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RESEARCH ARTICLE

Stability Indicating HPLC Method for Estimation of Palonosetron Hydrochloride in Tablet Dosage Form

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ABSTRACT

To develop precise, accurate and reproducible stability indicating HPLC method for determination of Palonosetron hydrochloride in its tablet dosage form. Stability indicating HPLC method was developed using BDS Hypersil C8 column (250 x 4.6mm, 5µm) with ACN: Water (70:30) as mobile phase with flow rate was 1.0ml/min, injection volume was 20µl and detection wavelength 242nm. Retention time of Palonosetron hydrochloride was found to be 4.387 min. Palonosetron hydrochloride was found to degrade significantly under Acidic, Alkaline, Neutral and Oxidative conditions and comparatively stable under photolytic condition. The proposed stability indicating HPLC method can be successfully employed in estimation of tablet dosage form in regular QC and stability analysis.

KEYWORDS

Palonosetron Hydrochloride, Stability Studies, HPLC, Forced Degradation

INTRODUCTION

Palonosetron hydrochloride is an antiemetic and antinauseant agent. Palonosetron hydrochloride is used in the prevention and treatment of chemotherapy-induced nausea and vomiting. Palonosetron is a 5-HT3 receptor antagonist with a strong binding affinity for this receptor and little or no affinity for other receptors.[1] Chemically, Palonosetron hydrochloride is: (3aS)-2-(3S)-1-Azabicyclo[2.2.2]oct-3-yl-2,3,3a,4,5,6-hexahydro-1H-benz[de]isoquinolin-1-one mono hydrochloride. The empirical formula is $C_{19}H_{24}N_2O$ HCl, with a molecular weight of 332.87gm/mol. Palonosetron hydrochloride is a white to off-white crystalline powder. It is freely soluble in water, soluble in propylene glycol, and slightly soluble in ethanol and 2-propanol.[2,3] Palonosetron hydrochloride exists as a single isomer and has the following structural formula:

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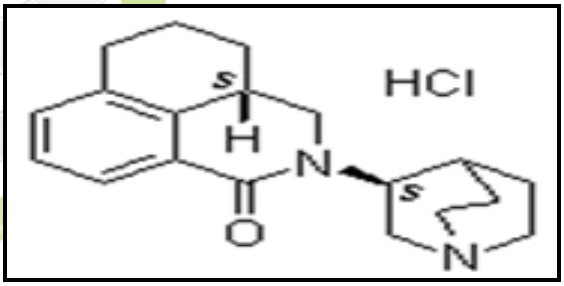

Figure 1: Structure of Palonosetron Hydrochloride

Stability Studies

A Stability Indicating Assay Method (SIAM) is a "Quantitative analytical procedure used to detect a decrease in the amount of the active pharmaceutical ingredient (API) present due to the degradation[4]."

Purpose of Stability Studies

- SIAM is developed routinely by stressing the API under conditions exceeding those normally used for accelerated stability testing.

- In addition to demonstrating specificity in SIAM, stress testing, also referred to as forced degradation, also can be used to provide information about degradation pathways and products that could form during storage and helps to facilitate formulation development, manufacturing, and packaging.
- Stressing the API in both solutions and in solid-state form generates the sample that contains the products most likely to form under most realistic storage conditions, which is in turn used to develop the SIAM.
- In simplest terms, the goal of the SIAM is to obtain baseline resolution of all the resulting products (the API and all the degradation products) with no co-elutions.
- Generally, the goal of these studies is to degrade the API 5-10 %. Any more than this and relevant compounds can be destroyed, or irrelevant degradation product produced.[5]

MATERIAL AND METHODS

Instruments

Agilent technologies 1200 infinity series HPLC system with PDA detector. BDS Hypersil C8 (250×4.6, 5µm particle size), Sonicator of Digital ultrasonic cleaner (LMUC series LABMAN), Analytical balance of Libror AEU-210 (Shimadzu).

Reagents

Palonosetron hydrochloride API was supplied by Intas Pharmaceutical Pvt. Ltd, Ahemdabad. Acetonitrile of HPLC grade was purchased from E. Merck (India) Ltd., Mumbai. Hydrochloric acid, Sodium hydroxide, Hydrogen peroxide (50%) of AR grade was obtained also from E. Merck (India) Ltd., Mumbai. EMEOD tablets (Containing 0.5mg Palonosetron hydrochloride) were procured from local market.

