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NEW DERIVATIVE SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF ONDANSETRON HYDROCHLORIDE

Medikonda Sai Kusuma, Mukthinuthalapati Mathrusri Annapurna*, and Bukkapatnam Venkatesh

Department of Pharmaceutical Analysis & Quality Assurance,

GITAM Institute of Pharmacy, GITAM University, Visakhapatnam, India-530045.

Email: mathrusri2000@yahoo.com

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Abstract

Five simple and sensitive first order derivative spectrophotometric methods (D_1) were developed for the determination of Ondansetron hydrochloride in pharmaceutical formulations using Sodium acetate buffer pH-4 (Method A), phosphate buffer pH-3.6 (Method B), phosphate buffer pH-5.0 (Method C), phosphate buffer Ph-7.0 (Method D) and borate buffer pH-9.0 (Method E). Beer's law was obeyed over concentration range 0.1-60 $\mu\text{g/mL}$ for Method A and 0.5-60 $\mu\text{g/mL}$ for the Methods B, C, D and E. The linear regression equations were found to be $y = 0.0014x + 0.0008$ in acetate buffer pH-4 $y = 0.0014x + 0.0008$, $y = 0.0012x + 0.0018$, $y = 0.0012x + 0.0011$ in phosphate buffer pH- 3.6, 5.0, 7.0 and $y = 0.006x + 0.0016$ in Borate buffer pH-9.0 respectively. The five methods were validated and no interference of the excipients was observed.

Keywords: Ondansetron HCl, Derivative spectrophotometry, Validation

Introduction

Ondansetron (OND) is a 5HT₃- receptor antagonist used as an antiemetic. Chemically it is 9-methyl-3-[(2-methyl-1H-imidazol-1-yl)-methyl]-1, 2, 3, 9-tetrahydro- 4H-carbazol-4-one hydrochloride dehydrate¹ with molecular weight 365.86 g/mol. It acts both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the postrema. It is indicated for the prevention of nausea and vomiting associated with cancer chemotherapy, radiotherapy and anesthesia and surgery².

Literature survey revealed that Ondansetron HCl was determined by Spectrophotometry³⁻¹⁴, and RP-HPLC¹⁵⁻¹⁶ in pharmaceutical formulations. At present the authors have proposed five simple UV spectrophotometric methods for the analysis of Ondansetron in tablets and validated as per ICH guidelines¹⁷.

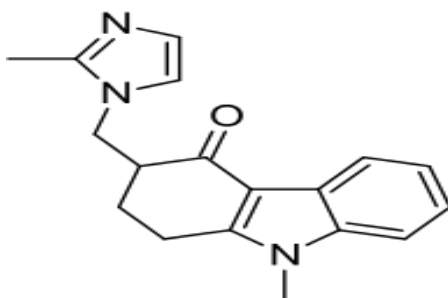


Figure 1: Chemical structure of Ondansetron.

Materials and Methods

Instrumentation

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe was employed with spectral bandwidth of 1 nm and wavelength accuracy of ± 0.3 nm with a pair of 10 mm matched quartz cells. For scanning, the wavelength range selected was 400 nm to 200 nm with medium scanning speed. All weights were taken using electronic balance (Denver, Germany). All experiments were performed at room temperature (25 ± 1) °C.

Reagents and chemicals:

Preparation of acetate buffer (pH 4.0) (Method A):

2.86 ml of glacial acetic acid and 1.0 ml of a 50 per cent solution of sodium hydroxide were taken in a 1000 ml volumetric flask, add diluted up to the mark with distilled water.

Preparation of Phosphate Buffer (pH- 3.6) (Method B):

Dissolve 0.900 g of anhydrous disodium hydrogen phosphate and 1.298 g of citric acid monohydrate in sufficient water to produce 1000 ml.

Preparation of phosphate buffer (pH 5.0) (Method C):

6.8 grams of potassium di hydrogen phosphate was taken in 1000ml of water and adjusted pH to 5.0 with 10M potassium hydroxide.

Preparation of Phosphate Buffer (pH- 7.0) (Method D):

Place 50.0 ml of 0.2 M potassium dihydrogen phosphate in a 200 ml volumetric flask, add 29.1 ml of 0.2 M sodium hydroxide and dilute with water to 1000 ml.

Preparation of Borate Buffer (pH- 9.0) (Method E):

Dissolve 6.20 g of boric acid in 500 ml of water, adjust to pH 9.0 with 1M sodium hydroxide (about 41.5 ml) and dilute with water to 1000 ml.

