The Influence of Plasticizer Type and Concentration on Acid Resistance of Tablets Coated with a New Aqueous Delayed Release Film Coating System

ABSTRACT SUMMARY

The influence of plasticizer type and concentration, added to a new aqueous delayed release (DR) film coating system, on acid resistance was evaluated. Incorporating PEG 8000 (8-15%), TEC (12-25%), or triacetin (12-30%) in the DR coating system resulted in acid resistance (2 hours) and complete disintegration in buffer (pH 6.8), as desired.

INTRODUCTION

Enteric protection from DR film coating systems has been shown to be influenced by the hydrophilic and lipophilic properties of the plasticizer, level of plasticizer, and amount of polymer applied to the substrate.[1] Furthermore, the properties of the substrate, in conjunction with the plasticizer type, were found to influence the degree of enteric protection.[2]

Therefore, the purpose of this study was to evaluate the influence of three plasticizers at various levels on acid resistance in a new aqueous DR film coating system (Acryl-EZE®, aqueous acrylic enteric system, 93A Series). The tablets were tested in two different media, 0.1N HCl (pH 1.2) and 0.5M sodium acetate buffer (pH 4.5), to simulate the stomach pH of a fasted human and the increase in stomach pH (above pH 4.0) from food and/or multiple doses of proton pump inhibitors (PPIs), respectively. A multiple dose regimen of PPIs results in a decrease in gastric acid secretion with a subsequent elevation in gastric pH.[4-5]

The properties of the substrate (placebo cores) and amount of polymer applied to the substrate (7.6mg/cm^2) were held constant. Polyethylene glycol 8000 (8-15%), triethyl citrate (12-25%), or triacetin (12-30%) was added to water, followed by Acryl-EZE 93A, to form a pigmented aqueous DR coating dispersion. Placebo tablets were coated with the DR coating dispersion to 10% theoretical weight gain. Acid uptake in 0.1N HCl and acetate buffer (pH 4.5), as well as disintegration time in phosphate buffer (pH 6.8), were determined.

EXPERIMENTAL METHODS

Materials

Polyethylene glycol 8000 (PEG 8000), triethyl citrate (TEC), and triacetin were obtained from Clariant (USA), Morflex (USA), and Tessenderlo Fine Chemicals (UK), respectively. Simethicone emulsion (30%, Dow) was used as an anti-foam to deaerate the DR coating dispersion, was purchased from Dow (USA). Placebo tablets, Opadry®, complete film coating system, YS-1-7027, and Acryl-EZE 93A18597 were obtained from Colorcon (USA).

Preparation and Characterization

A seal coat dispersion was prepared by dispersing (low shear) Opadry in water and mixing for 30 minutes. The solids content of the final coating dispersion was 12.5% (w/w).

The enteric coating dispersion was prepared by dispersing the plasticizer and simethicone emulsion (0.5% w/w, respect to total dispersion) in water and mixing (low shear) for 5 minutes. Acryl-EZE 93A was added (20% solids, w/w, respect to water) and mixed for an additional 30 minutes, achieving a uniform DR pigmented coating dispersion. The dispersion was screened (250µm) and slowly stirred during spraying.

Placebo tablets (3/8" (9.57mm) convex, 307mg) were seal coated (4% theoretical weight gain) and enteric coated (10% theoretical weight gain) according to recommended coating conditions (Colorcon, Table 1).

Table 1. Seal Coating and Delayed Release Coating

O'Hara Labcoat I	**Opadry YS-1-7027**	**Acryl-EZE 93A18597**
Tablet Charge (kg)	1	1
Inlet Air Temp. (ºC)	70-74	39-42
Drying Air Volume (cfm)	180	125
Tablet Bed Temp. (ºC)	43-46	28-32
Exhaust Air Temp. (ºC)	52-55	28-32
Atomization Air (psi)	30	9
Pattern Air (psi)	30	15
Spray Rate (g/min)	15	10
Pan Speed (rpm)	18	20

Table 2 shows the plasticizer type and level (w/w, with respect to polymer) and the solids content of the final coating dispersions.

