

**SIMULTANEOUS ESTIMATION OF OLMESARTAN MEDOXOMIL AND HYDROCHLOROTHIAZIDE IN TABLET DOSAGE FORM
BY UV- SPECTROPHOTOMETRIC METHOD****Sonali P. Mahaparale^{1*}**, Yogesh S. Andhale¹, Vishwajeet H. Sonawane¹ and Indrajeet D. Gonjari²¹Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune-411 044, Maharashtra, India.²Government college of Pharmacy, Vidyanagar, Karad- 415 110 Maharashtra, India.**ABSTRACT**

Olmesartan medoxomil is a selective AT₁ subtype angiotensin II receptor antagonist and used as antihypertensive. Hydrochlorothiazide (HCT) is one of the oldest and widely used thiazide diuretics. Two simple, accurate and economic methods; Q analysis and first order derivative method have been described for the simultaneous spectrophotometric estimation of olmesartan medoxomil and hydrochlorothiazide in tablet dosage form. Absorption maxima of olmesartan medoxomil and hydrochlorothiazide in distilled water were found to be 256.0 nm and 271.5 nm respectively. Beer's law was obeyed in the concentration range 5-40 µg/ml for olmesartan medoxomil and 5-40 µg/ml for hydrochlorothiazide. In Q analysis method, absorbances were measured at the selected wavelengths, 231.0 nm (isoabsorptive point) and 271.5 nm (λ_{max} of HCT). In first order derivative method, zero crossing point of OLM and HCT were selected at 256.0 nm and 271.5 nm respectively. The analysis of binary pharmaceutical formulation was carried by both methods. Results of two methods were validated statistically by recovery studies and were found to be satisfactory.

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Ultraviolet spectrophotometry, Q
- Analysis method and First order
method.**INTRODUCTION**

Olmesartan medoxomil is a selective AT1 subtype angiotensin II receptor antagonist and used as antihypertensive¹. Chemically it is 2, 3-dihydroxy-2-butenyl-4-(1-hydroxy-1-methylethyl)-2-propyl-1-[p-(o-1-Htetrazol-5-ylphenyl) benzyl] imidazole-5- carboxylate, cyclic-2, 3-carbonate². Hydrochlorothiazide (HCT) is one of the oldest and widely used as thiazide diuretics. Chemically it is 6-chloro-1, 1-dioxo-3, 4-dihydro-2 H-1, 2, 4-benzothiadiazine-7-sulfonamide^{3,4}. Olmesartan medoxomil (OLM) and Hydrochlorothiazide (HCT) are available in tablet dosage form in the ratio 20:12.5. Olmesartan medoxomil is official in Martindale, The Extra Pharmacopoeia¹ and The Merck Index², whereas Hydrochlorothiazide is official in I. P.³, B. P.⁴, U. S. P.⁵ and Martindale, The Extra Pharmacopoeia¹. Literature survey reveals that many analytical methods such as spectrophotometric^{6,7} and RP-HPLC^{7,8} methods are reported for determination of olmesartan medoxomil individually from pharmaceutical dosage form and RP-HPLC⁹⁻¹² and HPTLC^{12,13} methods are reported for determination of OLM and HCT in combined dosage form. Some RP-HPLC methods¹⁴⁻¹⁷ are reported for determination of OLM or HCT combined with other drugs. This paper represents two simple, rapid, accurate, precise, reproducible and economic UV spectrophotometric methods for simultaneous estimation of OLM and HCT in bulk and tablet dosage form.

MATERIALS AND METHODS

Instrument

A UV/ VIS double beam spectrophotometer, model 1700, with matched quartz cells corresponding to 1 cm pathlength and spectral bandwidth of 2 nm was used in the study.

Materials

Standard gift samples of olmesartan medoxomil (OLM) and hydrochlorothiazide (HCT) were procured from EMCURE Pharmaceuticals Ltd, Pune. Combined olmesartan medoxomil and hydrochlorothiazide tablets were purchased from local market.

