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DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF ONDANSETRON IN BULK AND PHARMACEUTICAL FORMULATION

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ABSTRACT

To develop simple, economical, precise and less time consuming UV method for the estimation of Ondansetron in bulk and pharmaceutical formulations. The method is based on UV spectroscopic technique. Ondansetron shows the maximum absorbance at 310nm in absorption maxima method. Drug followed the linearity in the range of 4-24µg/ml for this method with correlation coefficient (r^2) of 0.999. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method. The method was validated as per the International Conference on Harmonization (ICH) guidelines. The proposed method is recommended for routine analysis since it is rapid, simple, accurate and sensitive.

Keywords: Ondansetron, HPLC, UV spectrophotometry, absorption maxima method.

INTRODUCTION

Ondansetron [1-2] is chemically named as 9-methyl-3-[(2-methyl-1H-imidazol-1-yl)methyl]-2,3,4,9-tetrahydro-1H-carbazol-4-one, is official in IP, BP and USP[3-5]. It is 5-HT3 receptor antagonist used mainly as an antiemetic (to treat nausea and vomiting) [6]. The antiemetic activity of the drug is brought about through the inhibition of 5-HT3 receptors present both centrally (medullary chemoreceptor zone) and peripherally (GI tract) [7-8]. Literature review shows that there are developed methods including spectrophotometric, HPLC and HPTLC methods for the estimation of Ondansetron alone and in combination of other drugs like Omeprazole, Rabeprazole etc.There are developed Spectrophotometric methods [9-12] of analysis in single or in combination. Ondansetron shows absorption in UV-visible range in

acidic media produced by hydrochloric acid was measured in absorption maxima method. In the present investigation simple and sensitive UV spectrophotometric method have been developed for the quantitative estimation of Ondansetron in bulk and its marketed formulations with good accuracy and economy. The structure of Ondansetron is shown in (Figure 1).

EXPERIMENTAL WORK

All the chemicals used during the experimental work are of Analytical grade. A Shimadzu UV-1800 UV/VIS Spectrophotometer was used with 1cm matched quartz cells. Tablets of ONDEM- 4mg were procured from local market.

Preparation of standard solution

The pure drug of about 10 mg was weighed and transferred in to a 10ml volumetric flask. The drug was dissolved completely in a few ml of 0.1N HCL and made up to the final volume with HCL to get a stock solution of concentration 1000µg/ml. Aliquots of standard stock solution were pipette out and diluted suitably with 0.1N HCL to get the final concentration of standard solutions.

Absorption maxima method

The solutions were scanned in the range of 400-200 nm against 0.1N HCL as reference, and the peaks were observed in the spectra at 310nm. The wavelength selected for analysis of drug was 310nm (Figure 2). The drug obeys the lamberts law in the range of 4-24 µg/ml. By using linearity plot (Figure 3) the quantification was carried out.

Optical characteristics

Optical characteristics such as Beer's law limit (µg/mL)**,** Correlation coefficient, Regression equation, Slope (m), and Intercept (c) were calculated (Table-1).

Analysis of tablet formulation

For the estimation of Ondansetron in pharmaceutical formulation by above method, 10 tablets of ONDEM-4 brand were weighed and triturated to a fine powder. Tablet powder equivalent to 10mg was weighed and transferred to 100ml volumetric flask and dissolved in few ml of 0.1N HCL with the aid of ultra-sonication for 15min; this was filtered through whatman filter paper no. 41 to get the stock solution of 100 µg/ml various dilutions were prepared from

tablet solution and analyzed for six times and the concentration for both the methods was calculated by using calibration curve (Table-2).

VALIDATION OF ANALYTICAL METHOD

The analytical method was validated according to ICH validation parameters [13].

Linearity

Fresh aliquots were prepared from standard stock solution ranging from 4-24 µg/ml and the absorbance values of each concentration was recorded at 310nm for this method using 0.1N HCL as blank. The drug shows linearity between 4-24 µg/ml for this method (Table-3).

Precision

In intraday study, concentration of replicates of drug was calculated on the same day for three times. In inter-day study the concentration of drug were calculated on three successive days which expresses the laboratory variation in different days. In both intra and inter day precision study for the methods %RSD was calculated (Table-4(a), 4(b).

Accuracy

Accuracy of the developed method was confirmed by performing recovery studies at three different concentration ranges 80%, 100%, 120% each one in triplicate (Table-3). From the recovery studies it was clear that the method is very accurate for quantitative estimation of tablet as the statistical results were within the acceptance range (Table-5).

Limit of Detection and Limit of Quantification

The limit of detection and limit of quantification of Ondansetron by proposed methods were determined using calibration graphs. LOQ and LOD were calculated as

LOD = 3.3 X S.D/S

LOQ = 10 X S.D/S

Where S is the slope of the calibration curve and SD is the standard deviation of response of least concentration of calibration curve in three replicates.(Table-6).

Robustness

Robustness of the method was determined by carrying out the analysis at five different wavelengths (±0.5nm). The respective absorbance was noted and the result was indicated by % RSD (Table-7).

Ruggedness

Ruggedness of the method was determined by carrying out the analysis by two different analysts and the respective absorbance was noted. The result was indicated by % RSD (Table-7).

RESULTS AND DISCUSSION

The developed method was found to be precise as the %RSD values for intra-day and inter-day were found to be less than 2%. Good recoveries (98.75% to 100.45%) of the drug were obtained at each added concentration, which indicates that the method was accurate. The LOD and LOQ were found to be in sub-microgram level, which indicates the sensitivity of the method. The method was also found to be robust and rugged as indicated by the %RSD values which are less than 2%. The results of assay show that the amount of drug was in good agreement with the label claim of the formulation as indicated by % recovery (101.6%).