Preparation of stock and sample solution:

Ondansetron HCl stock was prepared by dissolving 25 mg of the drug in methanol in 25 ml volumetric flask (1000 µg/ml) and dilutions were made from the stock solution with acetate buffer, phosphate buffer and borate buffer for method A, B, C, D and E respectively. The above solutions were scanned (200- 400 nm) against their reagent blank and the absorption spectra were recorded for method A, B, C, D and E respectively.

Procedure:

Linearity of the method was established by preparing a calibration curve. For this a series of drug solutions were prepared for method A (0.1-60.0 µg/mL), B, C, D and E (0.5-60 µg/mL) scanned (200- 400 nm) against their reagent blank. The absorption spectra was recorded for the three methods A, B, C, D and E respectively and transformed in to first order derivative spectra (D₁). The derivative spectrum shows maxima at 297 nm in method A and 296 nm in methods B, C, D and E.

Assay procedure for the commercial formulations:

Twenty tablets (branded) were procured from pharmacy store and extracted using methanol. The filtrate obtained during the extraction was diluted as per the requirement and the percentage recovery was determined. The stock solution was further diluted with Sodium acetate buffer pH-4.0, phosphate buffers (pH-3.6, 5.0, 7.0) and borate buffer pH-9.0 separately for method A, B, C, D and E respectively.

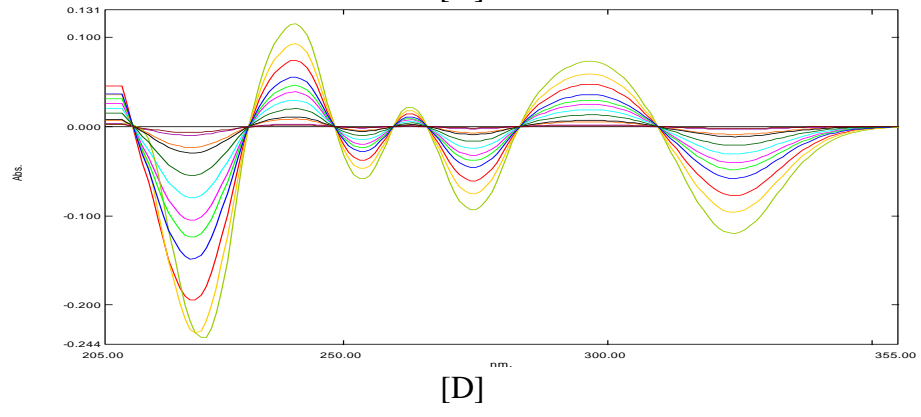
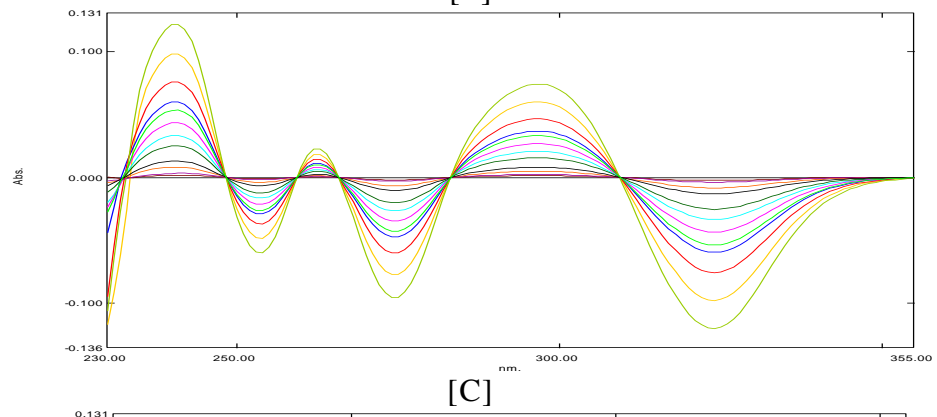
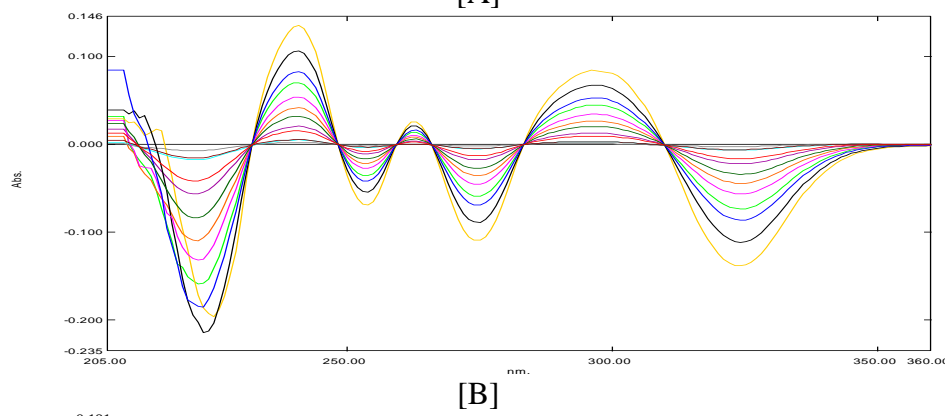
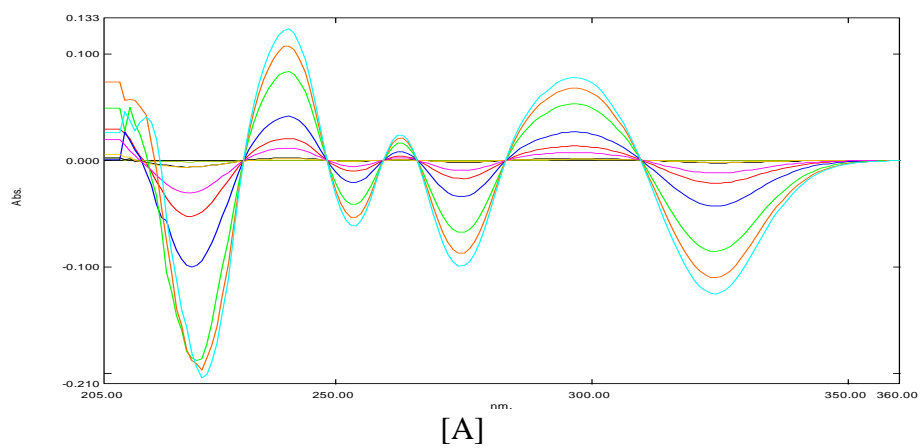
Precision and accuracy:

