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TO DEVELOP AND VALIDATE A NOVEL ANALYTICAL METHOD FOR ESTIMATION OF IN-VITRO DISSOLUTION DRUG RELEASE OF DOLASETRON BY USING RP- HPLC

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ABSTRACT

A rapid and precise reverse phase high performance liquid chromatography method has been developed and validated as per current regulatory approaches, to estimate the percentage drug release of the dissolution in dolasetron tablet dosage form. Chromatography was carried out on a kinetex XB C18 (150X4.6mm,2.6µ) column using a mixture of acetonitrile and phosphate buffer (50:50v/v) as the mobile phase at a flow rate of 0.8mL/min, the detection was carried out at 215nm. The retention time of the dolasetron was about 3min and the run time was 8min. The method produces linear response to the concentration ranges of 25-125ppm of dolasetron. The recovery was done 25% of the lower strength to 150% of higher strength on the active component. In this study the dissolution method has been optimized by different approaches as per the current regulatory guidelines. The method precision for the determination of % drug release in dissolution media 0.1N HCl at 30min time point. The above 90% of the drug release has been achieved with %RSD below 3.0%. The method can be able to evaluate the invitro % drug release of dolasetron for the commercial marketed drug product.

KEYWORDS: *Dolasetron, RP-HPLC, Validation, Dissolution and Regulatory guideline.*

1. INTRODUCTION

Dolasetron is an antinauseant and anti-emetic agent indicated for the prevention of nausea

and vomiting associated with moderately-emetogenic cancer chemotherapy and for the prevention of postoperative nausea and vomiting. Dolasetron is a highly specific and selective serotonin 5-HT3 receptor antagonist. It works by blocking the action of serotonin, a natural substance that may cause nausea and vomiting. Dolasetron is a BCS Class-III drug which can be freely soluble in water and has an excellent bioavailability of oral dolasetron is about 75-80%. The dissolution is the main tool to check the quality and consistency of the drug product. In the part of product development, the invitro study plays an important role in assessing the quality and consistency of the any dosage form. The dissolution profile test is one of the most useful methods used in different stages of the drug product life cycle. The high-performance liquid chromatography technique is the most widely used technique to quantify the % drug release. The aim of this paper was to develop a suitable dissolution method and HPLC method for the dolasetron marketed dosage form.

2. MATERIALS AND METHOD

Chemicals: HPLC grade acetonitrile, Milli-Q water potassium dihydrogen phosphate Emparta grade and all other chemicals were AR grade.

Instrumentation: HPLC Shimadzu LC-2030 prominence equipped with UV detector, Dissolution make Electrolab model 08lx. Column kinetex XB C18(150X4.6mm, 2.6µ).

Chromatographic conditions

Table 1: Chromatographic parameters.

Column	Kinetex XB, C18
Flow	0.8mL/min
Column temperature	30°C
Sample temperature	25°C
Injection volume	15µL
Wavelength	215nm
Elution mode	Isocratic mode

Dissolution parameters

Table 2: Dissolution conditions.

Medium	0.1N HCl
Volume	900mL
Apparatus	USP Type-II
RPM	75RPM
Filters used	10µ
Sampling point	30min point
Temperature	37±0.5

As per the regulatory guideline (USP chapter <1092>) the most used apparatus for the study of dissolution in tablets and capsules dosage form is Basket and Paddles. This study was executed by using the paddles apparatus with the rpm of 75 and the 900mL media volume has been chosen for the test. The temperature of the medium is 37°C±0.5. The media selection was done based on the solubility of the drug substance in different pH ranges from 1.2 to 6. 8buffer. The 0.1N HCl media was selected as per the saturation solubility of dolasetron drug substance. The media which has meets the sink condition was selected for the study. The 0.1N HCl media has an excellent sink condition which is about 2.5X range. The HPLC method parameters were selected based on the different study trials. Isocratic elution mode has been chosen with a flow rate of 0.8mL/min and run time is 6min and detection wavelength 285nm.Validaion of the method was done in accordance with USP and ICH Guidelines.

Guidelines for Validation

Every analytical method has required a validation process establishing through documented evidence, it provides the high degree of assurance that an analytical method will consistently yield results that accurately reflect the quality characteristic of the product tested. Validated the method as per the current ICH guidelines Q2 (R2).

Parameters to be Validated

Specificity and system precision, method precision (repeatability, Intermediate precision and ruggedness), Linearity, accuracy or recovery and robustness.

