

Development of an Enteric Coating Process and Stability Evaluation of PCcaps®

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Introduction

A study to test a promising drug in animals is performed before reaching Clinical Trial stage. The pre-clinical studies are designed for pharmacokinetic, pharmacodynamic, and safety studies with rodents. To accommodate rodent dosing, a small size capsule specifically designed is utilized by filling either raw drug or binary blends with very limited formulation-development work. To support rodent studies, the acidic degradation and dyspeptic side effects associated with some compounds are overcome by enteric coating of the capsules. This work is an evaluation of the ability of commercially available enteric, aqueous film-coating systems to confer their enteric release properties on gelatin capsules which can support pre-clinical rodent studies.

Objectives

To develop a robust methacrylic acid co-polymer type C (Acryl-EZE®, Colorcon) and cellulose acetate phthalate (Aquacoat® CPD, FMC BioPolymer) enteric coating process for PCcaps® (Capsugel) and evaluate the compatibility/stability of the coated PCcaps®.

Methods

Capsule Coating

The PCcaps® and commercial Capsugel size 3 CS gelatin capsules were filled with anhydrous lactose, NF, DT (Kerry BioSciences) by hand filling and with a hand-held Feton® encapsulator (ChemiPharm), respectively. The Acryl-EZE® or Aquacoat® enteric coating was performed on a mixture of filled PCcaps® (50/batch) and size 3 capsules (0.5 L) in a LDCS 5 Hi-Coater® (Vector) fitted with a 1.3 L (11.5") partially perforated coating pan. PCcaps® were coated to a level of approximately 13 % weight gain for Acryl-EZE® and 8 % for Aquacoat®.

Table 1: Enteric Coating Process Parameters

Coating System	Acryl-EZE®	Aquacoat® CPD
Inlet Temperature (°C)	53-54	53-60
Exhaust Temperature (°C)	35-38	29-43
Atomizing Air Pressure (psi)	7	10
Air Volume (CFM)	27-29	31-42
Spray Rate (g/min)	1-5	1-4
Pan Speed (RPM)	10	10
Gun to Bed Distance (inches)	5-6	5-6

Scanning Electron Microscopy (SEM)

SEM (Hitachi S-800) images were obtained to assess how well the coating materials covered the junction between the capsule body and cap (Figure 1).

Stability Packaging and Storage

44 coated PCcaps® were added into 30cc white HDPE bottles before capping and induction sealing. Packaged PCcaps® were placed at 25°C/60% relative humidity (RH) [data available upon request] and 40°C/75% RH storage conditions for evaluation at initial, 2, 4, 8, and 12 week time points.

Weight Variation

The integrity of the coating was evaluated with respect to weight change by performing weight variation of the coated PCcaps® at each time point.

Disintegration Testing

The efficacy of the enteric coating was evaluated by performing USP <701> disintegration test for delayed-release (enteric-coated) tablets.

Capsule Fill Moisture Content

The moisture content values of the coated PCcaps® fill (anhydrous lactose) was obtained by using the TA Instruments Q500 TGA (Thermogravimetric Analyzer). The fill content was analyzed by TGA using the Hi-Res Dynamic method and ramped from ambient temperature to 850°C at 50°C/minute (Sensitivity 1.0 and Resolution 4.0).

Results

SEM images of the coated PCcaps® surfaces (Figure 1) reveal differences in coating texture and coverage at the body/cap junction. Acryl-EZE® enteric coat appeared to closely bridge the gap at the body/cap junction while Aquacoat® coated PCcaps® displayed a more prominent visible gap due to lesser coating quantity on the capsule.