HPLC Conditions

A chromatographic separation of drug was achieved using BDS Hypersil, 4.6 × 250mm, 5µm C_8 column with Mobile phase of Acetonitrile: Water (70:30, V/V). Drug and degradants were monitored at detection wavelength of 242nm, the flow rate was 1 ml/min, injection volume was 20 µl. Retention time of Palonosetron hydrochloride was about 4.38 minute.

Preparation of Standard Solution: 20ppm Palonosetron Hydrochloride

50 mg of Palonosetron hydrochloride was weighed and transferred to 50ml volumetric flask and volume was made up to the mark with diluent.(stock solution 1000ppm). From this stock solution 2.5ml of solution was pipetted out in 25 ml of volumetric flask and volume was made up to the mark with diluent (100ppm). From this solution 2 ml of solution was pipetted out in 10ml volumetric flask and volume was made up to the mark with diluent (20ppm).

Chromatographic Trials

Trial 1

Table 1: Chromatographic conditions for 1st trial

1	Column	YMC Pack Pro C8 (250 x 4.6 mm, 5µm)
2	Mobile phase	ACN : Water (50:50)
3	Flow rate	1.0 ml/min
4	Injection volume	20µl
5	Column temp	25ºC
6	Diluent	ACN : Water (70:30)
7	Detection	242nm

Trial 2

Table 2: Chromatographic conditions for 2nd trial

1	Column	YMC Pack Pro C8 (250 x 4.6 mm, 5µm)
2	Mobile	ACN : Water (60:40)

	phase	
3	Flow rate	0.8 ml/min
4	Injection volume	20µl
5	Column temp	25ºC
6	Diluent	ACN : Water (70:30)
7	Detection	242nm

Trial 3

Table 3: Chromatographic conditions for 3rd trial

1	Column	Zorbax eclips plus C8 (250 x 4.6 mm, 5µm)
2	Mobile phase	ACN : Water (60:40)
3	Flow rate	1.0 ml/min
4	Injection volume	20µl
5	Column temp	25ºC
6	Diluent	ACN : Water (70:30)
7	Detection	242nm

Trial 4

Table 4: Chromatographic conditions for 4th trial

1	Column	SUPELCOSIL™ LC-ABZ (15cm x 4.6 mm, 5µm)
2	Mobile phase	ACN : Water (50:50)
3	Flow rate	1.0 ml/min
4	Injection volume	20µl
5	Column temp	25ºC
6	Diluent	ACN : Water (70:30)
7	Detection	242nm

Trial 5

Table 5: Chromatographic conditions for 5th trial

1	Column	SUPELCOSIL™ LC-ABZ (15cm x 4.6 mm, 5µm)
2	Mobile phase	ACN : Water (60:40)
3	Flow rate	1.0 ml/min
4	Injection volume	20µl
5	Column temp	25ºC
6	Diluent	ACN : Water (70:30)
7	Detection	242nm

Final Chromatographic Condition

Table 6: Final Chromatographic conditions for optimized method

1	Column	BDS HYPERSIL C8 (250 x 4.6 mm, 5µm)
2	Mobile phase	ACN : Water (70:30)
3	Flow rate	1.0 ml/min
4	Injection volume	20µl
5	Column temp	25ºC
6	Diluent	ACN : Water (70:30)
7	Detection	242nm

Acidic Degradation

2 ml of 20ppm solution from standard preparationwas pipetted out in to 10 ml volumetric flask and 1 ml of 0.1 N HCl was added. It was refluxed for 1 hour at 60^0C then neutralized by adding 1 ml 0.1 N NaOH and volume was made up to the mark with diluent. After making final dilution the standard solution was injected in HPLC and the peak area and peak shapes were observed.

Alkali Degradation

2 ml of 20ppm solution from standard preparation was pipetted out in 10 ml volumetric flask and 1 ml of 0.1 N NaOH was added. It was refluxed for 1 hour at 60^0C then neutralized by adding 1 ml 0.1 N HCl and volume was made up to the mark with diluent. After making final dilution the standard solution was injected in HPLC and the peak area and peak shapes were observed.

