

Simultaneous Estimation of Ondansetron and Pantoprazole in Solid Dosage Form by First Derivative Spectroscopy Method

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Abstract: The objective of this work was to develop and validate simple, rapid, and accurate UV spectrophotometric method for simultaneous determination of Ondansetron and Pantoprazole in enteric coated tablet dosage form. UV spectrophotometric method involves first derivative spectroscopy using 288.5 nm and 310 nm as zero crossing point for Pantoprazole and Ondansetron respectively. For spectrophotometric method, water was used as a solvent. Both the drug and their mix obeyed Beer- Lambert's law at selected wavelength was observed in concentration range of 0.5-2.5ug/ml of Ondansetron and 5-25ug/ml of Pantoprazole. Results of analysis were analyzed and validated for various parameters according to ICH guidelines. This method was found to be simple, precise, accurate, selective and rapid and can be successfully applied for the determination of pure laboratory mixtures and tablet formulations.

Keywords: First derivative spectroscopy, Ondansetron (OND), Pantoprazole (PAN), marketed formulation, and Beer-Lambert Law.

I. Introduction

Ondansetron (OND), 9-Methyl-3-(2-Methyl-1H-imidazol-1-yl)-2, 3-dihydro-1H-carbazol-4(9H)-one, antagonizes 5HT-3 receptor both peripherally as well as centrally, block the initiation of the reflux, so is used as antiemetic. Ondansetron combination with proton pump inhibitors has recently been introduced in the market for the treatment of peptic ulcer, gastroesophageal reflux disease (GERD) and to prevent nausea [1]. Ondansetron is official in USP [2], BP [3], and reported in Martindale [4], and Merck index [5]. Pantoprazole (PAN), 5-(Difluoromethoxy)-2-[[3,4-dimethoxy-2-pyridinyl]Methyl]sulfinyl-1H-Benzimidazole, is a proton pump inhibitor, which suppresses gastric acid secretion by H⁺/K⁺-ATPase enzyme system at the secretory surface of the gastric parietal cell [6]. This drug is used for the treatment of duodenal, gastric and esophageal ulceration. Pantoprazole is not an official drug but is reported in Merck index [7], Martindale [8]. Literature survey revealed that several methods are reported for the determination of Ondansetron by UV [9] [10], HPTLC [11], RP-LC-UV [12], HPLC [13]. Ion pair RP-HPLC [14] [15], LC [16] in solid dosage form and biological fluids. For Pantoprazole, method reported as HPLC [17] in human plasma, simultaneous estimation by HPLC, HPTLC [18], UV [19] [20]. As no analytical method has so far been indicated for the Ondansetron combination with Pantoprazole, an attempt has been made to estimate them by first order derivative spectrophotometry.

II. Materials And Method

2.1 Materials

Ondansetron reference standard was obtained as a gift sample from Neon Lab LTD., Mumbai, while Pantoprazole from Zim Lab., Nagpur and Cadila pharma Ltd, Ahmadabad. The drug sample (Tablet), Vomizen-P manufactured by Wintech Pharma, Mumbai was procured from the market. Label claim for PAN and OND were 40 mg and 4 mg respectively. All other reagents used were of analytical grade for spectrophotometry. Water was used as a mobile phase. Shimadzu UV/Vis double beam spectrophotometric method.

2.2 Methods

Accurately weighed amount of standard OND (25mg) and PAN (25mg) were transferred to 100ml volumetric flask separately, dissolved and diluted up to mark with water. The resulting solution was filtered through Whatman filter paper No.41. All solutions were prepared freshly. An aliquot portion of the standard stock solution of OND and PAN were further diluted with water to get the series of concentration of 0.5-2.5 ug/ml for OND and 5-25ug/ml for PAN. The 10ug/ml standard solution of both the drug were scanned in spectrum mode from 400-200nm and the absorption spectra so obtained (Fig 1 and Fig 2 for OND and PAN respectively) were derivatized to obtain first order derivative spectra which are shown in Fig 3 and Fig 4 for OND and PAN respectively and overlain spectra to obtain zero cross point is shown in Fig 5. From first order derivative spectra of PAN and OND in water, zero crossing point 288.5nm and 310nm for PAN respectively were selected for simultaneous estimation of two drugs. The absorption of above were diluted were recorded in 1st order derivative in quantitation mode at 288.5nm for estimation of OND and 310nm for PAN. Respective calibration curve were plotted between amplitudes observed at 1st order (n=1), for two drugs at two wavelengths

