

Spectrophotometric Simultaneous Estimation of Ranitidine Hydrochloride and Ondansetron hydrochloride from Tablet Formulation

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Three simple, accurate, economical and reproducible UV spectrophotometric methods for simultaneous estimation of two component drug mixture of ranitidine hydrochloride and ondansetron hydrochloride from combined tablet dosage form have been developed. First developed method involves formation and solving of simultaneous equations at 267.2 nm and 314.4 nm. Second method was developed making use of first order derivative spectroscopy using 340.8 nm and 276.0 nm as zero crossing points for estimation of ranitidine hydrochloride and ondansetron hydrochloride respectively. Third method is based on two wavelength calculation, wavelengths selected for estimation of ranitidine hydrochloride were 266.1 nm and 301.8 nm and for ondansetron hydrochloride 305.7 nm and 319.2 nm. The results of analysis have been validated statistically and by recovery studies.

Ranitidine hydrochloride, chemically 1,1-ethenediamine-N-[2-[[[5-[(dimethylamino)methyl]-2-furanyl]-methyl]thio]ethyl]-N'-methyl-2-nitro hydrochloride is an H₂-receptor antagonist indicated for the duodenal ulcer¹. Literature survey reveals that for ranitidine hydrochloride HPLC^{3,4}, spectrophotometric⁵ and capillary electrophoresis^{6,7} methods have been reported for its determination from human plasma and

commercial formulation. Ondansetron hydrochloride, chemically 4H-carbazol-4-one-1,2,3,9-tetrahydro-9-methyl-3-[(2-methyl-1H-imidazole-1-yl) methyl] hydrochloride is a selective 5-HT₃ receptor antagonist indicated for the prevention of nausea and vomiting². Three HPLC⁸⁻¹⁰ and one LC¹¹ methods have been reported in literature for estimation of ondansetron hydrochloride from human plasma and commercial formulation. However no spectrophotometric method is yet reported for simultaneous analysis of two drugs from combined pharmaceutical dosage form.

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A systronics UV/Vis spectrophotometer (model 2101) with 1 cm matched quartz cells was used for spectrophotometric analysis. Spectra were recorded using specific program of instrument, having specifications as, spectral band width 2 nm, wavelength accuracy ± 0.5 nm, wavelength readability 0.1 nm increment. Double distilled water was used for the preparation of 0.1N hydrochloric acid. The tablet samples of combined dosage form of ranitidine hydrochloride and ondansetron hydrochloride [Ranidom-O (Mankind Laboratories, New Delhi), Doran-O (Bestochem Formulation Ltd, Delhi), Rani-O (Prime Life Pharmaceuticals, New Delhi)] were procured from the local market.

For method I pure drug sample of ranitidine hydrochloride and ondansetron hydrochloride were dissolved separately in 0.1 N hydrochloric acid so as to give six dilutions of standard in concentration range of 50-500 $\mu\text{g/ml}$ of ranitidine hydrochloride and 2-30 $\mu\text{g/ml}$ of ondansetron hydrochloride. All solutions were scanned in wavelength range of 220 nm and 380 nm. Fig. 1 represents the overlain spectra of ranitidine hydrochloride and ondansetron hydrochloride in 0.1N hydrochloric acid. Two wavelengths selected for formation and solving of simultaneous equations were 267.2 nm and 314.4 nm. Absorptivity coefficients of both the drugs were determined at selected wavelengths. Absorptivity coefficient for ranitidine

hydrochloride at 267.2 nm and 314.4 nm were 25.32 and 35.78 $\text{cm}^{-1}\text{g}^{-1}$, while respective values for ondansetron hydrochloride were 461.0 and 481.66 $\text{cm}^{-1}\text{g}^{-1}$. Set of two simultaneous equations thus formed are $A_1 = 461.0C_1 \pm 25.32C_2$ and $A_2 = 481.66C_1 \pm 35.78C_2$, where A_1 and A_2 are absorbance of sample solution at 267.2 nm and 314.4 nm, respectively. C_1 and C_2 are concentration of ranitidine hydrochloride and ondansetron hydrochloride respectively in sample solution in g/l. Validity of above formed equations was checked by preparing five mixed standards using pure drug sample of two drugs, results of which are reported in Table 1.