Solvent used

Methanol AR grade and distilled water were used as solvents in the study.

Stock solutions

The stock solution (100 μ g/ml) of OLM and HCT were prepared separately by dissolving accurately about 10 mg of each drug in 25 ml methanol AR grade in 100 ml volumetric flask. The volume was adjusted up to the mark with distilled water.

Preparation of calibration curves

Working standard solutions of OLM and HCT were prepared separately from standard stock solution. These solutions were scanned in the spectrum mode from 400.0 nm to 200.0 nm. The maximum absorbance of OLM and HCT was found to be 256.0 nm and 271.5 nm respectively. The linearity of OLM and HCT was found to be in the concentration ranges of 5-40 μ g/ml and 5-40 μ g/ml, respectively, at their respective maximas. The coefficients of correlation were found to be 0.9991 for OLM and 0.9996 for HCT, respectively.

Method I: Q - Analysis method

In the quantitative assay of two components by C analysis method, absorbances were measured at two wavelengths, one being the isoabsorptive point and other being the wavelength of maximum absorption of one of the two components. Solutions of 10 μ g/ml of OLM and HCT were prepared separately. Both the solutions were scanned in the spectrum mode from 400.0 nm to 200.0 nm. From overlain spectra of OLM and HCT, absorbances were measured at the selected wavelengths i.e. 231.0 nm (isoabsorptive point) and 271.5 nm (λ_{max} of HCT). (Fig. 1)

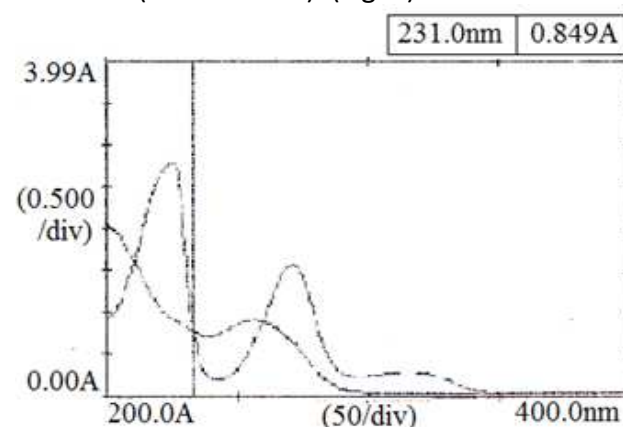


Fig. 1: Overlain UV spectra of Olmesartan medoxomil and Hydrochlorothiazide

The mixed standards having concentrations 10, 15 and 20 µg/ml of OLM and 10, 15 and 20 µg/ml of HCT respectively were prepared and scanned in the spectrum mode from 400 nm to 200 nm. The absorbances of mixed standards were measured at selected wavelength. The concentration of each component can be calculated by mathematical treatment of the following mentioned equation.

For olmesartan medoxomil,

$$C_1 = \frac{Q_m - Q_y}{Q_x - Q_y} \times \frac{A_1}{a_1}$$

For hydrochlorothiazide,

$$C_2 = \frac{Q_m - Q_x}{Q_y - Q_x} \times \frac{A_1}{a_2}$$

Where, C_1 = concentration of OLM

C_2 = concentration of HCT

A_1 = Absorbance of sample at isoabsorptive wavelength 231.0 nm.

a_1 and a_2 = Absorptivity of OLM and HCT at isoabsorptive wavelength 231.0 nm respectively.

$$Q_x = \frac{\text{Absorptivity of OLM at 271.5 nm}}{\text{Absorptivity of OLM at 231.0 nm} + \text{Absorptivity of HCT at 271.5 nm}}$$

$$Q_y = \frac{\text{Absorptivity of HCT at 231.0 nm} + \text{Absorptivity of sample solution at 271.5 nm}}{\text{Absorptivity of sample solution at 231.0 nm}}$$