against the concentration in the range of 0.5-2.5ug/ml and 5-25ug/ml for OND and PAN respectively. Estimation of these two drug was done by solving the regression equation i.e. OND, $y=0.001x-0.0011$ and for PAN $y=-0.0118x+0.0117$. The concentration of individual drug present in the mixture was determined against calibration curve in quantitation mode. Validity of proposed method was checked by preparing five mixed standard in the ratio 1:10 w/w for OND and PAN respectively. Absorbance value were measured at respective selected zero cross point and concentration of two drugs, using respective calibration curve were determined. Validation studies gave satisfactory results. Twenty tablets were accurately weighed and finely powdered. An accurately weighed amount equivalent to 40mg of PAN (equivalent to 4 mg of OND) was transferred to 100ml volumetric flask with 50ml of water. The flask was mechanically shaken for 10 min; finally volume was made to mark with water and filtered. An aliquot of 2.5 ml from stock solution was transferred to different volumetric flasks having 50ml capacity and volume was made to the mark with the water to give a solution containing 2ug/ml of OND and 20 ug/ml of PAN. This solution was analyzed spectrophotometrically at 288.5 nm and 310 nm.

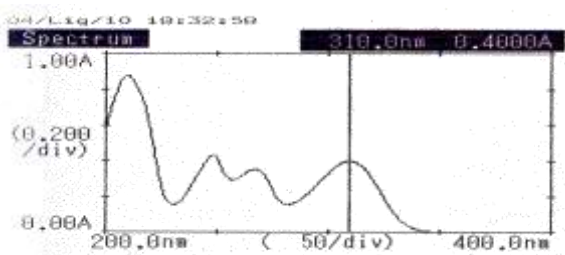


Fig 1. UV spectrum of Ondansetron

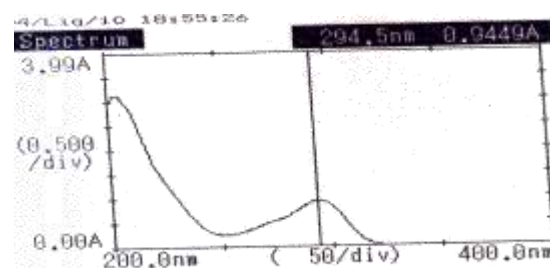


Fig 2. UV spectrum of Pantoprazole

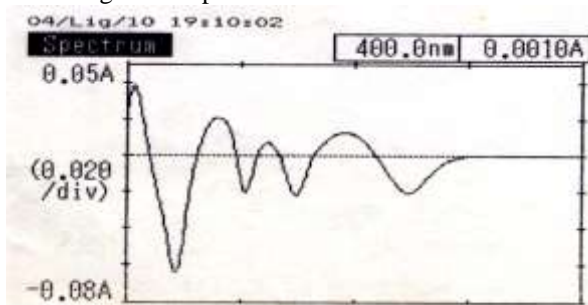


Fig 3. Derivative spectra of Ondansetron

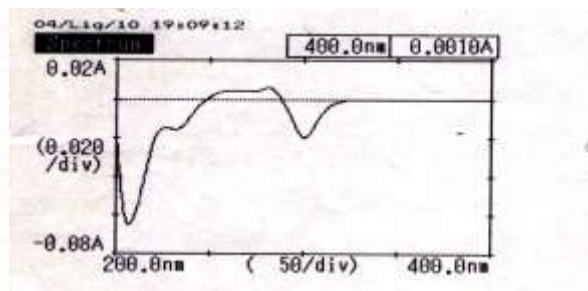


Fig 4. Derivative spectra of Pantoprazole

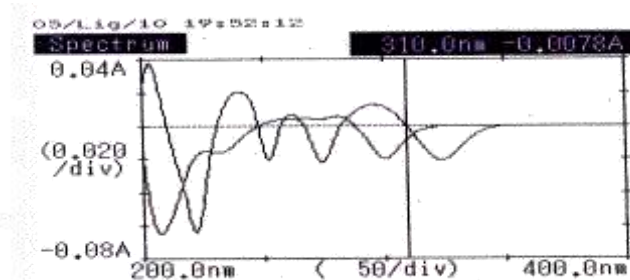


Fig 5. Overlain first order derivative spectrum of PAN and OND

III. Results And Discussion:

First derivative absorbance at these wavelengths was substituted in the straight line equation to calculate the amount of the drug present. Result of analysis is reported in Table 1.

Table 1 Assay result of marketed formulation

Formulation	Actual concentration (mg/tab)		%OND	%PAN
	OND	PAN		
Tablet	4	40	100.17	1000.42

Accurate, reproducibility and precision of the proposed method were studied with the help of recovery studies that was carried out by addition of standard drug solution to pre analyzed sample at three different levels. The mean of % recovery was calculated by using formula, $\% \text{ Recovery} = (T-A)/S \times 100$, where, T is total amount

