

# The Use of Acrylic Resins for Improved Aqueous Enteric Coating

Charles A. Signorino,\* Stephen Levine, Aaron Barkley, and Lou Forcellini



Recent technology improvements have made **acrylics the preferred system for the aqueous enteric coating of tablets.**

**Charles A. Signorino, PhD,** is the president of Emerson Resources, Inc., 600 Markley St., Norristown, PA 19401, tel. 610.279.7450, ext. 223, charlie@emersonresources.com.

**Stephen Levine** is a senior scientist, **Aaron Barkley** is a group leader, and **Lou Forcellini** is a manager of manufacturing, all at Emerson Resources, Inc.

\*To whom all correspondence should be addressed.

In the past few years, many published articles have detailed the developments in the enteric coating process (1). Significant progress has been made in the coating of both hard gelatin capsules and softgels (2–4), and some progress has been made in the coating of small particles such as beads and granules. In addition, improvement has been seen in the enteric coating systems for tablets. One example is the advances in applying colored latex enteric films.

In particular, there has been great interest in the enteric coating of aspirin (6, 7). The resins available for enteric coating have undergone some changes during the past five years. The current situation is as follows:

- cellulose acetate phthalate is still used and is applied from organic solvent and as an aqueous latex
- hydroxypropyl methylcellulose phthalate is still used and is applied from organic solvent or from an ammoniated aqueous solution
- polyvinyl acetate phthalate is still available, but the manufacturer of this resin is now aggressively promoting an acrylic system

- hydroxypropyl methylcellulose succinate acetate is promoted as a dispersible powder and a hot-melt resin
- shellac is useful as an ammoniated solution but releases at a high pH (usually at  $\text{pH} \geq 7.5$ )
- zein is no longer actively used for enteric coatings
- acrylics now are the system of choice and competition has made several suppliers available. Chemically similar alternate materials are available, but their equivalence must be tested.

### Acrylics are the system of choice

Historically, acrylic coatings have been unstable and have tended to agglomerate easily, making them difficult to use. Because of the improvements that have been made to acrylic systems and the techniques for applying them, however, acrylics currently are the most widely used resins for aqueous enteric coatings. The resins are now more stable, and they can now be used with glycerides

Table I: Tablet cores used in the study.

Dosage (mg)	Tablet weight (mg)	Hardness (Kp)	Friability
81	175.5	6–10	$\leq 0.4\%$
325	390.0	8–12	$\leq 0.4\%$
500	600.0	9–13	$\leq 0.4\%$

as detackifiers instead of talc, thereby making their application much easier. In addition, the ability to add color to the enteric coating has reduced the complexity of the coating process. Because color can now be incorporated into the enteric system, a final color layer over a clear enteric film is no longer required.

### A study using acrylic enteric emulsions

The following study of the use of acrylic enteric emulsions in aspirin provides a clear indication of the improvements that have been made in these systems.

**Tablet cores.** Three commonly marketed dosages of aspirin tablets (81, 325, and 500 mg) were compacted as listed in Table I.

**Aqueous coating formulations and**

Table II: HPMC subcoat formulation.

Material description	Function	Supplier	Solids	% Solution	% Film
Spectrablend*					
50857	Film/plasticizer	Sensient	96.0%	12.50	100.00
Deionized water, USP	Medium	Emerson	0.0%	87.50	0.00
Total seal coat solution	Seal coat	Emerson	12.0%	100.00	100.00

\*Spectrablend (Sensient Technologies Co., South Plainfield, NJ) is a 96% solids granulation of HPMC and includes a plasticizer, which in the case of 50857 is triethyl citrate at 10% of HPMC.

**Table III: Acrylic enteric topcoat formulation for 81-mg aspirin.**

Material description	Function	Supplier	% Solids	% Suspension	% Film
Eudragit L30D55*	Film formation	Degussa	30.0	49.22	73.66
Plasacryl†	Detackifier/plasticizer	Emerson	20.0	4.91	4.90
Triethyl citrate, PG, NF	Plasticizer	Morflex	100.0	1.47	7.33
Spectraspray‡ Yellow SS-1243	Color	Sensient	41.0	6.90	14.11
Deionized water, USP	Spray medium	Emerson	0.0	37.50	0.00
Total enteric suspension	Enteric coat	Emerson	20.0	100.00	100.00

\* Eudragit L30D55 (Degussa, Röhm America, Piscataway, NJ) is a copolymer dispersion of methacrylic acid and ethyl acrylate, at 30% solids. This film solubilizes at a pH >5.5.

† Plasacryl (Emerson Resources, Norristown, PA) is 20% solids emulsion, which functions as a detackifier and as a plasticizer. Plasacryl is specially formulated for use in aqueous acrylic coating suspensions.

