Formulation of the Racecadotril Capsules (100mg), Method Validation and Stability Studies.

Wajeeha Ishtiyaq[1,3], Arslan Tariq[2], Nasir Abbas[1], Kanwal Ashiq[4], Mayyda Asif Bajwa[4]*
[1]Department of Pharmaceutics, University College of Pharmacy, University of the Punjab Lahore, Pakistan.
[2]Drug Regulatory Authority of Pakistan, Islamabad, Pakistan.
[3]DHQ Hospital Kallar Syedan, Rawalpindi, Pakistan.
[4]Faculty of Pharmaceutical Sciences Superior College, Superior University Lahore, Pakistan.
Corresponding author: Kanwal Ashiq kanwal.ashiq@superior.edu.pk

ABSTRACT
Product characterization is aimed at identifying attributes that are critical for the quality of a drug product. Such are design, analytical method validation, and stability studies strengthening the product development data. Undertaken, Racecadotril 100mg Capsules for diarrheal treatment entails the entire development study. Six formulations of Racecadotril 100mg Capsules were prepared with different excipients at varied concentrations. Amongst all formulations, F6 was the best fit having a comparatively good dissolution profile with 76.9% release in 60 minutes. HPLC system was suitable as %RSD was 0.619147% that is within the acceptance criteria. Other parameters like specificity, accuracy and recovery, precision, quantitation limit, detection limit, range, linearity, and robustness laid within the acceptance criteria. The percent degradation of Racecadotril after photolytic (sunlight for 6 hr.), oxidative (3% H2O2), acidic and basic stress was found to be 6.5%, 5.8%, 11.4%, and 28.4%, respectively. The product remains unchanged after thermal stress. F6 was marked successful amongst all with HPLC method validation. Accelerated stability studies and forced degradation studies enforced that the F6 formulation of Racecadotril 100mg Capsule is stable while the model-independent approach comprising of similarity and difference factors confirmed that the undertaken product is comparable with the marketed brand.
Keywords: Racecadotril, Anti-diarrheal, HPLC, Method Validation, ICH Q2R, Stability Indicating Method, Accelerated Stability Studies.

INTRODUCTION

According to several guidelines, concomitant use of Racecadotril with oral rehydration solution is recommended for the treatment of acute diarrhea in children. Racecadotril has greater tolerability than Loperamide in patients with acute diarrhea. Maximum absorption occurs when drug is administered orally at different doses i.e 30 mg, 100 mg and 300 mg and *C*max is achieved within 1 hour. According to BCS, Racecadotril belongs to Class-II drug (high permeability ,low solubility). The study is aimed to design, characterize a stable capsule solid dosage form of Racecadotril. Further, stability testing, HPLC method validation and comparative dissolution testing for Racecadotril 100mg Capsules were also performed.

MATERIAL AND METHODS

HPLC method was validated on analytical parameters recommended by ICH Q2R guidelines. Forced degradation studies were performed as per Stability Indicating Method (SIM) under various conditions. Accelerated stability studies were performed and kept for 6 months. The dissolution profile of the stable formulation was compared with the innovator brand.

RESULTS AND DISCUSSION

Among six formulations of Racecadotril 100mg Capsule, F6 was the best fit having comparatively good dissolution profile with 76.9% release in 60 minutes. The HPLC system was suitable as %RSD was 0.619147% which is within the acceptance criteria. Furthermore, analytical parameters including specificity, accuracy and recovery, precision, quantitation limit, detection limit, range, linearity and robustness lies within the acceptance criteria. The percent degradation of Racecadotril after photolytic (sunlight for 6 hr.), oxidative (3% H_2O_2), acidic (0.1N HCl) and basic (0.1N NaOH) stress was found to be 6.5%, 5.8%, 11.4% and 28.4%, respectively. While the product remain unchanged after thermal stress

Table 1. Composition of different Formulations of Racecadotril 100mg capsules

Sr no	Ingredients	F1	F 2	F3	F4	F5	F6	Role of ingredient
		mg	Mg	mg	Mg	mg	mg	
1	Racecadotril	100	100	100	100	100	100	Active
2	Maize Starch	15		10			30	Lubricant Disintegrant
	Stearic acid	2	2	1				Lubricant
3	Mg Stearate				5	5	1	Lubricant
4	Talcum powder	3	3	5				Glidant
5	Colloidal silicon dioxide	0.5			3	1	0.5	Glidant
6	Lactose Monohydrate	50	50		50	45	66.5	Diluent
7	Microcrystalline cellulose PH 102	31.5	30	75				Diluent
8	Mannitol					10		Diluent
9	Methyl cellulose				45	40		Disintegrant
10	Crosscarmelose sodium		15	10				Disintegrant
	Total fill weight per capsule	200	200	200	200	200	200	

Table 2. System suitability test (SST).

Reference standard	Peak Area (milli volt/ml)	Mean Peak Area	S.D.*	R.S.D. (%)**
01	11243686			
02	11097937			
03	11172360	11204623	69373	0.619147
04	11242053			
05	11267079			

*S.D., Standard Deviation; **R.S.D. (%), Percent Relative Standard Deviation

Table 3. Accuracy and recovery of Racecadotril HPLC assay at 50%, 100% and 150% standards.

