Acryl-EZE®
Aqueous Acrylic Enteric System

Colorcon®

Evaluation of Enteric Coating of Mini-Tabs in Different pH Media Using Acryl-EZE® II System

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Introduction

Multiparticulate (MP) drug delivery systems provide a consistent and reliable in vivo drug release, with a reduced risk of local irritation along the gastrointestinal tract (1, 2). Mini-tabs or small tablets with a size of 2-3 mm in diameter combine the advantages of MP dosage forms with the benefits of established tableting techniques, including excellent size uniformity, a regular shape, and a smooth surface. Mini tabs can be packaged in a variety of dosage forms, including hard shell capsules and sachets, which makes them suitable for a wide range of populations, including pediatric, geriatric, and those who report having difficulty swallowing. This study aimed to evaluate the performance of Acryl-EZE® II, Optimized High Performance Enteric Coating applied onto placebo mini-tabs containing blue dye as a substitute for a water-soluble active. Enteric performance, as determined by acid uptake and disintegration, was evaluated across a range of pH media up to pH 5.0 acetate buffer.

Methods

Placebo mini-tabs (3 mm, 18 mg) containing 1% of FD&C Blue No. 1 dye were compressed with 3.7 KN force using a XP 1 single punch tablet press (Korsch AG, Germany) fitted with 3 mm round concave 14-tip tooling. The placebo formulation is shown in Table 1.

Table 1. Core Formulation

Ingredient	Qty (%w/w)
Microcrystalline cellulose	98.5
FD&C Blue No.1	1.0
Magnesium stearate	0.5
Total	100.0

1 kg of placebo mini-tabs was seal-coated with 5% WG of Opadry (HPMC-based system), then enteric coated with 20% WG of Acryl-EZE II followed by 10% WG of an Acryl-EZE II top-coat. The coating was performed in a Labcoat IIX (O'Hara Technologies, Canada) fitted with a 12" fully perforated pan, following the coating process parameters described in Table 2. After coating, the enteric performance of the mini-tabs with and without the Acryl-EZE II top-coat was assessed by measuring the non-compendial acid uptake, which determined the weight increase after exposing the mini-tabs to various acid phase media including pH 1.2 (0.1N HCl), 4.5 or 5.0 acetate buffer (N=6) in a disintegration tester set to 37°C for 2 hours. To accurately calculate acid uptake values, it was assumed that the water-soluble Acryl-EZE II top-coat would dissolve during acid uptake testing, therefore, the initial tablet weight was recorded as the tablet weight before the addition of the top-coat.

Table 2. Coating Process Parameters

Parameter	Opadry Seal-coat	Acryl-EZE II	Acryl-EZE II Top-coat
Charge (Kg)	1	1	1
Solids Content (%w/w)	10	20	10
Spray Rate (g/min)	9	11	13
Bed Temp (°C)	44 – 47	32-33	42-44
Intel Air Temperature (°C)	64 – 65	47-48	65-69
Air Flow (cfm/m³/hr)	170/289	170/289	170/289
No. of Guns	1	1	1
Pan Speed (rpm)	Schlick 970	Schlick 970	Schlick 970
Atomization Air (psi/bar)	10/0.7	14/1.0	14/1.0
Pattern Air (psi/bar)	10/0.7	14/1.0	14/1.0
Coating WG (%w/w)	5	20	10

Results

Uncoated mini tabs showed consistency with excellent uniformity in weight, size, and tablet hardness, as shown in Table 3.

Table 3. Tablet Properties

Parameter	Value
Weight (mg)	8.11 ± 0.36
Thickness (mm)	2.84 ± 0.01
Hardness (kP)	3.1 ± 0.4

The enteric performance of Acryl-EZE II coated mini-tabs, as described by the acid uptake results, are shown in Figure 1, with tablet discoloration in Figures 2 and 3. The tablets before testing are shown in Figures 2a and 3a, respectively. Tablets coated with Acryl-EZE II provided excellent enteric protection in 0.1N HCl and pH 4.5 acetate buffer, as indicated by a low acid uptake value and no significant color change as shown by Figure 2b and 2c. When subjected to pH 5.0 acetate buffer, one of the tablets cracked and partially disintegrated, while the remaining tablets had extremely high acid uptake (79%) and significant discoloration as shown by Figure 2d. After application of the Acryl-EZE II top-coat, the enteric coated tablets exhibited enhanced enteric protection up to pH 5.0 and showed low acid uptake and no significant discoloration or disintegration as shown by Figure 3b-3d.