‡ Spectraspray (Sensient Technologies Co.) is a pigment disperser. SS-1243 is specifically designed for compatibility with acrylic emulsions.

procedures for enteric aspirin. An HPMC subcoat formulation for 81-, 325-, and 500-mg aspirin tablets, as listed in Table II, was applied as a seal coat to enhance the performance of the aspirin tablets in accelerated stability testing.

**Subcoat procedure for all tablets.** The first step in the subcoat procedure for all three dosages of aspirin was to mix Spectrablend into water until a solution was formed. Next, a 15-in. side-vented pan was charged with 2-kg aspirin cores and sprayed to 1.5% weight gain of solution at approximately 20 g/min, with exhaust temperature at 45–50 °C, process air at 250 cfm, atomizing air at 40 psi, and at a speed of 12–15 rpm.

**Acrylic enteric topcoat formulation for 81-mg aspirin.** The acrylic enteric topcoat formulation for 81-mg aspirin is listed in Table III.

**Enteric topcoat procedure for 81-mg aspirin.** The following procedure was used to prepare the topcoat for the 81-mg tablets:

- Mix Eudragit (screened), Plasacryl (screened), and triethyl citrate in 80% of the additional water for 60 min.
- Combine Spectraspray with the remaining 20% of the additional water.
- Combine the two suspensions and mix for 10 min; rescreen the resulting suspension and continue gentle mixing throughout the coating run.

Table IV: Acrylic enteric topcoat formulation for 325- and 500-mg aspirin.

Material description	Function	Supplier	% Solids	% Suspension	% Film
Eudragit L30D55	Film formation	Degussa	30.0	49.22	73.78
Plasacryl	Detackifier/ plasticizer	Emerson	20.0	4.91	4.91
Triethyl citrate, PG, NF	Plasticizer	Morflex	100.0	1.47	7.35
Spectraspray Orange D-489	Color	Sensient	40.5	6.90	13.96
Deionized water, USP	Spray medium	Emerson	0.0	37.50	0.00
Total enteric suspension	Enteric coat	Emerson	20.0	100.00	100.00

Table V: Analytical testing results for 81-mg aspirin.

Stability test conditions	Desiccant	Time (months)	Potency %	Free SA %	Diss.† acid %	Diss.† buffer %
RT*	Without	0 (initial)	98.3	0.1	0.4	100
RT	With	3	97.3	0.1	1.0	104
RT	Without	3	97.3	0.2	0.0	102
Accelerated	With	1	97.6	0.3	0.7	100
Accelerated	With	3	98.4	0.7	0.0	103
Accelerated	Without	1	98.7	0.5	0.9	97
Accelerated	Without	3	96.9	1.7	1.0	103

\* room temperature

† dissolution

- Charge a 15-in. side-vented pan with 2030 g of subcoated 81-mg aspirin tablets and spray to 9% weight gain with a suspension at 20–25 g/min, with inlet air at ~55 °C at 250 cfm, exhaust air at 35–40 °C, atomizing air at 30 psi, and a pan speed of 15–18 rpm.

Enteric topcoat formulation for 325- and 500-mg aspirin. The topcoat formulation for the 325- and 500-mg aspirin tablets is listed in Table IV.

Enteric topcoat procedure for 325- and 500-mg aspirin. The following

procedure was used to apply the enteric topcoat to the 325- and 500-mg tablets:

- Follow the topcoat suspension preparation procedure used for the 81-mg aspirin.
- Charge a 15-in. side-vented pan with 2030 g of subcoated 325-mg aspirin tablets and spray to a 8% weight gain of suspension, as indicated above for the 81-mg aspirin, but with the pan speed at 15 rpm.
- Charge a 15-in. side-vented pan with 2030 g of subcoated 500-mg

Table VI: Analytical testing results for 325-mg aspirin.

Stability test conditions	Desiccant	Time (months)	Potency %	Free SA %	Diss. acid %	Diss. buffer %
RT	Without	0 (initial)	99.1	0.1	0.3	98.0
RT	With	3	101.2	0.1	1.0	104
RT	Without	3	99.6	0.1	0.0	103
Accelerated	With	1	99.3	0.2	1.3	99
Accelerated	With	3	102.7	0.6	1.0	103
Accelerated	Without	1	101.7	0.2	0.9	100
Accelerated	Without	3	102.4	0.5	1.0	102

RT is room temperature

Table VII: Analytical testing results for 500-mg aspirin.

