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Research Article

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF ONDANSETRON AND RANITIDINE IN PURE AND ITS TABLET DOSAGE FORM BY RP-HPLC

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ABSTRACT

A rapid and precise reverse phase high performance liquid chromatographic method has been developed for the validated of Ondansetron and Ranitidine, in its pure form as well as in tablet dosage form. Chromatography was carried out on a Hypersil C18 (4.6×250mm, 5µ) column using a mixture of Water and Acetonitrile (50:50) as the mobile phase at a flow rate of 1.0ml/min, the detection was carried out at 235nm. The retention time of the Ondansetron and Ranitidine was 2.079, 4.045 ± 0.02 min respectively. The method produce linear responses in the concentration range of 5-25µg/ml of Ondansetron and 93.75-468.75µg/ml of Ranitidine. The method precision for the determination of assay was below 2.0 %RSD. The method is useful in the quality control of bulk and pharmaceutical formulations.

KEYWORDS: *Ondansetron, Ranitidine, RP-HPLC, validation.*

INTRODUCTION

Ondansetron is chemically named as 9-methyl-3-[(2-methylimidazol-1-yl)methyl]-2,3-dihydro-1H-carbazol-4-one [1]. It is a drug marketed under the brand name Zofran, is a medication used to prevent nausea and vomiting caused by cancer chemotherapy, radiation therapy, or surgery [2]. It is also useful in gastroenteritis [3, 4]. It has little effect on vomiting caused by motion sickness [5].

Ranitidine is chemically named as (E)-1-N'-[2-[[5-[(dimethyl amino)methyl]furan-2-yl]methylsulfanyl]ethyl]-1-N-methyl-2-nitro ethene-1,1-diamine [6]. It is a drug sold under the trade name Zantac among others, is a medication which decreases stomach acid production [7]. It is commonly used in treatment of peptic ulcer disease, gastroesophageal reflux disease, and Zollinger–Ellison syndrome [7]. There is also tentative evidence of benefit for hives [8].

In the scientific literature, analysis of Ondansetron and Ranitidine has been reported as individual ingredients and in combination with other compounds [9-11].

No other chromatographic methods are found for simultaneous analysis of Ondansetron and Ranitidine in a combined dosage form. The method described is rapid, economical, precise, and accurate and can be used for routine analysis of tablets. It was validated as per ICH guidelines [12-14].

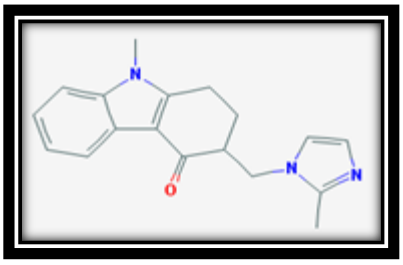

Fig. 1: Chemical Structure of Ondansetron

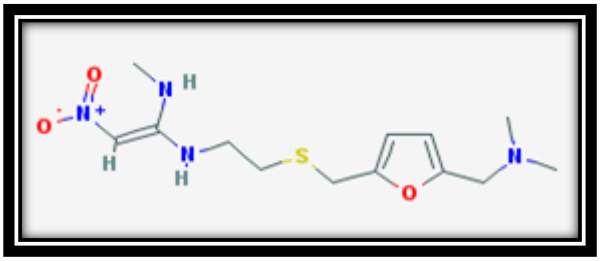

Fig. 2: Chemical Structure of Ranitidine

MATERIALS AND METHODS

Experimental:

Materials:

Pharmaceutical grade working standards Ondansetron and Ranitidine were obtained from Hetero Labs, Jedcharla, India. All chemicals and reagents were HPLC grade and were purchased from Merck Chemicals, Mumbai, India.

Instrumentation:

The analysis was performed using Waters-2695 (Modal Alliance) High Performance liquid chromatography, analytical balance (Mettler Toledo), PDA Detector (Standard cell) and data handling

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system (Empower 2), pH meter (lab India), Sonicator. The column used is Hypersil C18 (4.6 x 250mm, 5µm) with the flow rate 0.9ml/min (isocratic).

Preparation of mobile phase:

Accurately measured 500 ml (50%) of Water, 500ml of Acetonitrile (50%) were mixed and degassed in digital ultrasonicater for 10 minutes and then filtered through 0.45 µ filter under vacuum filtration.

Preparation of Standard Solution:

Accurately weigh and transfer 10 mg of Ondansetron and 10mg of Ranitidine working standard into a 10ml of clean dry volumetric flasks add about 7mL of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 0.15ml (15µg/ml) of the Ondansetron and 2.81ml (281µg/ml) of the Ranitidine stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

Preparation of Sample Solution:

Take average weight of Tablet and crush in a mortar by using pestle and weight 10 mg equivalent weight of Ondansetron and Ranitidine sample into a 10mL clean dry volumetric flask and add about 7mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent.

