methods for delayed release ASA and diclofenac sodium tablets, or a modified method for acetaminophen and ibuprofen.

RESULTS

Drug Release - Multiple Actives

Acetaminophen, ibuprofen, and diclofenac sodium were enteric coated with an Acryl-EZE formulation containing 3% (w/w) FD&C Yellow #6 aluminum Lake as the pigment.

Figure 1 highlights the delayed release dissolution profiles for ibuprofen and acetaminophen at various stability intervals.

Figure 1.

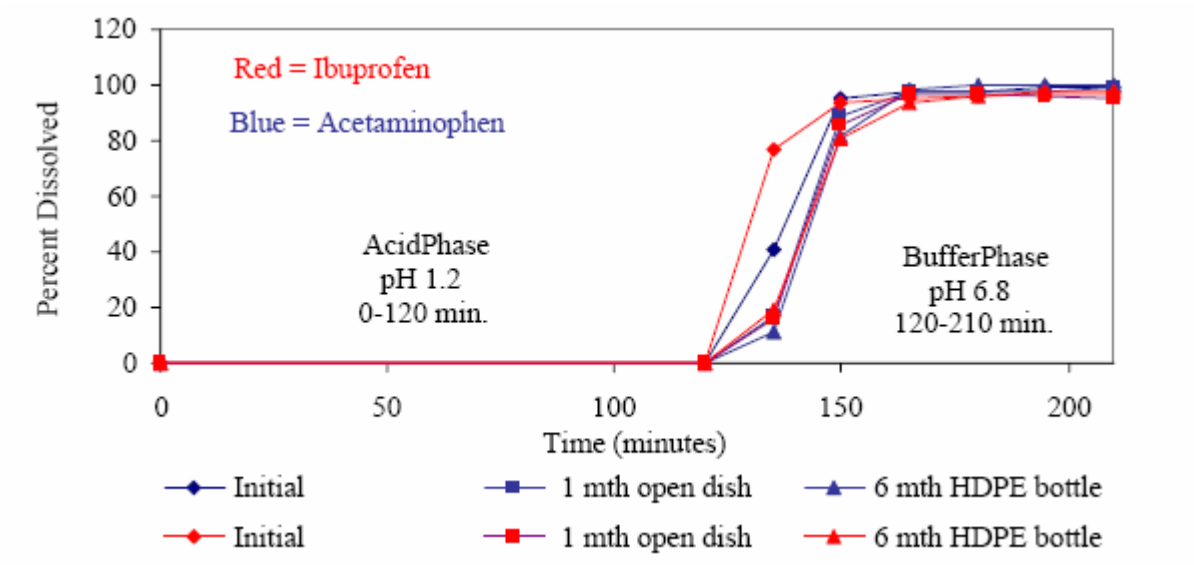
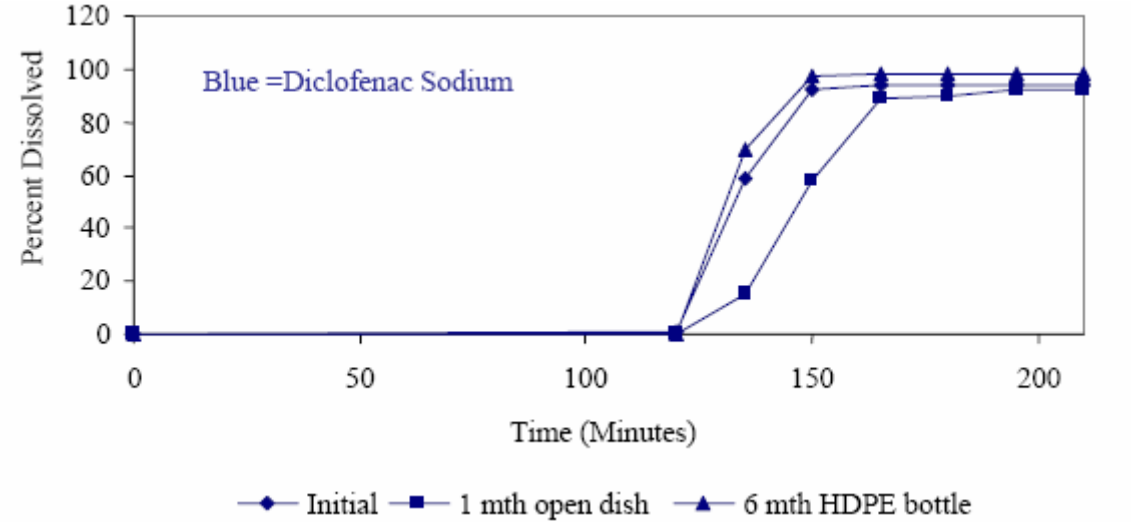


Figure 1 indicates that greater than 80% of acetaminophen and ibuprofen is released after 30 minutes in the buffer phase (150 min. overall) at all stability conditions. The results of diclofenac sodium under similar conditions are plotted in Figure 2.

Figure 2.

