Evaluation of Aqueous Enteric Coating Materials for a Colon Delivery Drug

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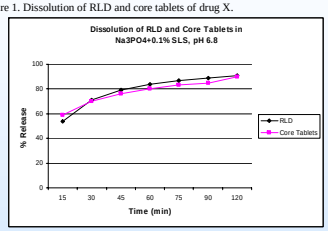
Abstract (# W4072)

Dissolution profile of core tablets of drug X complies with RLD, a delayed-release tablet with multiple coatings for colon delivery. To achieve the best colonic targeting of drug X, different aqueous enteric coating materials were screened by dissolution study to evaluate their bio-performance. Core tablets of drug X were used as the coating substrate. Enteric coating materials of Eudragit®FS30D (Evonik), Eudragit®L-100 (Evonik), Acryl-EZE®93O (Colorcon), Acryl-EZE®93F (Colorcon), and a mixture of Surelease®, Opadry® and Acryl-EZE®93O (Colorcon) were applied separately. Target weight gains from 7% to 20% (w/w). Both Eudragit® and Acryl-EZE® systems showed good acid resistance in 0.1 N HCl. In buffer stage at pH 6.8, similarity factor (F2) for Eudragit®FS30D, Eudragit®L-100, Acryl-EZE®93O, Acryl-EZE®93F and the mixture of Surelease®, Opadry® and Acryl-EZE®93O are 51, 60, 59, 60, and 55, respectively. However, in acetate buffer at pH 4.5, Acryl-EZE®93O containing systems could not protect tablets from disintegrating. Since Eudragit® requires the addition of plasticizer and more preparation steps than Acryl-EZE®, Acryl-EZE®93F was chosen for sufficient enteric protection. Core tablets of drug X were successfully coated with Acryl-EZE®93F to achieve the desired colonic performance.

Purpose

Dissolution profile of core tablets of drug X complies with RLD, a delayed-release tablet with multiple coatings for colon delivery at approximately pH 7 (Figure. 1). Multiple coatings of RLD include enteric coating and sugar coating, which is not practical for nowadays in-house practice. Furthermore, it has been found that there is a direct relationship between cumulative drug X dissolution and it's efficacy. Therefore, different aqueous enteric coating materials were screened by each dissolution profile to evaluate their bio-performance, and ultimately one enteric coating material would be selected and optimized for the best colonic targeting of drug X.

Figure 1. Dissolution of RLD and core tablets of drug X.



Methods

•Coating trials were conducted in an O'Hara Lab Coater IIX equipped with a 15" pan. Core tablets (180 mg/tablet) of drug X were used as the coating substrate. Enteric coating materials of Eudragit®FS30D (Evonik), Eudragit®L-100 (Evonik), Acryl-EZE®93O (Colorcon), Acryl-EZE®93F (Colorcon), and a mixture of Surelease®, Opadry® and Acryl-EZE®93O (Colorcon) were applied separately. Batch size was about 2 kg for each trial and target weight gains from 7% to 20% (w/w) (Table 1).

•Dissolution study of the enteric coated tablets and RLD were performed per current USP <711> for delayed-release dosage forms. Tablets were put in 1000 mL of 0.1 N HCl at 37ºC with apparatus II (paddle) at 75 rpm for 2 hours, then transferred to acetate buffer or phosphate buffer under the same condition. In phosphate buffer solution (0.2 M Sodium Phosphate with 0.1% SLS) at pH 6.8, 10 mL aliquots were taken at every 15 minutes and were analyzed by HPLC to determine %Release of drug X.

•Dissolution analysis was conducted by HPLC method with UV detector at 265 nm. A Phenomenex® C18 column (3.9×300 mm, 10 μm) with 2.0 mL/min flow rate and 50 μL injection volume was applied.

Table 1. Coating trials with different enteric coating materials.

Aqueous Enteric Coating Materials	Batch Size	Core Tablet Weight	Coating Weight Gain (w/w)
Eudragit®FS30D	2 Kg	180 mg	9%*
Eudragit®L-100			20%*
Acryl-EZE®93O			7%*
Acryl-EZE®93F			10% - 20%**
Surelease®+Opadry®+Acryl-EZE®93O			15%*

*Coating trials were conducted by manufactures, weight gain is suggested by manufactures.

**Coating was performed in-house, weight gain below 10% could not protect tablets from acid.

Results

1. Dissolution of Different Enteric Coated Tablets

Figure 2. Dissolution comparison of RLD and different enteric coated tablets.

	% Release					
Time (min)	RLD	Eudragit®FS30D	Eudragit®L-100	Acryl-EZE®93O	Acryl-EZE®93F	Surelease®+Opadry®+ Acryl-EZE®93O
15	44	43	56	56	50	46
30	68	58	68	67	64	60
45	77	67	74	73	71	68
60	83	72	78	78	76	74
75	86	76	81	81	79	78
90	89	79	83	83	81	80
F2		52	60	59	60	55

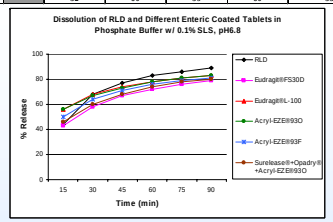


Table 2. Dissolution properties of different enteric coating materials in multi-pH dissolution medium.