	Concentration (mg/mL)					
	At 50 percent		At 100 percent		At 150 percent	
Replicates	Percent assay	Conc. Recovered	Percent assay	Conc. Recovered	Percent assay	Conc. Recovered
1.	51.3	0.2052	101.0	0.404	151.9	0.6076
2.	50.8	0.2032	101.1	0.4044	151.4	0.6056
3.	51.0	0.2040	101.8	0.4072	151.1	0.6044
Average	51.033	0.204	101.300	0.405	151.467	0.606
SD*	0.252	0.001	0.436	0.002	0.404	0.002
RSD** (%)	0.493	0.493	0.430	0.430	0.267	0.267

*SD, Standard Deviation; **RSD, Relative Standard Deviation

Table 4 Results of linearity at different concentration

Sr. No.	Concentration (mg/mL)	Area (millivolt/min)
1.	0.1	2820753
2.	0.2	5588404
3.	0.3	8332772
4.	0.4	11088989
5.	0.5	14168943
6.	0.6	16805884
7.	0.7	19779778

Table 5. Results of robustness at different test conditions

Test Conditions		Sample	Conc. (%)	Average	SD	RSD%
Change in mobile phase ratio	Buffer : Acetonitrile, 50: 50	1	100.8			
	Buffer : Acetonitrile, 60: 40	2	101.3			
Change in pH	2.3	3	101.1	100.66	0.476	0.4729
	2.6	4	100.1			
Change in injection rate (ml/minute)	1.5	5	100.4			
	2	6	100.3			

SD, standard deviation; RSD%, percent relative standard deviation

Table 6 Limit of detection (LOD) and limit of quantitation (LOQ).

Sr. No.	Conc.(mg/mL)	Area (mv/min)	Avg.	S.D.	Slope	SD/Slope	LOD (mg)	LOQ (mg)
1	0.1	2820753						
2	0.2	5588404						
3	0.3	8332772						
4	0.4	11088989	11226503	6107145	30000000	0.20357151	0.610715	2.035715
5	0.5	14168943						
6	0.6	16805884						
7	0.7	19779778						

Conc., Concentration; mg, milligram; mL, milli liter; mv, milli volt; Avg., average; S.D., Standard Deviation; LOD, limit of detection; LOQ, limit of quantitation.

Table 7 Results of Repeatability and intermediate precision of Racecadotril HPLC Assay

Sample	Concentration % (At same conditions)	Concentration % (At same conditions, different analyst)
1	101.1	100.8
2	100.4	101.3
3	101.3	100.2
4	101.0	101.1
5	100.8	100.3
6	101.8	100.4
Average	101.07	100.68
SD	0.472	0.454
RSD%	0.4669%	0.4504%

SD, standard deviation; RSD%, percent relative standard deviation

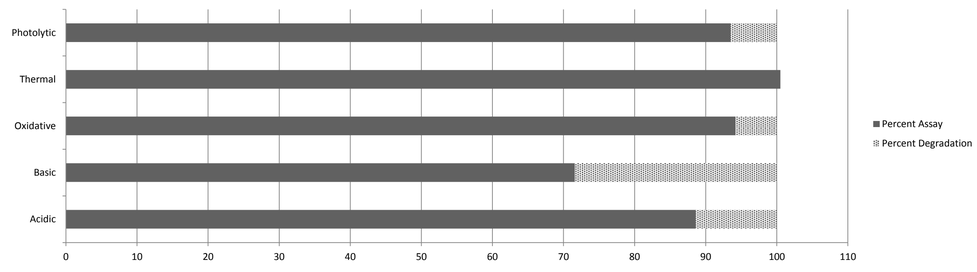

Figure 1. Forced degradation study of Racecadotril capsule 100mg.

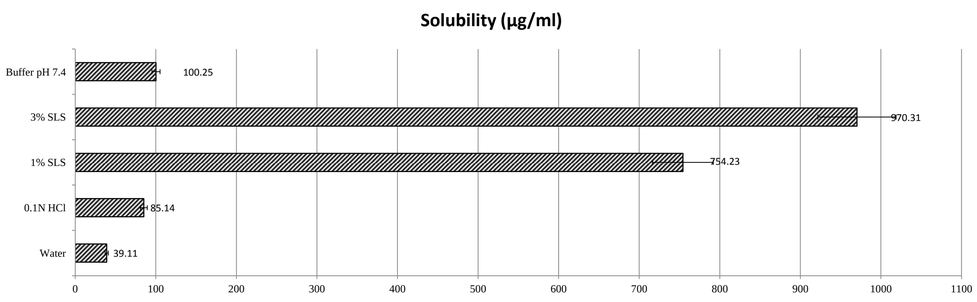

Figure 2. Graphical representation of solubility trend of Racecadotril in different solvent

CONCLUSIONS

F6 was marked successful amongst all with HPLC method validation. Accelerated stability studies and forced degradation studies enforced that the F6 formulation of Racecadotril 100mg Capsule is stable.

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