Further pipette 0.15ml (15µg/ml) of the Ondansetron and 2.81ml (281µg/ml) of the Ranitidine stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

RESULTS AND DISCUSSION

The simultaneous estimation of Ondansetron and Ranitidine was done by RP-HPLC and in the optimized method the mobile phase consists of buffer (500ml of Water, 500ml of Acetonitrile). Then finally filtered using 0.45µ membrane filter paper and degassed in sonicator for 15 minutes. The detection is carried out using PDA detector at 244 nm. The solutions are following at the constant flow rate of 0.9 ml/min.

The retention time for Ondansetron and Ranitidine was 2.079 & 4.045 min respectively. Linearity ranges for Ondansetron and Ranitidine were 5 - 25µg/mL and 93.75 - 468.75µg/mL respectively and the results were found in the acceptable as (R^2) = 0.9998 for Ondansetron and (R^2) = 0.9994 for Ranitidine. LOD were 0.56µg/ml and 17.2µg/ml and LOQ were 1.7µg/ml and 52.2µg/mL for Ondansetron and Ranitidine respectively. The all parameters value of RSD is less than 2.0% indicating the accuracy and precision of the method. The percentage recoveries were found 98.98 - 101% and 99 – 99.7% for Ondansetron and Ranitidine respectively.

Table No. 1: Optimized Chromatographic Conditions

Parameters	Method
Stationary phase (column)	Hypersil C18 (4.6 x 250mm, 5µm)
Mobile Phase	Acetonitrile: Water (50:50v/v)
Flow rate (ml/min)	0.9
Run time (minutes)	8.0
Column temperature (°C)	40
Volume of injection loop (µl)	10
Detection wavelength (nm)	235
Drugs RT (min)	2.079 & 4.045

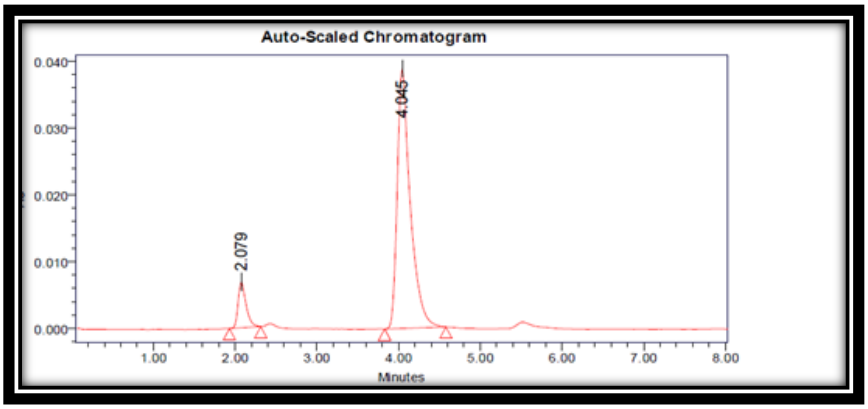

Fig. 3: Optimized Chromatogram of Ondansetron and Ranitidine at 235nm

Table No. 2: Linearity Data of Ondansetron and Ranitidine

Analyte	Concentration range (µg/mL)	Correlation Coefficient (R^2)	Slope	Intercept
Ondansetron	5 – 25	0.9998	3062.7x	5.7143
Ranitidine	93.75 - 468.75	0.9994	1517.4x	3648.2