The precision study was done by recording the absorbance of six replicates for method A, B, C, D and E (20 µg/mL) and the %RSD was calculated. Accuracy was evaluated from the percent recovery studies by the addition of 80%, 100% and 120% of pure sample solution to the pre-analysed formulation solution. Ondansetron HCl extracted drug solution from the formulation (10µg/mL) was spiked with 80%, 100% and 120% of pure API solution and the % recovery was calculated.

Results and Discussion

The first order derivative spectrum of Ondansetron HCl in Sodium acetate buffer pH-4.0 (Method A) was shown in figure 2 indicating the maxima (297 nm). The zero crossing points were observed at 213.64nm, 231.94nm, 248.33 nm, 259.25 nm, 266.08 nm, 283.01 nm, 309.51 nm. The first order derivative spectra of Ondansetron HCl for Method B (maxima 296 nm) was shown in figure 3 and the Zero crossing points were found to be at 212.13 nm, 232.31 nm, 248.55 nm, 259.13 nm, 266.02 nm, 283.73 nm, 309.56 nm. The first order derivative spectra of

Ondansetron HCl for Method C (maxima 296nm) was shown in figure 4 and the zero crossing points were found to be at 248.25 nm, 259.17 nm, 265.52 nm, 283.17 nm, 309.17 nm. The first order derivative spectra of Ondansetron HCl for Method D (maxima 296nm) was shown in figure 5 and the zero crossing points were found to be at 210.24 nm, 232.38 nm, 248.33 nm, 259.52 nm, 265.71 nm, 283.33 nm, 309.52 nm. The first order derivative spectra of Ondansetron HCl for Method E (maxima 296nm) was shown in figure 6 and the zero crossing points were found to be at 210.24 nm, 232.14 nm, 248.33 nm, 259.76nm, 265.71nm, 283.33 nm, 309.52nm.