3. RESULTS AND DISCUSSION

The test results were obtained by different parameters and were within the acceptance criteria, as per the regulatory guidelines. Specificity of the test has not shown any interference at the retention time of dolasetron. The %RSD for the System precision was found to be 0.3%. Method precision for 6units dissolution found to be 90% and %RSD was below 2.0%. Method is linear over concentration ranges from 25% to 125% and plotted the linearity graph, found the correlation coefficient was 0.9999. Recovery of the drug substance was done on placebo solution and results were found to be comparable and 95-105%. Robustness has been performed little changes in method parameters. The outcome of this study is to check the quality of the drug product by a simple, precise and accurate analytical method.

Tables 3: Robustness conditions.

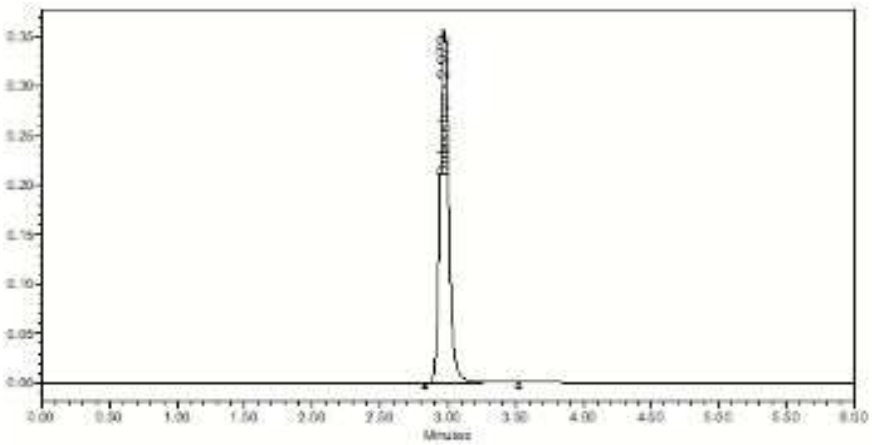
S. No	Parameter	Optimized condition	Changes±
1	Flow	0.8mL/min	±0.2mL/min
2	Temperature	30°C	±5
3	pH	pH 3.2	±0.2

Table 4: Outcome of the system precision.

S. No	Standard Inj	Peak area	%RSD
1	Unit-1	3564231	1.0*
2	Unit-2	3499123	
3	Unit-3	3523617	
4	Unit-4	3501563	
5	Unit-5	3591345	
6	Unit-6	3522341	

** The % RSD for the 6 replicate injections is 1.0%*

Reference chromatogram for dolasetron standard injection



Reference chromatogram for blank injection

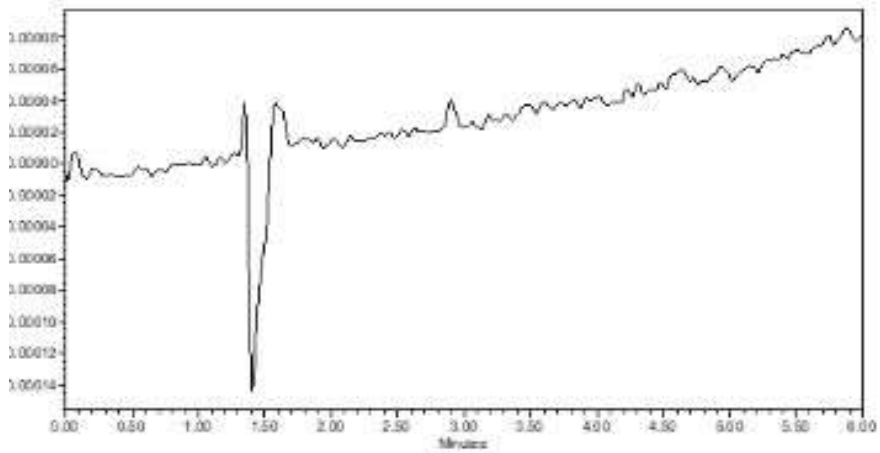
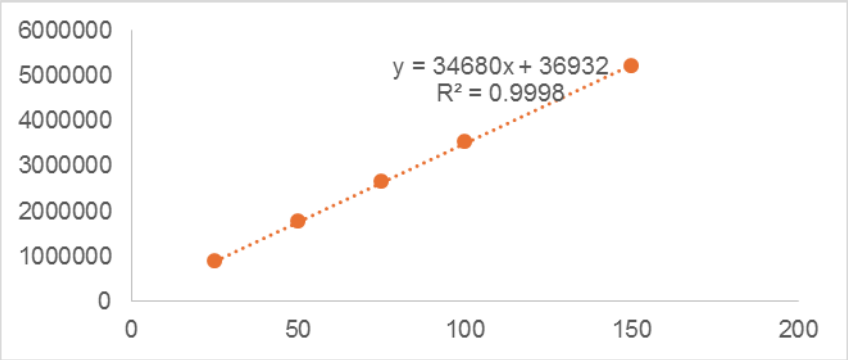


Table 4: Recovery at 25%, 100% and 150% levels.