Oxidative Degradation

2 ml of 20ppm solution from standard preparationwas pipetted out in to 10 ml volumetric flask and 1 ml of 3% $H_2O_2$was added. It was refluxed for 1hour at 60^0C and volume was made up to the mark with diluent.After making final dilution the standard solution was injected in HPLC and the peak area and peak shapes were observed.

Neutral Degradation

2 ml of 20ppm solution from standard preparation was pipetted out in to 10 ml volumetric flask. It was refluxed for 1 hour at 60^0C and volume was made up to the mark with diluent. After making final dilution the standard solution was injected in HPLC and the peak area and peak shapes were observed.

Photo Degradation

2 ml of 20ppm solution from standard preparation was pipetted out in to 10 ml volumetric flask and volume was made up to the mark with diluent. It was exposed in sun light for 1 hour. After making final dilution the standard solution was injected in HPLC and the peak area and peak shapes were observed.

RESULTS AND DISCUSSION

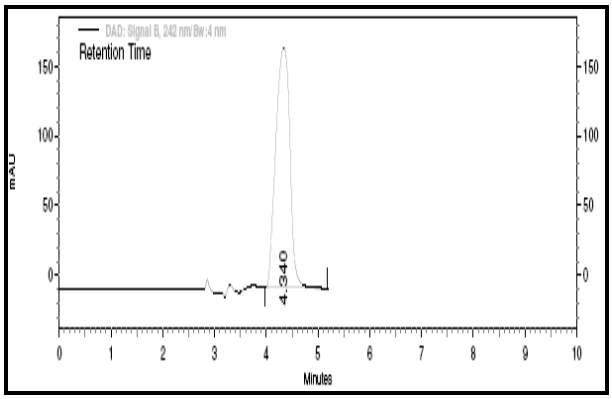

Figure 2: Chromatogram of Palonosetron for 1st trial