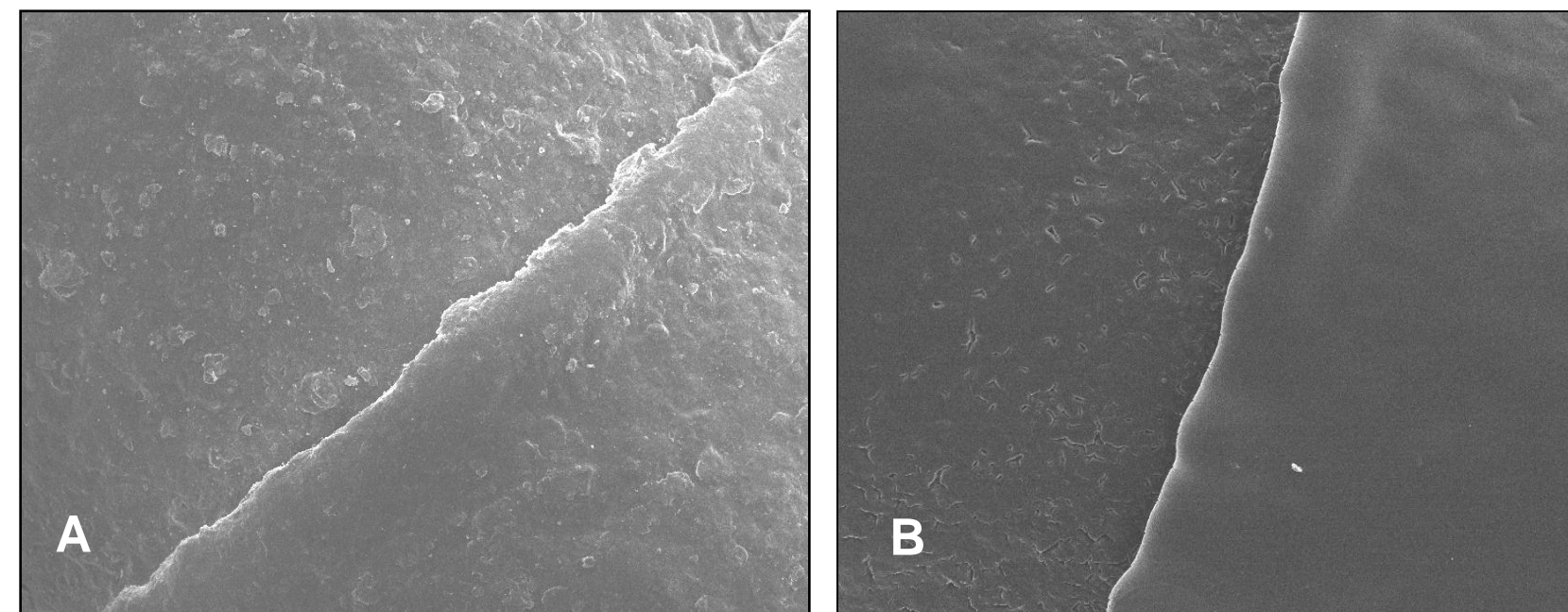


Figure 1: (A) PCcaps® coated with Acryl-EZE® (~13 % weight gain) (B) PCcaps® coated with Aquacoat® CPD (~8 % weight gain)

The weight variation data in Table 2 does not demonstrate change in weight ($\pm 3.0\%$) on stability at 40°C/75% RH storage condition (n=6).

Table 2: Weight Variation of 40°C/75% RH Storage Samples (mg)

Coating	Initial	2 weeks	4 weeks	8 weeks	12 weeks
Acryl-EZE®	27.1	27.3	27.6	27.4	27.8
Aquacoat®	26.3	26.7	26.6	26.5	26.1

Disintegration testing showed that Acryl-EZE® coating material (13 % weight gain) to be effective as enteric coating agent while the amount of Aquacoat® coated (8 % weight gain) to be not sufficient. Acryl-EZE® coating material kept the PCcaps® intact during disintegration testing in Simulated Gastric Fluid (SGF) and released in Simulated Intestinal Fluid (SIF) Test Solution. Table 3 below shows the disintegration times of the PCcaps® in SIF subsequent to 1 hour of disintegration testing in SGF (n=3).

Table 3: Disintegration Time of 40°C/75% RH Storage Samples in SIF (min:secs)

Coating	Initial	2 weeks	4 weeks	8 weeks	12 weeks
Acryl-EZE®	6:00	8:15	6:27	5:23	6:22
Aquacoat®	Capsules disintegrated in SGF				

The data in Table 4 below demonstrates that the PCcaps® fill weight loss was similar for both Acryl-EZE® and Aquacoat® coated PCcaps®. The capsule coating weight gain of Acryl-EZE® (13 % weight gain) and Aquacoat® (8 % weight gain) does not seem to play a role on the PCcaps® content moisture values (n=1).

Table 4: Moisture Loss of PCcaps® Content (% Weight Loss)

Coating	Initial	2 weeks	4 weeks	8 weeks	12 weeks
Acryl-EZE®	1.1	2.4	2.7	Not tested	4.0
Aquacoat®	1.1	2.5	3.0	Not tested	4.0

Conclusions

Development of a successful Acryl-EZE® coating process on PCcaps® that is robust, stable, and similar to enteric coating of tablets while Aquacoat® CPD should be tried at higher coating level to provide enteric properties.

References

1. Capsugel. "PCcaps®," Retrieved on September 27, 2010, from <http://www.capsugel.com/products/pccaps.php>
2. Colorcon. "Acryl-EZE®," Retrieved on September 27, 2010, from <http://www.colorcon.com/products/coatings/enteric-delayed-release/acryl-eze>
3. FMC BioPolymer. "Enteric Drug Delivery," Retrieved on September 27, 2010, from <http://www.fmcbiopolymer.com/Pharmaceutical/Applications/EntericDrugDelivery.aspx>