of drug contributed by tablet powder and S is the amount of pure drug added. The result of recovery studies for OND and PAN was found to be around 99-100%, indicating that the method are free from interference from excipient and reported in Table 2. The concentrations of two drug were measured three times on the day at intervals of 3 h and on three different days over a period of one week for intra and inter day study respectively. The limit of detection (LOD) and limit of quantitation (LOQ), were calculated by use of the equation $LOD = 3.3 / s$ and $LOQ = 10 / s$, where s is the standard of the blank and S is the slope of the calibration curve, which are shown in Table 3. The linear regression equation obtained were: absorbance at 288.5 nm, $y = 0.001x - 0.0011$ (for OND $r^2 = 0.9994$) and 310nm, $y = -0.0118x + 0.0117$ (For PAN $r^2 = 1$). Assay values of OND and PAN were found to be 100.17 and 100.42 respectively with standard deviation of < 1.0 (Table 1). In first derivative UV spectroscopy, proper selection of zero crossing point completely eliminates the interference of unwanted component and thus concentration of two component can be easily calculated without prior separation of components from combined dosage form.

Table 2 Analysis data and recovery studies

Sample Code	Statistical Data	%Label Claim	
		OND	PAN
Laboratory Mixture (%Estimation)	Mean	99.77	100.19
	SD	0.7092	0.5349
	RSD	0.0071	0.0053
Vomizen- P Tablet (%Label Claim)	Mean	100.17	100.42
	SD	0.2106	0.2730
	RSD	0.0021	0.0027
Recovery Study (%Recovery)	Mean	100.13	99.96
	SD	0.2027	0.0918
	RSD	0.0020	0.0009
	LOQ	0.67	0.30
	LOD	2.03	3.92

Table 3 Result of ruggedness studies

Parameter	Statistical Data	OND	PAN
Intraday	Mean	100.40	99.93
	SD	0.5656	0.0989
	RSD	0.0056	0.0009
	CV	0.5634	0.0990
	SE	0.3265	0.0571
	LOQ(ug/ml)	0.5656	0.0083
	LOD(ug/ml)	0.1866	0.0027
Interday	Mean	99.97	99.93
	SD	0.0472	0.0989
	RSD	0.0004	0.0009
	CV	0.0472	0.0990
	SE	0.0272	0.0571
	LOQ(ug/ml)	0.0472	0.0083
	LOD(ug/ml)	0.0155	0.0027
Different Analyst	Mean	99.96	99.86
	SD	0.0472	0.0989
	RSD	0.0004	0.0009
	CV	0.0472	0.0991
	SE	0.0272	0.0571
	LOQ(ug/ml)	0.0472	0.0083
	LOD(ug/ml)	0.0155	0.0027

IV. Conclusion

From the result it can be concluded that the proposed first derivative spectrometric method is accurate, simple, rapid and selective for simultaneous estimation of Ondansetron and Pantoprazole in tablet dosage form. Hence it can be conveniently adopted for routine quality analysis of the solid dosage form.

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