Analysis of tablet formulation

Each tablet contains 20 mg of OLM and 12.5 mg of HCT. Twenty tablets were weighed and average weight of tablet was determined and crushed to fine powder. The powder sample equivalent to 10 mg of OLM and 6.25 mg of HCT was weighed and transferred to 100 ml volumetric flask. Accurately weighed 3.75 mg of pure HCT was added to the above powder in the volumetric flask to obtain the required concentration of HCT. The total powder mixture obtained was equivalent to 10 mg of OLM and 10 mg of HCT. The powder mixture was dissolved in 25 ml of methanol AR grade and was kept in ultrasonicator for 45 min. Finally, the volume was made up to the mark with distilled water. The solution was filtered through Whatmann filter paper No. 41. The filtrate was further diluted to obtain mixed sample solutions in Beer's-Lambert's range for each drug in the ratio of 1:1 having concentrations 10, 15 and 20 µg/ml of OLM and 10, 15 and 20 µg/ml of HCT, respectively. The absorbances of mixed sample solutions were measured at 231.0 nm and 271.5 nm. These values were equated in the above mentioned equations and the concentration of each drug was calculated (Table 1). Recovery studies were carried out at 80 %, 100 % and 120 % level of label claim (Table 2).

Table 1: Analysis of Tablet Formulation

Metho d	Tablet sample	Label claim (mg/tablet)	Amount found* mg/tablet	% Label claim found*	% RSD
I	OLM	20	19.94	99.70	0.40
	HCT	12.5	12.44	99.52	0.48
II	OLM	20	19.91	99.87	0.29
	HCT	12.5	12.40	99.78	0.32

***Mean of six estimations**

OLM and HCT denote Olmesartan medoxomil and Hydrochlorothiazide respectively.

Table 2: Recovery studies

Method	Level of % Recovery	% Recovery found *		± Standard Deviation		Standard Error	
		OLM	HCT	OLM	HCT	OLM	HCT
I	80	99.91	99.89	0.18	0.20	0.10	0.11
	100	99.93	99.95	0.14	0.11	0.08	0.06
	120	99.85	99.68	0.22	0.35	0.12	0.17
II	80	99.60	99.75	1.04	0.57	0.42	0.23
	100	99.91	99.70	0.16	0.60	0.11	0.25
	120	99.66	99.81	0.82	0.12	0.33	0.06

***Mean of six estimations**

OLM and HCT denote Olmesartan medoxomil and Hydrochlorothiazide respectively.

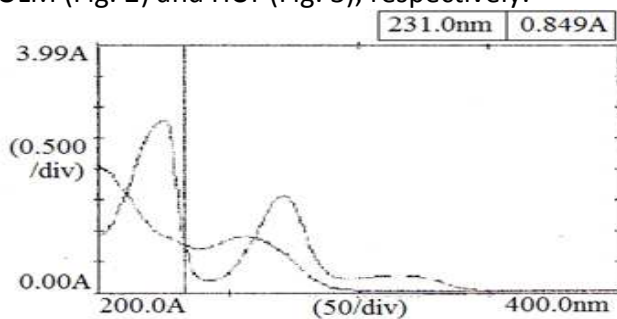
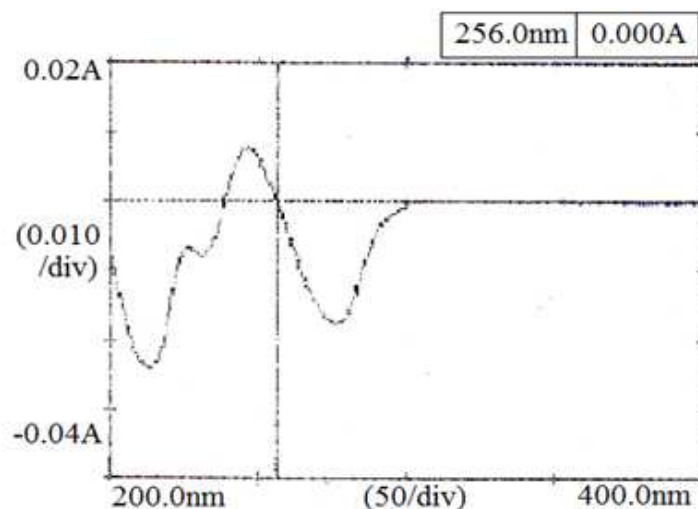
Method I is Q analysis.