Figure 1. Acid Uptake of Acryl-EZE II ((a) Without Top-coat, (b) With Top-coat) Coated 3 mm Mini-Tabs in 0.1N HCl, pH 4.5 or 5.0 Acetate Buffer for 2 Hours

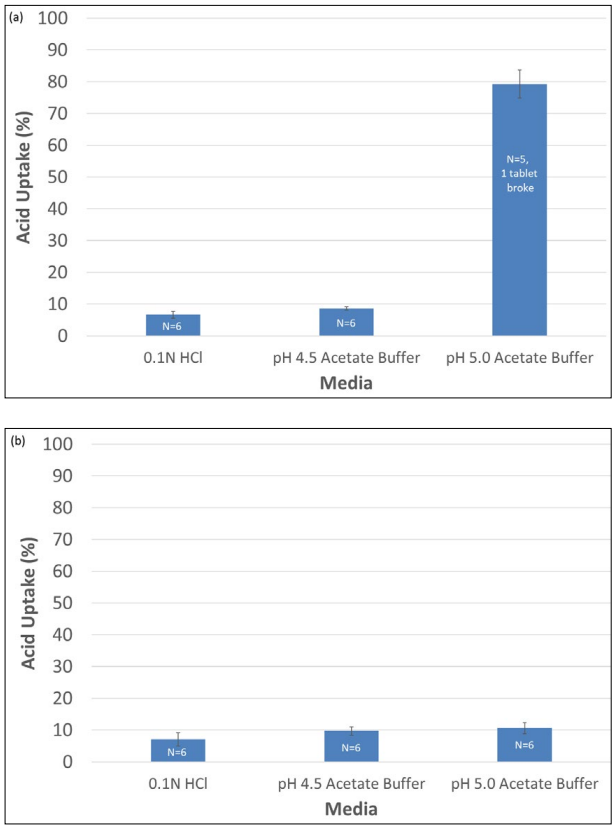


Figure 2. Acryl-EZE II Coated Tablets Without Top-coat: (a) Before Acid Uptake Test, (b) After Acid Uptake Test in 0.1N HCl, (c) After Acid Uptake Test in pH 4.5 Acetate Buffer, (d) After Acid Uptake Test in pH 5.0

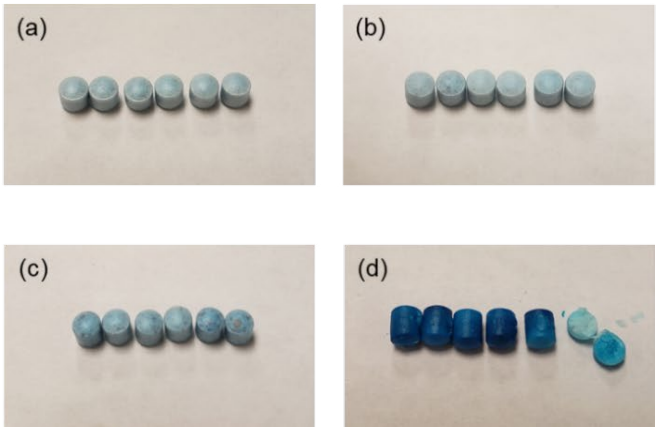
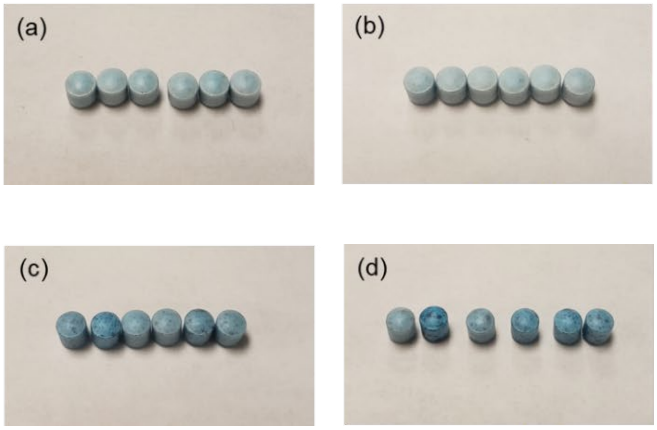


Figure 3. Acryl-EZE II Coated Tablets with Top-coat: (a) Before Acid Uptake Test, (b) After Acid Uptake Test in 0.1N HCl, (c) After Acid Uptake Test in pH 4.5 Acetate Buffer, (d) After Acid Uptake Test in pH 5.0



Conclusions

Acryl-EZE II, optimized high performance enteric coating, was used to coat 3 mm placebo mini-tabs and provided enteric protection across a range of pH media up to pH 5.0 acetate buffer, as shown by low acid uptake results and no significant tablet discoloration. On its own, the Acryl-EZE II enteric coating protected up to pH 4.5 acetate buffer. With the addition of the Acryl-EZE II top-coat, enteric protection extended to pH 5.0 acetate buffer. This makes Acryl-EZE II coatings an excellent choice for actives requiring protection from high pH conditions like those found in the stomach of patients who take proton pump inhibitor (PPI) drugs, or to protect highly sensitive biologic actives.

References

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2. Riis T., Bauer-Brandl A., Wagner T., Kranz H., pH-independent drug release of an extremely poorly soluble weakly acidic drug from multiparticulate extended-release formulations. Eur. J. Pharm/ Biopharm., 65 (2007) 78-84.

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