

Process Development, Compatibility, and Stability of Aqueous Acryl-EZE® and Sheffield™ Clear ENT Enteric Coat on Vcaps®



Balaji V. Kadri, Aran M. Johnson, Danica M. Cartwright, & Paul F. Skultety
Xcelience®, LLC. 5415 W. Laurel Street, Tampa, FL 33607, U.S.A.



Introduction

The formulation of drugs into capsules is often utilized in early phase development due to the relatively quicker formulation-development process. The bioavailability of the poorly soluble drugs can be significantly increased when formulated in a solubilized form in a capsule (i.e. liquid or semi-solid filled capsules). Acidic degradation and dyspeptic side effects associated with some compounds are overcome by enteric coating of the dosage form. This work is an evaluation of the ability of commercially available enteric, aqueous film-coating systems to confer their enteric release properties on hydroxypropyl methylcellulose (HPMC) capsules.

Objectives

To develop a robust methacrylic acid co-polymer type C (Acryl-EZE®, Colorcon) and Methacrylic acid/ethylacrylate (Sheffield™ Clear ENT, Sheffield) enteric coating process for Vcaps® and evaluate the compatibility/stability of the coated Vcaps®.

Methods

Capsule Coating

Commercial Capsugel Vcaps® (Hypromellose, HPMC) were filled with anhydrous lactose, NF (Sheffield™ Pharma Ingredients) using a hand-held Fetor® encapsulator (ChemiPharm). One liter of filled capsules were enteric coated with either Acryl-EZE® (Colorcon®) or Sheffield™ Clear ENT (Sheffield™ Pharma Ingredients) using a LDSC 5 Hi-Coater® (Vector Corporation) with a 1.3L (9.5") partially perforated coating pan. Capsules were coated to a target coating level of more than 10 % weight gain. Capsules coated at 75% of the target level were collected for evaluation.

Table 1: Enteric Coating Process Parameters

Coating System	Acryl-EZE®	Sheffield™
Inlet Temperature (°C)	55	56-60
Exhaust Temperature (°C)	35-37	41-42
Atomizing Air Pressure (psi)	30	30
Air Volume (CFM)	30-50	47-51
Spray Rate (g/min)	5-10	3.5-5.5
Pan Speed (RPM)	10-12	10-12
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

30 coated capsules were added into 100cc white HDPE bottles with a 1g silica-gel desiccant before capping and induction sealing. Packaged capsules were placed at 25°C/60% relative humidity (RH) [data not included due to limited poster space] and 40°C/75% RH storage conditions for evaluation at initial, 8, 12, and 16 week time points.

Weight Variation

The integrity of the coating was evaluated with respect to weight change by performing weight variation of the coated capsules 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

Initially and at each stability time-point the anhydrous lactose capsule fill of the coated capsules was assayed for water per USP <921> Water Determination method 1a (direct titration). For each coating material, water determinations were performed on the combined contents of three capsules from the 10% coating levels.

Results

SEM images of the coated capsule surfaces (Figure 1) reveal differences in coating texture and coverage at the body/cap junction. Sheffield™ Clear ENT coated capsules displayed a visible gap at the body/cap junction while the Acryl-EZE® enteric coat appeared to bridge this gap.

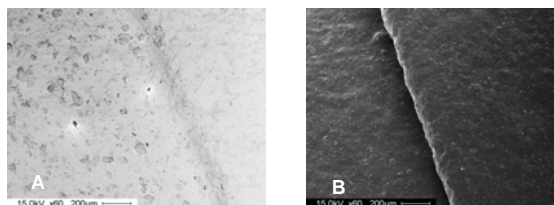


Figure 1: (A) Capsule coated with Acryl-EZE® (~10% weight gain)
(B) Capsule coated with Sheffield™ (~10% weight gain)

The weight variation data in Table 1 does not demonstrate change in weight on stability at 40°C/75% RH storage condition (n=10).

Table 1: Weight Variation of 40°C/75% RH Storage Samples (mg)

Coating	Initial	8 weeks	12 weeks	16 weeks
Acryl-EZE®	600.8	599.3	590.4	599.1
Sheffield™	604.4	616.9	611.2	610.6

Disintegration testing showed the two coating materials to be effective as enteric coating agents on the Vcaps®. Both coating materials kept the capsules intact during disintegration testing in SGF and released in USP Simulated Intestinal Fluid (SIF) Test Solution, which became longer on stability study and was through the domed ends of the capsules. Table 2 below shows the disintegration times of the capsules in SIF subsequent to 1 hour of disintegration testing in SGF (n=6).

Table 2: Disintegration Time of 40°C/75% RH Storage Sample in SIF (min:secs)

Coating	Initial	8 weeks	12 weeks	16 weeks
Acryl-EZE®	17:24	19:54	35:48	48:15
Sheffield™	17:52	18:24	18:24	52:30

The data in Table 3 below demonstrates that the capsule fill had no significant increase in moisture content during stability storage and supports that both coating materials provided approximately the same protection from gastric media at comparable coating levels (n=3).

Table 3: Moisture Content of Capsule Fill Material (% Weight)

Coating	Initial	8 weeks	12 weeks	16 weeks
Acryl-EZE®	1.2	1.2	1.0	1.8
Sheffield™	0.5	0.4	0.5	0.6

Conclusions

The results demonstrate that the enteric coating process developed for Vcaps® is robust, stable, and similar to enteric coating of tablets.

References

- Colorcon. "Acryl-EZE®." Retrieved on September 14, 2009, from <http://www.colorcon.com/products/coatings/enteric-delayed-release/acryl-eze/Product%20Overview>
- Sheffield. "Sheffield™ Coating System Clear ENT," Retrieved on October 02, 2009, from http://www.sheffield-products.com/index.php?option=com_mtree/task,listcats/cat_id,693/Itemid,91/#product