Table1 Optical characteristics

Optical characteristics	Method A
Beer's law limit (µg/ml)	4-24
Correlation coefficient (r^2)	0.999
Regression equation	y = 0.040x + 0.009
Slope (a)	0.040
Intercept (b)	0.009
LOD	0.265µg/ml
LOQ	0.804µg/ml

Table 2 Analysis of Formulation

Drug	Label Claim (Mg/ Tablet)	Amount* Found (Mg/ Tablet)	% Amount Found	%Rsd
ONDANSETRON	4	4.05	101.25	0.012

*Mean of three readings

Table3 Linearity of Ondansetron

S.No	Concentration in µg/ml	Absorbance	
		UV Method	
1	4	0.176	
2	8	0.337	
3	12	0.512	
4	16	0.665	
5	20	0.832	
6	24	0.980	

Table4 (a) Intra-day precision

S.no	Conc (µg/ml)	Absorbance			%RSD
		Morning*	A.noon*	Evening*	
1.	8	0.521	0.523	0.524	0.42

Table4 (b) Inter-day precision

S.no	Conc (µg/ml)	Absorbance			%RSD
		Day1*	**Day2***	**Day3***	
1.	12	0.521	0.524	0.527	0.54

*Mean of six replicates

Table5 Accuracy studies of Ondansetron

Method	Amount of µg/ml		% of drug added	Amount recovered	%recovered	% RSD
	Tablet	Pure drug				
UV	4.0	3.2	80	7.18	99.72	0.41
	4.0	4.0	100	7.98	98.75	
	4.0	4.8	120	8.84	100.45	

Table6 LOD and LOQ of Ondansetron

Standard	LOQ	LOD
ONDANSETRON	0.265	0.804

Table7 Robustness and Ruggedness of Ondansetron

Parameter		%RSD
Robustness	Change in λmax **(±** 5 nm**)**	0.65
Ruggedness	1st analyst	0.86.
	2nd analyst	1.2

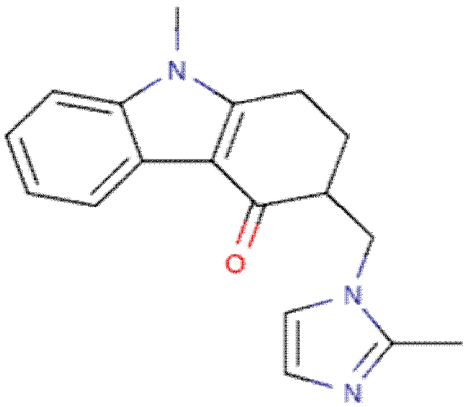

Figure1 Structure of Ondansetron

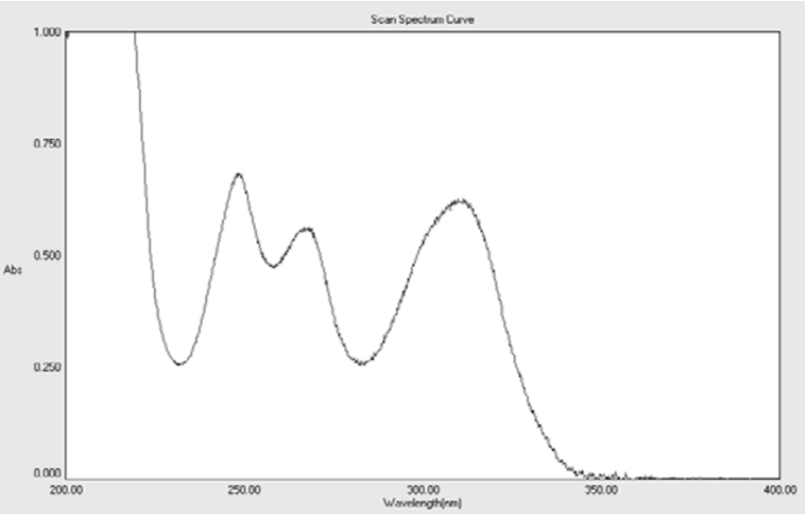

Figure2 Absorption maxima spectrum of Ondansetron

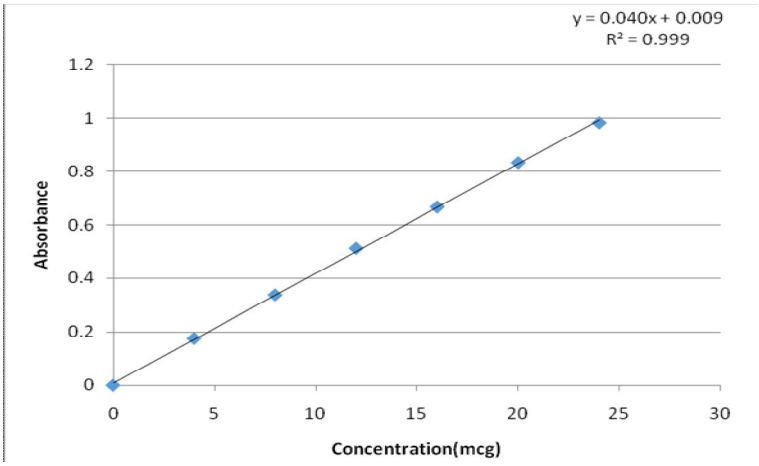

Figure3 Calibration curve of Ondansetron at 310nm

CONCLUSION

The proposed methods are simple, sensitive, and cost-effective. Validated in terms of precision, linearity and accuracy. The results are reproducible, and can be used successfully for the estimation of Ondansetron in bulk and its pharmaceutical formulations.

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