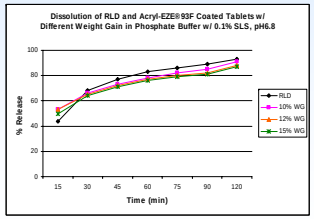
Aqueous Enteric Coating Materials	Resistance at pH 1.2	Protection at pH 4.5	Disintegration at pH 6.8
Eudragit®FS30D	X	X	X
Eudragit®L-100	X	X	X
Acryl-EZE®93O	X		X
Acryl-EZE®93F	X	X	X
Surelease®+Opadry®+Acryl-EZE®93O	X		X

•Both Eudragit® and Acryl-EZE® systems showed good acid resistance in 0.1 N HCl. However, in acetate buffer at pH 4.5, Acryl-EZE®93O containing systems could not protect tablets from disintegrating (Table 2). Since Eudragit® requires the addition of plasticizer and more preparation steps than Acryl-EZE®, Acryl-EZE®93F was chosen for sufficient enteric protection.

2. Dissolution of Acryl-EZE®93F Coated Tablets with Different Weight Gain

Figure 3. Dissolution comparison of RLD and Acryl-EZE®93F coated tablets w/ different weight gain (WG).

	% Release			
		Acryl-EZE®93F		
Time (min)	RLD	10% WG	12% WG	15% WG
15	44	53	53	50
30	68	66	65	64
45	77	73	72	71
60	83	78	77	76
75	86	82	80	79
90	89	85	82	81
120	93	91	88	87
F2		63	60	60

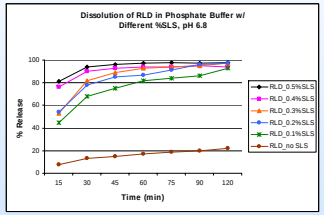


•Acryl-EZE®93F coated tablets with different weight gain showed similar dissolution profile, indicating that coating thickness is not the determinant factor to affect dissolution once it reaches certain weight gain. For better coating efficiency, 12% was selected as the target weight gain.

3. Dissolution of Acryl-EZE®93F Coated Tablets in Phosphate Buffer with Different %SLS

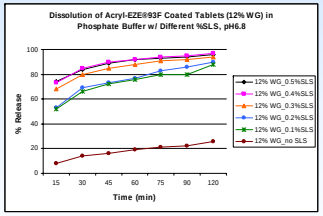
Figure 4. Dissolution comparison of RLD and Acryl-EZE®93F coated tablets (12% weight gain) in phosphate buffer w/ different %SLS.

	% Release of RLD					
Time (min)	no SLS	0.1% SLS	0.2% SLS	0.3% SLS	0.4% SLS	0.5% SLS
15	8	45	54	53	76	81
30	13	68	78	82	90	94
45	15	75	85	89	93	96
60	17	82	87	93	94	97
75	19	84	91	94	94	98
90	20	86	96	95	95	97
120	22	93	97	97	94	98



	% Release of Acryl-EZE®93F (12% WG)					
Time (min)	no SLS	0.1% SLS	0.2% SLS	0.3% SLS	0.4% SLS	0.5% SLS
15	8	52	53	68	73	74
30	14	66	69	80	85	84
45	16	72	73	85	90	89
60	19	76	77	88	92	92
75	21	80	83	91	94	93
90	22	80	86	92	95	94
120	26	88	90	94	97	96
F2	90	67	52	52	69*	53*

*Only 2 numbers are included in calculation (N =2).

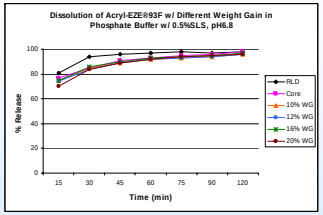


•Dissolution comparison between RLD and test product in phosphate buffer with different %SLS demonstrates that phosphate buffer with 0.1% SLS is a discriminatory condition for future comparative dissolution study.

4. Dissolution of Acryl-EZE®93F Coated Tablets with Different Weight Gain in Phosphate Buffer with 0.5% SLS

Figure 5. Dissolution comparison of RLD and Acryl-EZE®93F coated tablets w/ different weight gain in phosphate buffer w/ 0.5% SLS.

	% Release in Phosphate Buffer w/ 0.5% SLS, pH 6.8					
			Acryl-EZE®93F			
Time (min)	RLD	Core	10% WG	12% WG	16% WG	20% WG
15	81	77	75	74	75	70
30	94	85	85	84	86	84
45	96	91	89	89	90	89
60	97	93	92	92	93	92
75	98	95	93	93	94	94
90	97	96	94	94	95	95
120	98	98	96	96	97	96



•Phosphate buffer with 0.5% SLS could be used as test method to satisfy the dissolution specification (NLT 75% (Q) in 45 minutes) for Acryl-EZE®93F coated tablets with different weight gain.

Conclusion

Core tablets of drug X were successfully coated with Acryl-EZE®93F to achieve the desired colonic performance.

References

USP 32 – <711> Dissolution.

Booth # 2260