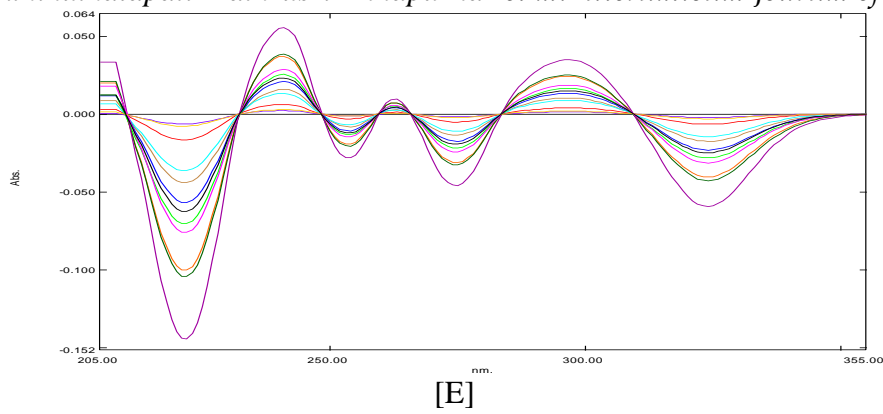
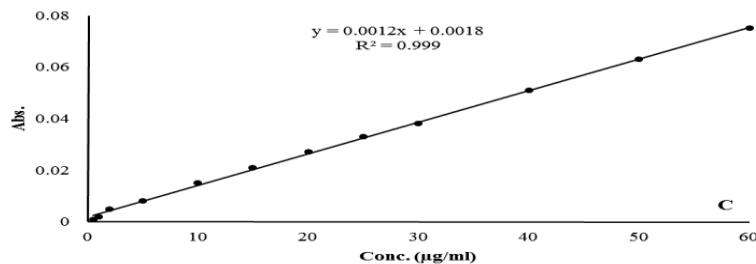
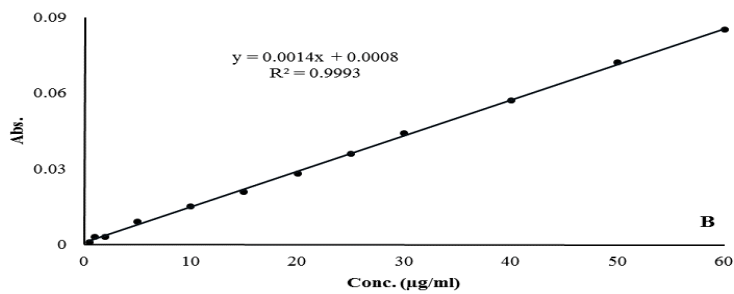
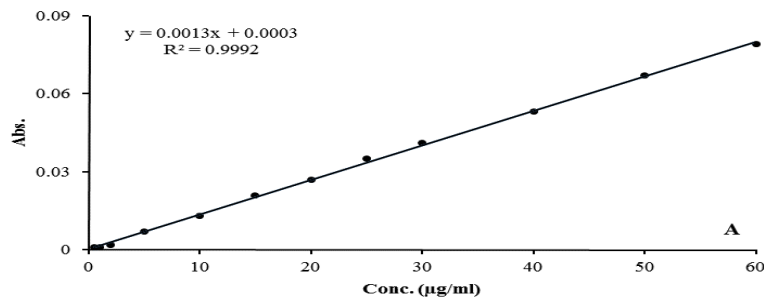


Figure 2: Overlay first order derivative spectrum of Ondansetron in sodium acetate buffer [A]

phosphate buffer pH 3.6 [B] phosphate buffer pH 5.0 [C] phosphate buffer pH 7.0 [D] borate buffer pH 9.0 [E]

A graph was drawn by taking the concentration on the x-axis and the corresponding derivative absorbance on the y-axis for the data obtained in method A, B, C, D and E. Beer-Lambert's law was obeyed over the concentration range 0.5-60 µg/mL for method A, B, C, D and E (Figure 8, 9, 10 and 11) respectively. The linear regression equations for method A, B, C, D and E were found to be $y = 0.0013x + 0.0003$ ($R^2=0.9992$), $y = 0.0014x + 0.0008$ ($R^2=0.9993$), $y = 0.0012x + 0.0018$ ($R^2=0.999$), $y = 0.0012x + 0.0011$ ($R^2=0.999$) and $y = 0.006x + 0.0016$ ($R^2=0.9992$).