Stability test conditions	Desiccant	Time (months)	Potency %	Free SA %	Diss. acid %	Diss. Buffer %
RT	Without	0 (initial)	98.5	0.04	0.3	94
RT	With	3	99.3	0.1	1.0	99
RT	Without	3	101.8	0.1	1.0	97
Accelerated	With	1	97.4	0.1	1.6	95
Accelerated	With	3	101.7	0.2	1.0	99
Accelerated	Without	1	98.5	0.2	1.1	98
Accelerated	Without	3	98.1	0.8	1.0	100

RT is room temperature

aspirin tablets; spray to 7% weight gain, as indicated in the coating procedure for the 325-mg aspirin.

The application of the subcoats and topcoats to the tablets of all three sizes was performed using a Compu-Lab Accela-Cota tablet coater (Thomas Engineering Inc., Hoffman Estates, IL) equipped with a 15-in. side-vented pan and using a single  $\frac{1}{4}$  JAU spray gun (Spraying Systems Co, Wheaton, IL) with a SS 40100 liquid cap.

### Stability study setup

Samples of the three dosages of enteric aspirin tablets were subjected to a stability study. Samples were taken monthly for analytical testing.

**Bottling.** Within seven days after coating, tablets of each dosage were transferred to high-density polyethylene-sealed bottles, with and without desiccants. Tests were conducted under room temperature (RT) and accelerated stability conditions, and the bottles were designated as time initial, one month, and three months.

**Storage.** The samples designed for RT storage were kept at  $25 \pm 3^\circ\text{C}$  and 40% relative humidity (RH). The samples in the accelerated stability study were kept at  $40^\circ\text{C}$  and 75% RH. Bottles were kept sealed until testing. The RT samples were pulled from stability and tested

three months after the date of packaging. The accelerated stability samples were pulled from stability and tested one month and three months after the date of packaging. One Time 0 (initial) sample was tested.

### Analytical testing

All testing was conducted within seven days of sample pulls. Samples were tested for potency, free salicylic acid (SA), and USP enteric coated dissolution. Testing was performed by Boston Analytical Inc. (Salem, NH).

**Aspirin potency.** Tablets were tested by HPLC assay according to the USP monograph for delayed-release aspirin tablets and reported in terms of percentage of label claim. A passing result was 95.0–105.0% of label claim.

**Limit of free SA.** Using USP salicylic acid RS, USP assay results were obtained in terms of percentage of free SA. A passing result was  $\leq 3.0\%$  free SA.

**USP enteric coated dissolution.** With the use of USP test 724, method B, six tablets of each sample were tested for enteric dissolution drug release as specified in the USP monograph for delayed-release aspirin tablets. A passing result for the in-gastric (acid) portion of the test is  $\leq 10\%$  dissolved. A passing result for the intestinal (buffer) portion of the test is  $\geq 75\%$  dissolved.

### Analytical results

The analytical testing results for 81-325-, and 500-mg aspirin are listed in Tables V, VI, and VII, respectively. The analytical results for all aspirin

tablets of all three dosages were passing results.

### Conclusion.

The analytical testing results for all three dosage forms (81-, 325-, and 500-mg aspirin), including both those stored at room temperature and those stored under accelerated stability conditions, with and without desiccant, were within the specified criteria for passing results. The positive results of these tests demonstrate the advances that have been made in acrylic polymers for aqueous enteric coating of tablets.

### References.

1. C.A. Signorino, "Aqueous Enteric Coating," *Pharm. Technol. Tableting & Granulation Yearbook*, 1999.
2. L.A. Felton and J.W. McGinity, "Enteric Film Coating of Soft Gelatin Capsules," *Drug Delivery Technol.* **3** (6), 34–39 (2003).
3. K. Thoma and K. Bechtold, "Enteric Coated Hard Gelatin Capsules," *Cap-sugel Technical Bulletin*, pp. 1–16 (1986).
4. R. Pissinati and P. Oliviera, "Enteric Coating Soft Gelatin Capsules by Spouted Bed," *Eur. J. Pharm. Biopharm.* **55**, 313–321 (2003).
5. K. Thoma and K. Bechtold, "Influence of Aqueous Coatings on the Stability of Enteric Coated Pellets and Tablets," *Eur. J. Pharm. Biopharm.* **47**, 39–50 (1999).
6. C.R. Cunningham and K.A. Fegley, "One-Step Aqueous Enteric Coating Systems: Scale-up Evaluation," *Pharm. Technol.* **25** (11), 36–44, (2001).
7. J. Yuan, N.M. Clipse, and S.H. Wu, "The Effects of Alternating Combinations of an Enteric Coating and HPMC as Inner and Outer Coatings on the Performance of Coated Aspirin Tablets," *Pharm. Technol.* **27** (11), 70–82 (2003). **PT**