S. No	Stock concentration	Recovery level	Spiked stock volume(mL)	Media volume	Added ppm	found ppm	% Recovery	%RSD
1	3000	25%_Unit-1	4	900	13.3	13.15	98.6	0.5
2	3000	25%_Unit-2	4	900	13.3	13.45	100.9	
3	3000	25%_Unit-3	4	900	13.3	13.2	99.0	
S. No	Stock concentration	Recovery level	Spiked stock volume(mL)	Media volume	Added ppm	found ppm	% Recovery	%RSD
1	3000	100%_Unit-1	15	900	50.0	49.75	99.5	0.5
2	3000	100%_Unit-2	15	900	50.0	49.69	99.4	
3	3000	100%_Unit-3	15	900	50.0	50.12	100.2	
S. No	Stock concentration	Recovery level	Spiked stock volume(mL)	Media volume	Added ppm	found ppm	% Recovery	%RSD
1	3000	100%_Unit-1	22.5	900	75.0	76	101.3	0.9
2	3000	100%_Unit-2	22.5	900	75.0	75.15	100.2	
3	3000	100%_Unit-3	22.5	900	75.0	74.65	99.5	

Table 5: Linearity solutions concentration levels.

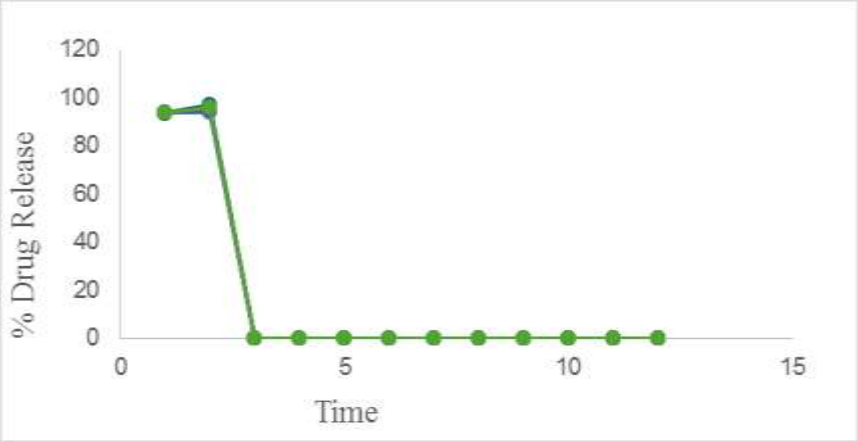
S. No	std stock ppm	Linearity Level in %	Conc in ppm
1	1008	25	12.60
2	1008	50	25.20
3	1008	75	37.80
4	1008	100	50.40
5	1008	125	63.00



The linearity plot for dolasetron drug substance

Table 6: Outcome of the method precision.

S. No	Unit-No	% drug release	%RSD
1	Unit-1	93	1.7
2	Unit-2	92	
3	Unit-3	92	
4	Unit-4	96	
5	Unit-5	95	
6	Unit-6	94	



Graph for % drug release of dolasetron drug

Calculation formula:

$$\% \text{ Release} = \frac{A1}{A2} \times \frac{W1}{Ds} \times \frac{Dt}{N} \times \frac{P}{100} \times \frac{100}{LC}$$

P: Potency of the Dolasetron standard as is basis

LC: Label claim in mg

A1: Area of Dolasetron peak from test solution

A2: Area of Dolasetron peak in standard solution

W1: Weight of the Dolasetron standard in mg

Ds: Dilution step for standard solution

Dt: Dilution step for test solution

N: Number of tablets

4. CONCLUSION

In this study a simple, precise and accurate RP-HPLC method was developed for the estimation of % drug release of dolasetron in pharmaceutical industry. The qualitative dissolution method was developed as per regulatory guidelines. The results obtained from this method were satisfactory and can be used for the routine quality control analysis for the dolasetron tablet dosage form.

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