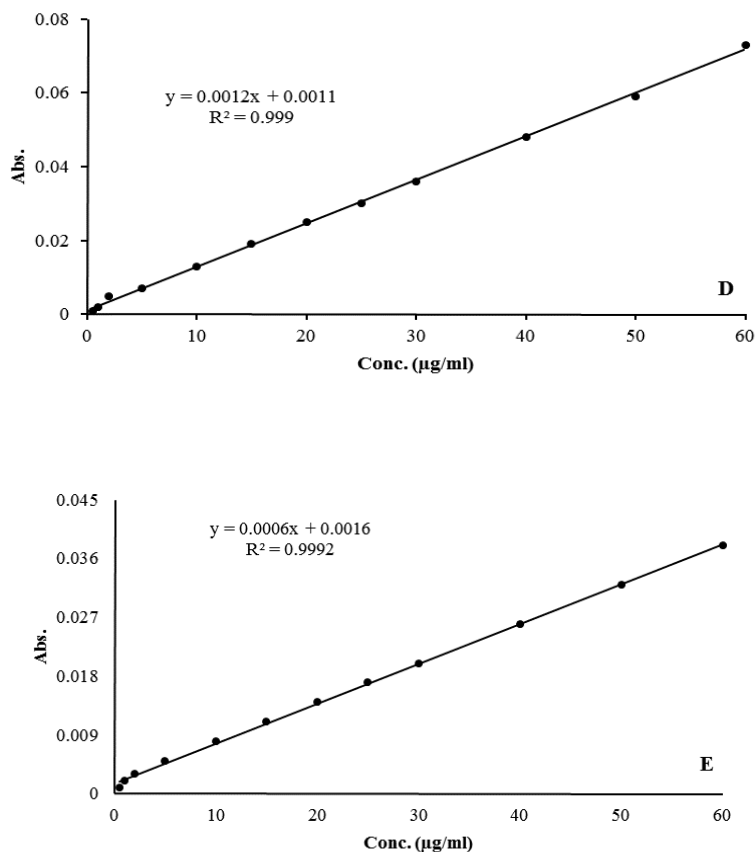


Figure 7: Linearity plot of Ondansetron hydrochloride in sodium acetate buffer pH 4.0 [A] phosphate buffer pH 3.6 [B] phosphate buffer pH 5.0 [C] phosphate buffer pH 7.0 [D] Borate buffer pH-9.0 [E].

The %RSD in precision and accuracy studies were found to be less than 2% in methods A, B, C, D and E indicating that the methods are more precise and accurate. The optical characteristics were shown in Table 1. The % recovery was found to be 99.5-99.9, 99.4-99.8, 99.5-99.7, 99.2-99.7 and 99.3-99.5 for methods A, B, C, D and E respectively in marketed formulations (Table 2).

Table 1: Optical characteristics of Ondansetron.

Parameters	Sodium Acetate buffer pH-4.0	Phosphate buffer pH-3.6	Phosphate buffer pH-5.0	Phosphate buffer pH-7.0	Borate buffer pH-9.0
Wavelength (maxima) (nm)	297nm	296 nm	296nm	296nm	296nm
Linearity range (µg/mL)	0.5-60	0.5-60	0.5-60	0.5-60	0.5-60
Slope	0.0013	0.0014	0.0012	0.0012	0.006
Intercept	0.0003	0.0008	0.0018	0.0011	0.0016
Correlation coefficient	0.9992	0.9993	0.999	0.999	0.9992

Precision (% RSD) Intra-day (n=3)	0.46	0.30	0.30	0.40	0.76
Inter-day (n=3)	1.00	0.61	0.60	1.11	1.52
Accuracy (% recovery) (% RSD)	98.56-98.62 (0.22)	98.92-99.16 (0.30)	99.78-100.01 (0.31)	99.64-99.80 (0.17)	99.69-100 (0.38)

Table 2: Analysis of Ondansetron commercial formulation (Tablets)

Brand	Labeled Amount (mg)	Amount obtained (mg)					% Recovery*					% RSD*				
		Method					Method					Method				
	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	
I	10	9.97	9.96	9.97	9.92	9.94	99.7	99.6	99.7	99.2	99.4	0.11	0.32	0.22	0.31	0.11
II	10	9.99	9.98	9.96	9.95	9.95	99.9	99.8	99.6	99.5	99.5	0.25	0.18	0.16	0.14	0.31
III	10	9.95	9.94	9.95	9.97	9.93	99.5	99.4	99.5	99.7	99.3	0.35	0.22	0.38	0.09	0.22

Conclusion:

The proposed methods are simple, precise and accurate and can be applied for the determination of Ondansetron HCl in pharmaceutical formulations successfully.

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Corresponding Author:

Mukthinuthalapati Mathrusri Annapurna*,

Email: mathrusri2000@yahoo.com