Method II is First order derivative method

Method II: First order derivative method

Solutions of 10 µg/ml of OLM and HCT were prepared separately.

Both the solutions were scanned in the spectrum mode from 400.0 nm to 200.0 nm. The absorption spectra thus obtained were derivatized from first to fourth order. First order derivative (n=1) was selected for analysis of both the drugs. The zero crossing wavelengths, 256.0 nm and 271.5 nm were selected for OLM (Fig. 2) and HCT (Fig. 3), respectively.

**Fig. 1:** Overlaid UV spectra of Olmesartan medoxomil and Hydrochlorothiazide**Fig. 2:** First order derivative of Olmesartan medoxomil**Preparation of calibration curves**

The standard dilutions of 5, 10, 15, 20, 25, 30, 35 and 40 µg/ml of OLM and 5, 10, 15, 20, 25, 30, 35 and 40 µg/ml HCT were prepared separately from stock solution and scanned in the spectrum mode from 400.0 nm to 200.0 nm. The absorption spectra obtained were derivatized to obtain first order derivative spectra. The absorbance of standard solutions of OLM and HCT were measured at

zero crossing point of HCT (271.5 nm) and zero crossing point of OLM (256.0 nm) respectively. The working calibration curves of both the drugs were plotted separately.

The mixed standard solutions in Beer's-Lambert's range from 10, 15 and 20 µg/ml of OLM and 10, 15 and 20 µg/ml of HCT, respectively were prepared. The concentration of individual drug present in the mixture was determined against calibration curve of each drug in quantitation mode.

Analysis of tablet formulation

Tablet solution was prepared in methanol AR grade as described earlier and was further diluted with distilled water to obtain mixed sample solutions in Beer – Lamberts' range for each drug in the ratio of 1:1 from 10, 15 and 20 µg/ml of OLM and 10, 15 and 20 µg/ml of HCT, respectively were prepared. The absorbances of mixed sample solutions were measured at 271.5 nm and 256.0 nm. The concentrations of OLM and HCT present in the sample solution were determined against calibration curve in quantitation mode (Table 1). Recovery studies were carried out at 80 %, 100 % and 120 % level of label claim (Table 2). The tablet analysis obtained by proposed method was validated by statistical evaluation^{18,19}.

RESULTS AND DISCUSSION

In Q analysis method, from overlain spectra of OLM and HCT two wavelengths were selected at 231.0 nm (isoabsorptive point) and 271.5 nm (λ_{max} of HCT). OLM and HCT follow linearity in the concentration range 5-40 µg/ml and 5-40 µg/ml respectively. This method is also a simple and easy method.

The first derivative spectrophotometric method requires spectral data processing and hence can be applied only on recording spectrophotometers with such facilities. This method was employed totally to eliminate the spectral interference from one of two drugs while eliminating the other drug. This was achieved by selecting the zero crossing point on the derivative spectra of one drug as the wavelength for estimation of

other drug. First derivative method is simple, less time consuming, no manual calculation is required and gives better results.

All the developed methods were found to be simple, rapid, accurate, precise, reproducible and economic for routine simultaneous estimation of OLM and HCT in bulk and tablet dosage form. The value of standard deviation was satisfactorily low and the recovery was close to 100 % indicating the reproducibility and accuracy of the methods.

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