Twenty tablets were accurately weighed and average weight per tablet was determined. Tablets were ground to fine powder and tablet powder equivalent to 150 mg of ranitidine hydrochloride was accurately weighed and extracted four times with 20 ml portions of 0.1 N hydrochloric acid and filtered through Whatman filter paper no. 41 in to a 100 ml volumetric flask, filter paper was washed with 0.1 N hydrochloric acid adding washings to the filtrate and volume was made up to the mark with the same. From the above filtrate 1 ml was further diluted to 10 ml with 0.1N hydrochloric acid. Absorbance of this final diluted solution was measured at 267.2 nm and 314.4 nm respectively and concentration of two drugs in the sample were calculated using the simultaneous equations. Results of

TABLE 1: RESULTS OF VALIDATION STUDIES FOR METHOD I, II & III USING MIXED STANDARDS

Sample No.	Conc present (mcg/ml)		% Conc. Found					
	RDN	OST	Method I		Method II		Method III	
			RDN	OST	RDN	OST	RDN	OST
01	500	04	99.96	98.75	101.36	98.44	99.82	99.12
02	400	08	101.60	102.12	101.25	98.34	98.29	98.48
03	300	12	100.38	100.30	98.16	96.90	98.96	98.72
04	200	16	101.72	100.29	100.71	98.34	100.20	100.45
05	100	20	99.60	98.94	99.78	99.36	99.02	98.75

RDN denotes ranitidine hydrochloride and OST is ondansetron hydrochloride

TABLE 2: RESULTS OF ANALYSIS OF COMMERCIAL FORMULATION

Method	Brand	Label claim (mg/tab)		% of label claim estimated*		Standard deviation		% Recovery**	
		RDN	OST	RDN	OST	RDN	OST	RDN	OST
Method I	A	150	04	99.77	99.58	0.464	0.542	99.65	99.02
	B	150	04	98.93	100.23	0.542	0.621	98.98	99.23
	C	150	04	99.22	101.04	0.422	0.508	99.29	99.11
Method II	A	150	04	99.48	99.12	0.489	0.512	100.11	99.58
	B	150	04	100.58	98.82	0.528	0.488	99.66	101.13
	C	150	04	100.62	98.97	0.569	0.501	101.21	100.72
Method III	A	150	04	99.83	99.22	0.569	0.603	98.62	100.19
	B	150	04	99.25	99.29	0.572	0.452	99.28	98.92
	C	150	04	100.01	98.94	0.621	0.585	98.98	99.44

RDN denotes ranitidine hydrochloride and OST is ondansetron hydrochloride. *Average of three determinations and **Average of determination at three different concentration levels. Brand A is Ranidom-O, Brand B is Doran-O and Brand C is Rani-O

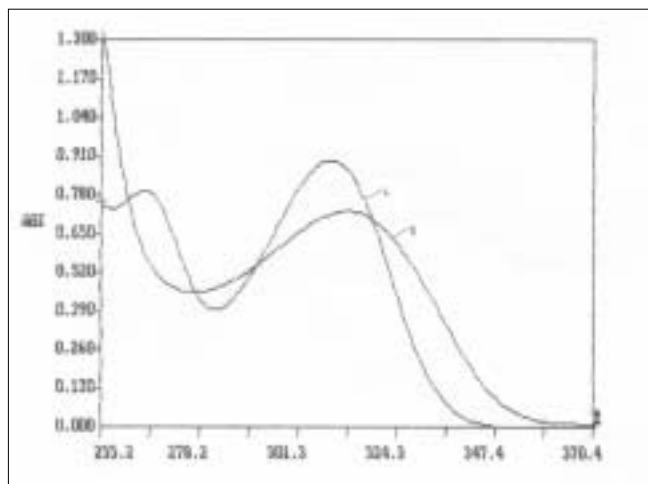


Fig. 1: Overlain spectra of two drugs

A: Spectra of ranitidine hydrochloride in 0.1 N hydrochloric acid and B: Spectra of ondansetron hydrochloride in 0.1 N hydrochloric acid.