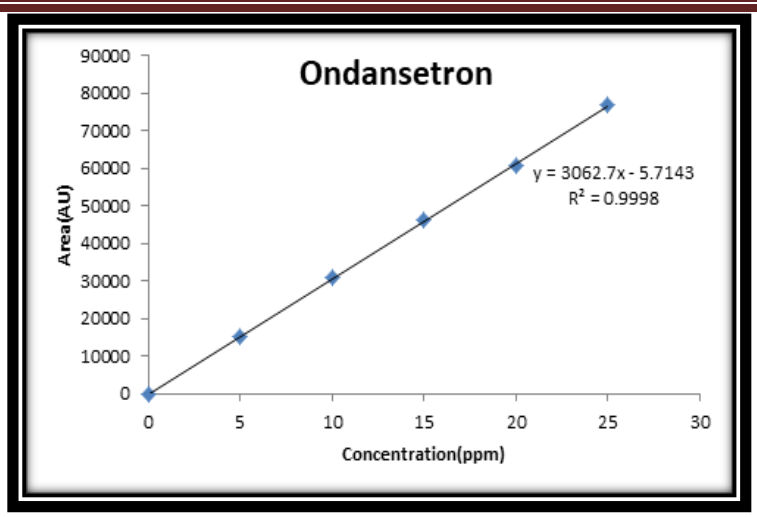

Fig. 4: Linearity Curve of Standard Ondansetron

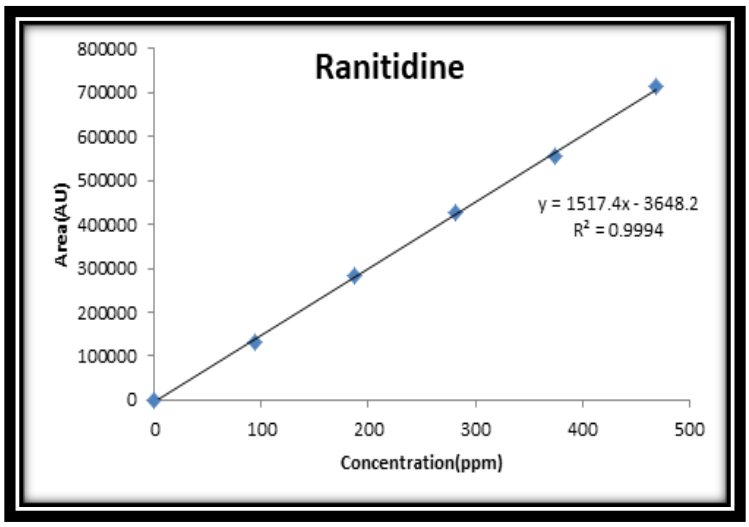

Fig. 5: Linearity Curve of Standard Ranitidine

Table No. 3: Repeatability and Reproducibility results of Ondansetron and Ranitidine

No. of Preparation	Ondansetron		Ranitidine	
	Repeatability	Reproducibility	Repeatability	Reproducibility
Pre-1	46054	46300	46054	46300
Pre-2	46803	46259	46803	46259
Pre-3	46150	46223	46150	46223
Pre-4	46056	46205	46056	46205
Pre-5	46247	46189	46247	46189
Mean	46262	46230	46262	46230
St. dev.	312.7099	41.88556	312.7099	41.88556
% RSD	0.675	0.09	0.675	0.09

Table No. 4: System suitability parameters for Ondansetron and Ranitidine

System suitability parameters	Ondansetron	Ranitidine
Retention time (min)	2.079	4.045
%RSD for Repeatability of peak area	0.675	0.22
Resolution (Rs)	-	3.62
Tailing factor (asymmetric factor)	1.27	1.17
USP plate count	5691	9762
LOD (µg/mL)	0.56	17.2
LOQ (µg/mL)	1.7	52.2

Table No. 5: Robustness study for analytical method validation of Ondansetron and Ranitidine

Parameters		Adjusted to	Mean Area [a]	Mean RT	% RSD
Ondansetron	Flow Rate ±0.1ml/min	0.8 ml/min	51177	2.29	0.86
		1.0ml/min	42190	1.890	0.72
	Mobile Phase (Acetonitrile: Water (50:50 v/v) (±5ml)	45:55	42402	1.885	0.73
		55:45	42112	1.908	0.91
Ranitidine	Flow Rate ±0.1ml/min	0.8 ml/min	472673	4.450	1.01
		1.0ml/min	392497	3.660	0.81
	Mobile Phase (Acetonitrile: Water (50:50 v/v) (±5ml)	45:55	391379	4.251	0.28
		55:45	391703	3.239	0.7

[a] = 5 *Replicates*

Tablet No. 6: Accuracy Results of Ondansetron and Ranitidine

Drug Name	%Concentration (at specification Level)	Area	Amount Added (ppm)	Amount Found (ppm)	% Recovery	Mean Recovery
Ondansetron	50%	22938.33	7.5	7.3	99.88	99.92%
	100%	45426	15	14.7	98.89	
	150%	70096.67	22.5	22.2	101	
Ranitidine	50%	209357	140.6	140.2	99.7%	99.23%
	100%	420697.7	281.25	281.1	99%	
	150%	631550.7	421.8	421.4	99%	

CONCLUSION

In the present investigation, a simple, sensitive, precise and accurate RP-HPLC method was developed for the quantitative estimation of Ranitidine and Ondansetron in bulk drug and pharmaceutical dosage forms. This method was simple, since diluted samples are directly used without any preliminary chemical derivatisation or purification steps. Ranitidine and Ondansetron was freely soluble in ethanol, methanol and sparingly soluble in water. Water and Acetonitrile (50:50) was chosen as the mobile phase. The solvent system used in this method was economical. The %RSD values were within 2 and the method was found to be precise. The results expressed in Tables for RP-HPLC method was promising. The RP-HPLC method is more sensitive, accurate and precise compared to the Spectrophotometric methods.

This method can be used for the routine determination of Ranitidine and Ondansetron in bulk drug and in Pharmaceutical dosage forms.

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