Table 2. Plasticizer Type and Level

Plasticizers (water solubility, 20ºC)	**Level (% w/w, respect to polymer)**	**Solids (%)**
PEG 8000 (1 in 25)	8, 9, 12, 15	21-22
TEC (1 in 15)	12, 15, 20, 25	22-23
Triacetin (1 in 14)	12, 15, 18, 20, 25, 30	22-24

Sample Analysis

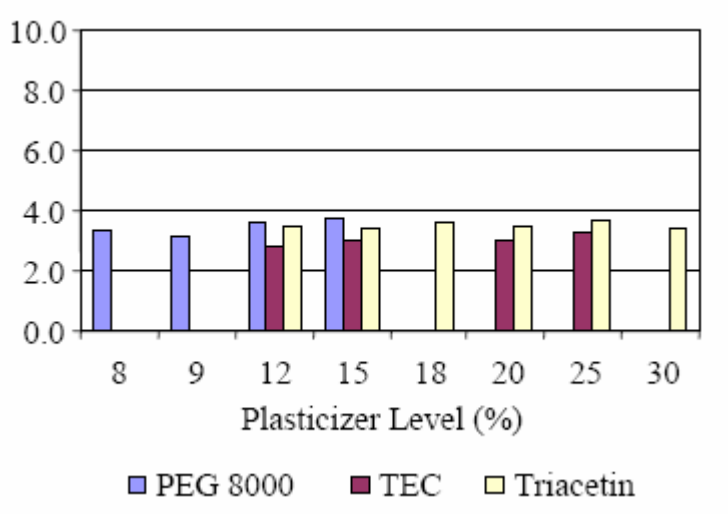
Disintegration and acid uptake testing was performed in a Vankel 35-1200 disintegration apparatus. The disintegration time of the uncoated and coated cores (n=6) in 900 ml of 0.1N HCl (pH 1.0), acetate buffer (pH 4.5) and phosphate buffer (pH 6.8) was recorded. The amount of media (HCl acid or acetate buffer) taken up by the coated placebo tablets (acid uptake) was determined by calculating the percent difference between tablet weights before and after exposure to media for 2 hours.

RESULTS AND DISCUSSION

The uncoated and seal coated cores disintegrated in the acid and buffer phases in less than 1 minute, as expected. The enteric coated placebo tablets remained intact for 2 hours in the acid phases (pH 1.0 and 4.5) and disintegrated in phosphate buffer (pH 6.8) in about 2 minutes, as desired.

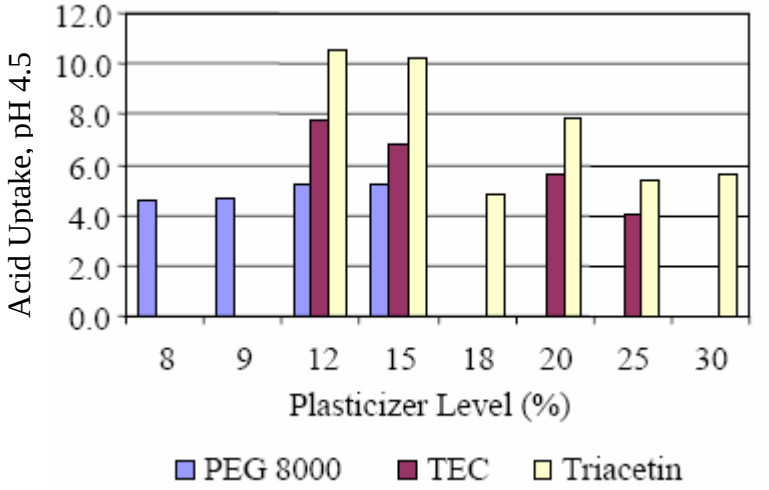
Historical data have shown that acid uptake less than 10% corresponds to acceptable enteric protection (no drug release or degradation in the acid phase of dissolution testing). Figure 1 shows that Acryl-EZE 93A plasticized with TEC, PEG 8000 or triacetin had less than 4% acid uptake when tested in 0.1N HCl acid.

Figure 1. Acid Uptake in 0.1N HCl (pH 1.0)



In acetate buffer (pH 4.5), Acryl-EZE 93A plasticized with PEG 8000 had the least acid uptake, followed by TEC and triacetin (Figure 2). PEG 8000 showed a fairly constant acid uptake (about 5%) at each plasticizer level (8-15%). In contrast, TEC and triacetin showed a decrease in acid uptake with an increase in plasticizer level. Specifically, acid uptake decreased from 7.7 to 4.1% as TEC increased from 12 to 25% and it decreased from 10.5 to 5.7% as triacetin increased from 12 to 30%.

Figure 2. Acid Uptake in Acetate Buffer (pH 4.5)



CONCLUSIONS

The degree of acid resistance was influenced by the plasticizer type and its concentration in the coating dispersion. All three plasticizers (PEG 8000, TEC and triacetin) at all tested concentrations with the Acryl-EZE film coating system provided the tablets with enteric protection.

Acryl-EZE 93A provides a flexible pigmented formulation for scientists, allowing them to select the type and level of the plasticizer used, while maintaining excellent enteric performance in intermediate pH media.

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