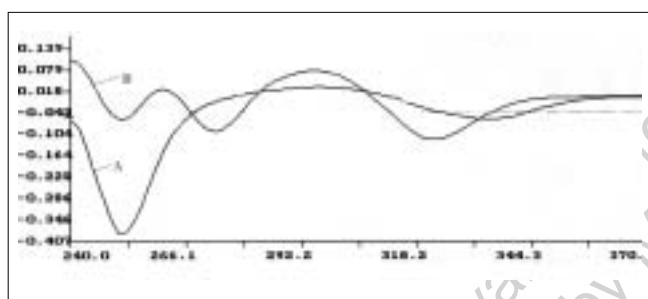


Fig. 2: Overlain first order derivative spectra of two drugs

A: First order derivative spectra of ranitidine hydrochloride in 0.1 N hydrochloric acid and B: First order derivative spectra of ondansetron hydrochloride in 0.1 N hydrochloric acid.

analysis of tablet formulation are reported in Table 2. The second developed method is first order derivative spectroscopy. From first order derivative spectra of ranitidine hydrochloride and ondansetron hydrochloride in 0.1 N hydrochloric acid (fig. 2) zero crossing points 340.8 nm and 276.0 nm were selected for simultaneous estimation of two drugs. Accurately weighed pure drug sample of ranitidine hydrochloride and ondansetron hydrochloride were dissolved in 0.1 N hydrochloric acid so as to give six dilutions in concentration range of 50-500 $\mu\text{g/ml}$ for ranitidine hydrochloride and 2-30 $\mu\text{g/ml}$ for ondansetron hydrochloride. The absorbance of these solutions was recorded in first derivative mode at 340.8 nm for estimation of ranitidine hydrochloride and 276.0 nm for estimation of ondansetron hydrochloride and respective calibration curves were prepared. Validity of proposed method was checked by preparing five mixed standards using pure drug sample of two drugs

and absorbance was measured at respective selected zero crossing points and determined concentration of two drugs using respective calibration curve. Results of validation studies are reported in Table 1.

Tablet sample solution was prepared in similar manner as for method I, absorbance of final sample solution was recorded at 340.8 nm and 276.0 nm from first derivative spectra of sample and amount of two drugs were calculated using respective calibration curve. Results of analysis are reported in Table 2.

The third developed method is two wavelength calculation method. From absorption spectra of ranitidine hydrochloride and ondansetron hydrochloride (fig.1), set of two wavelengths λ_1 (266.1 nm) and λ_2 (301.8 nm) for estimation of ranitidine hydrochloride and λ_3 (305.7 nm) and λ_4 (319.2 nm) for estimation of ondansetron hydrochloride were selected on basis of principle that absorbance difference between two points on a mixture spectra is directly proportional to concentration of component of interest and independent of interfering component¹². Five mixed standards containing different concentration of pure drug sample of two drugs were prepared in 0.1 N hydrochloric acid. All standards were scanned at respective set of selected wavelengths. Absorbance difference was measured and respective calibration curve was plotted.

Tablet sample solution was prepared in similar manner as for method I, final sample solution was analyzed by scanning at respective set of wavelength and absorbance difference values were noted, the concentration of ranitidine hydrochloride and ondansetron hydrochloride was calculated from the respective calibration curve. Result of analysis is reported in Table 2.

To study the accuracy, reproducibility and precision of the above developed methods recovery studies were carried out by addition 0.5, 1.0 and 1.5 ml of standard drug stock solution (100 $\mu\text{g/ml}$) to pre-analyzed tablet sample solutions. Results of recovery studies were found to be satisfactory and are reported in Table 2.

Three spectrophotometric methods have been developed for simultaneous estimation of ranitidine hydrochloride and ondansetron hydrochloride from combined tablet dosage form. The first developed

method involving formation and solving of simultaneous equations is very simple and requires only the accurately determined absorptivity of the two drugs at two selected wavelengths. The method just requires recording of absorbance and few calculations that can be manually done, thus method can be used with any model of spectrophotometer. Once the equations are framed the method is very fast. Framed equations were validated using laboratory prepared mixed standards of two drugs which gave satisfactory results.

Second developed method for simultaneous analysis of ranitidine hydrochloride and ondansetron hydrochloride from combined dosage form make use of first derivative ultraviolet spectrophotometry based on principle that at zero crossing point of one component the other component have substantial absorbance.

Third developed method for simultaneous analysis of ranitidine hydrochloride and ondansetron hydrochloride make use of two wavelength calculation so as to remove interference between two components. Proper selection of two wavelengths for estimation of a component is critical.

The results of analysis of two drugs from tablet formulation using all the three developed methods were found close to 100% for both ranitidine hydrochloride and ondansetron hydrochloride, standard deviation was satisfactorily low indicating accuracy and reproducibility of the methods. Recovery studies were satisfactory which shows that there is no interference of excipients. The developed methods were found to be simple, rapid, accurate and can be used for routine analysis of two drugs from tablet formulations.

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