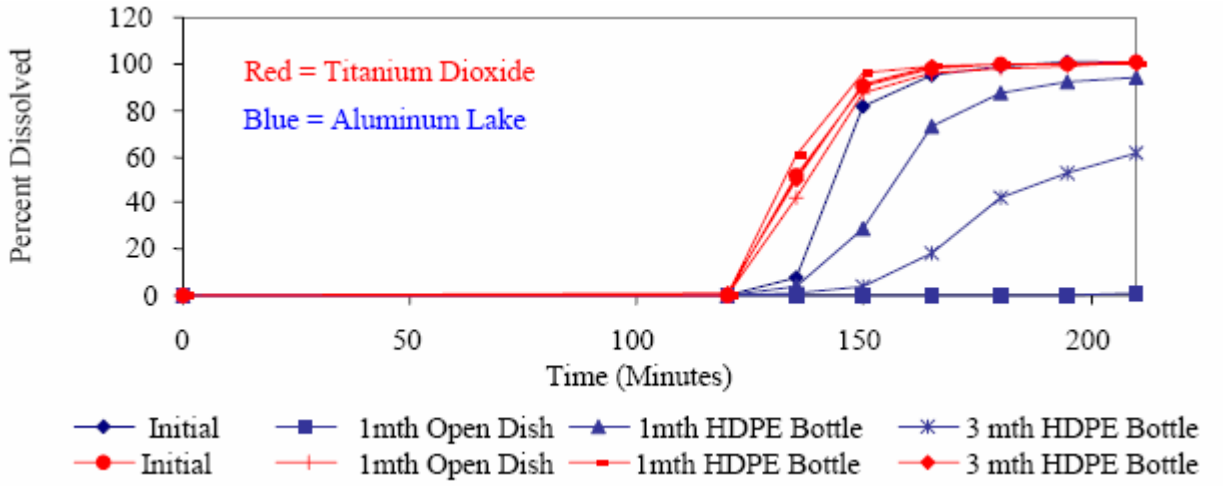


The results depicted in Figure 2 comply with the USP criteria for delayed release diclofenac sodium tablets. Figures 1 and 2 verify that even under "high stress" conditions such as "open-dish" for one month, that aluminum lake-pigmented Acryl-EZE is capable of providing enteric protection and complete drug dissolution through six (6) months 40°C/75%RH.

Acetylsalicylic Acid and Aluminium Lakes

Figure 3 represents the dissolution profiles of ASA enteric coated with FD&C Yellow #6 lake and separately, titanium dioxide pigmented coating formulations. Results indicate a decrease in the release rate of drug as the stability interval increases for the lake-pigmented system.

Figure 3.



Pigment Effect on ASA Release Rate

Enteric coated ASA was evaluated for the percent ASA dissolved at 90 minutes parameter (%ASA T90) utilizing Acryl-EZE formulations containing the pigments listed in Table 1. The results in Table 3 suggest that the retardation of ASA release rate is dependent on the aluminium lake and the aluminium substrate on which the dye is bound to during the "laking" process. The "non-aluminium" pigments do not retard the release rate of ASA.

Table 3.

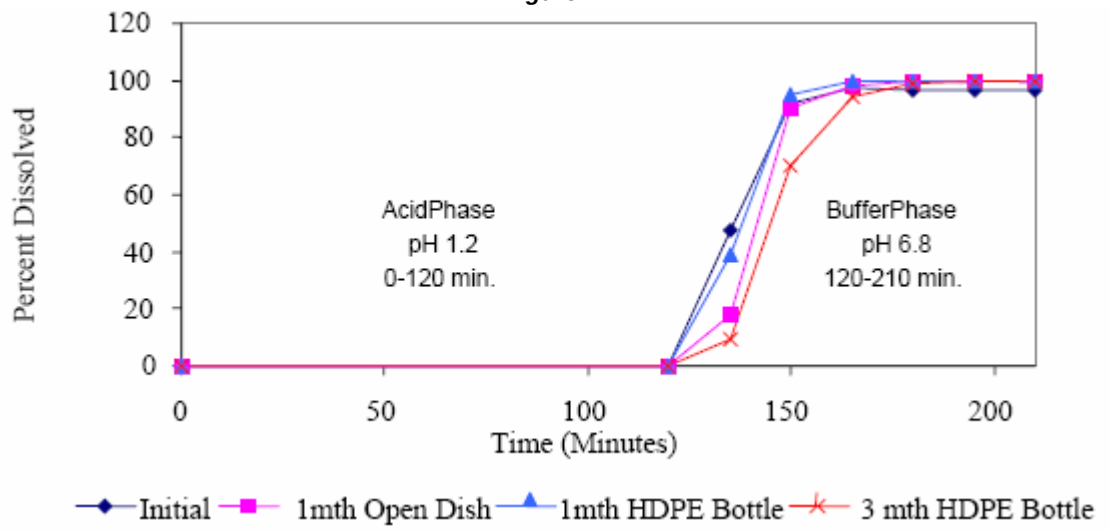
Percent ASA Released at 90 minutes (Buffer Phase) % ASA T_{90}		
Pigment Type	**One Month Open Dish**	**Three Month HDPE Bottle**
Titanium Dioxide	100	100
Yellow Iron Oxide	100	100
Riboflavin	100	100
FD&C Yellow #6 Dye	100	100
FD&C Yellow #6 Lake	**0**	**61**
Aluminum Hydrate	**4**	**10**

Coating Method for a Stable ASA Dissolution Rate

The findings in Table 3 and Figure 3 prompted an additional study to look at the application of a titanium dioxide pigmented acrylic layer (8% wgt/no sub-coat), followed by a lake-pigmented immediate release film-coating to provide the necessary color (85F13473, 2.5% wgt).

The dissolution plots in Figure 4 suggest that utilization of a separate, immediate release coloring layer will overcome the formulation difficulties observed with ASA and aluminium lake pigments.

Figure 4.



CONCLUSION

One-step, lake-pigmented Acryl-EZE formulations were applied to multiple pharmaceutical actives and yielded acceptable enteric protection and reproducible drug release over time.

Results of this study have prompted additional work to expand the color palette of commercially available Acryl-EZE formulations.

The presence of aluminium species in the acrylic film layer has been demonstrated to retard the dissolution release rate of ASA. Utilization of a distinct immediate release coloring layer after the enteric coat resulted in complete release of ASA from the dosage form within the specified interval.

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