Observation: Theoretical plate was less than 2000

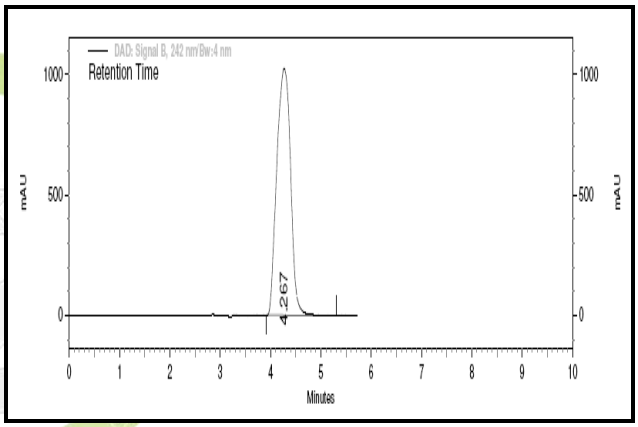

Figure 3: Chromatogram of Palonosetron for 2nd trial

Observation: Theoretical plate was less than 2000

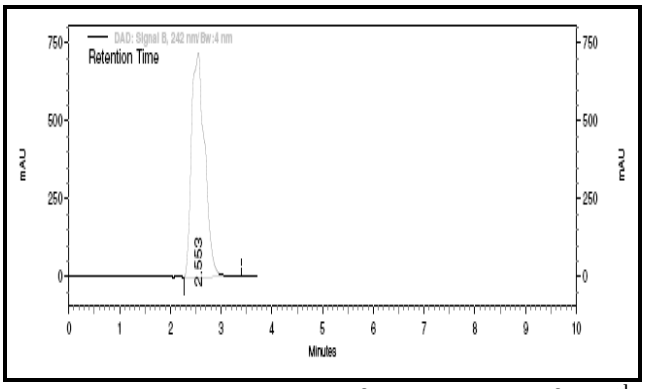

Figure 4: Chromatogram of Palonosetron for 3rd trial

Observation: Theoretical plate was less than 2000

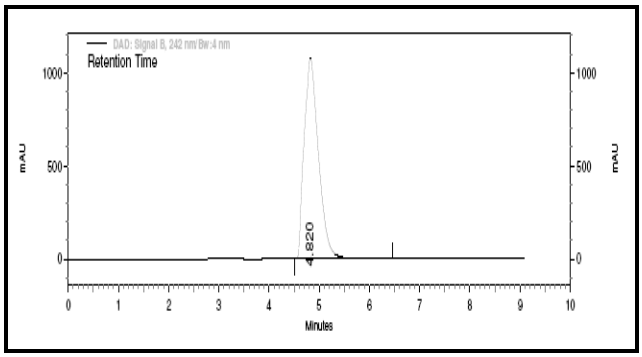

Figure 5: Chromatogram of Palonosetron for 4th trial

Observation: Theoretical plate was less than 2000

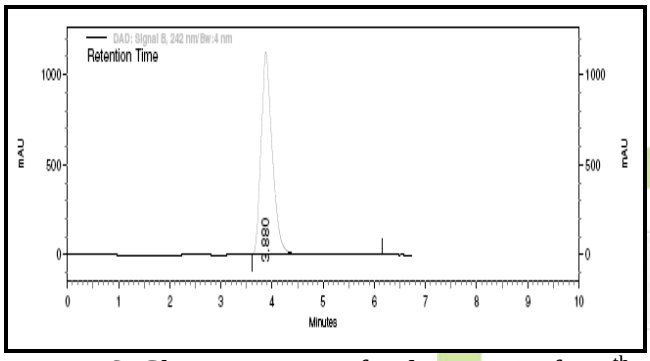

Figure 6: Chromatogram of Palonosetron for 5th trial

Observation: Theoretical plate was less than 2000

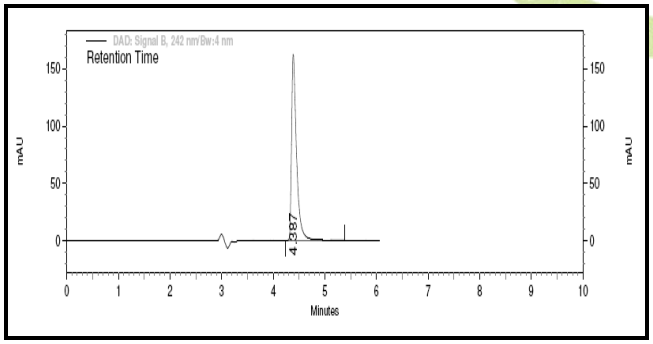

Figure 7: Chromatogram of Palonosetron hydrochloride

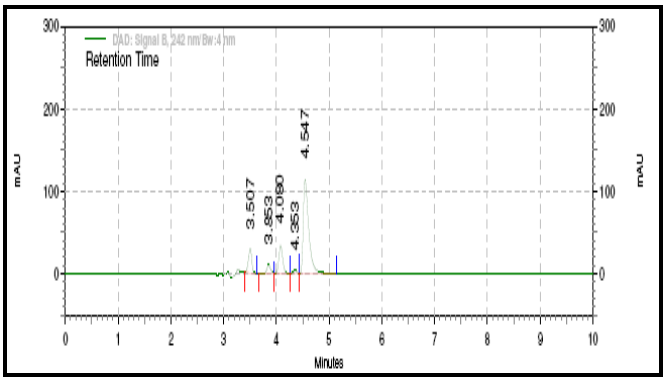

Figure 8: Chromatogram of Palonosetron_0.1N HCL @60°C for 1 hour

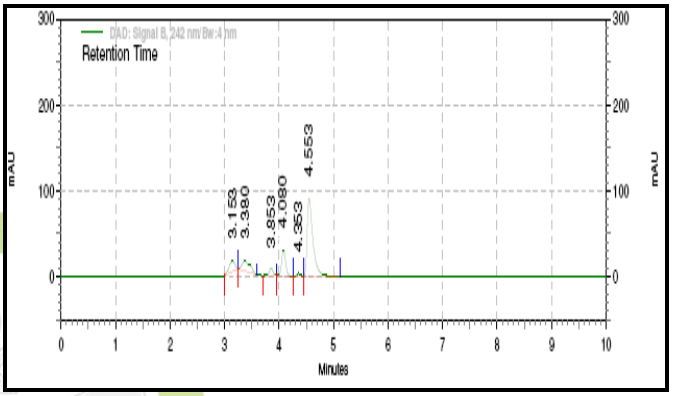

Figure 9: Chromatogram of Palonosetron_0.1N NaOH@60°C for 1 hour

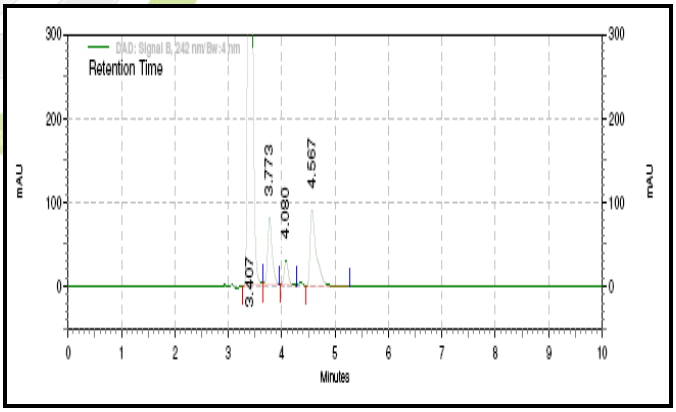

Figure 10: Chromatogram of Palonosetron_3% H_2O_2@ 60ºC for @ 1hour

Name	Retention time (min)	Area	Tailing	Resolution	Theoretical plate
Palonosetron hydrochloride	4.387	2292517	1.732	0.000	11885

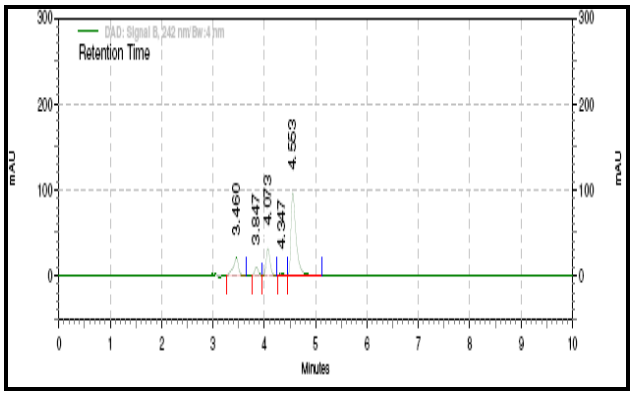

Figure 11: Chromatogram of Palonosetron_Thermal@60°C for 1 hour

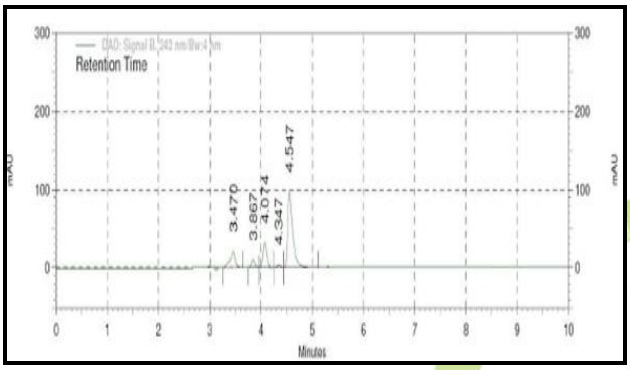

Figure 12: Chromatogram of Palonosetron_ Photo@ for 1 hour

Forced Degradation Summary

Table 7: Forced Degradation Summary

	Condition	% Degradation
Acid	Palonosetron_0.1N HCL at 60ºC for 1 hour	12.33%
Base	Palonosetron_0.1N NaOH at 60ºC for 1 hour	27.21%
Peroxide	Palonosetron_3%H_2O_2 at 60ºC for 1 hour	21.52%
Thermal	Palonosetron_ Thermal at 60ºC for 1 hour	28.17%
Photo	Palonosetron_ Photo for 1 hour	29.14%

CONCLUSION

A new Stability indicating HPLC method was developed for the estimation of Palonosetron hydrochloride tablet. The drug was found to degrade significantly under Acidic, Alkaline, Neutral, Oxidative and photolytic conditions. The simplicity of the method allows its application in the quality control and stability studies area for the formulated product.

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