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Spectrophotometric Method for Simultaneous Estimation of Olmesartan Medoximil and Hydrochlorothiazide in Tablets

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ABSTRACT

Two simple rapid and accurate UV spectrophotometric methods were developed for simultaneous determination of Olmesartan medoximil (OLME) and Hydrochlorothiazide (HCTZ) in pharmaceutical dosages forms. Method-1 Vierodts method and Method -2 Absorbance corrected for interference method. For Vierodts method readings were taken at 256.5 nm λ_{max} of (Olmesartan medoximil) and 271.0 nm λ_{max} of (HCTZ); In absorbance corrected for interference method, absorbance was measured at wavelength 256.5 nm and 318.5nm. Both the drugs obey Beer's law in the concentration range employed for these methods. The marketed tablet formulation analyzed by the above cited method shows good accuracy and precision for method.

Keywords: Olmesartan medoximil, Hydrochlorothiazide, Vierodts method, Absorbance corrected for interference method.

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INTRODUCTION

Olmesartan medoximil chemically (2,3-dihydroxy-2-butenyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-[p-(o-1H-tetrazol-5-ylphenyl)benzyl]imidazole-5-carboxylate, cyclic 2,3-carbonate), is a potent angiotensin antagonist used in treatment of hypertension [1]. Hydrochlorothiazide (6-chloro-3, 4-dihydro-2H-1, 2, 4-benzo-thiadiazine-7-sulfonamide 1, 1-dioxide) [2], is a benzodiazepine class of diuretic. Both the drugs are used in combination for hypertensive patients for whom monotherapy of drug is not effective enough. The combination is not official in any pharmacopeia. The literature survey reveals that number of methods have been reported for OLME and HCTZ individually or in combination with other drugs [3-8]. However there is no method reported for simultaneous estimation of these two drugs. This presents work describes two simple, accurate reproducible and rapid methods for simultaneous estimation of OLME and HCTZ in tablet formulations.

MATERIALS AND METHODS

Instrument

Shimadzu double beam UV visible spectrophotometer model 1700 with 1 cm matched quartz cell was used for all absorbance measurements.

Materials

The pure sample of Olmesartan medoximil and Hydrochlorothiazide were kindly provided by Macleods pharmaceutical Ltd, Daman. Two multicomponent tablet formulations of Olmesartan medoximil and hydrochlorothiazide, Tablet 1-Olmesar^{TM}-H 20 and Tablet 2-Olmesar^{TM}-H 40 were purchased from local pharmacy stores. All chemicals and reagents used were of analytical grade.

Preparation of Standard Stock Solution

Standard stock solution of OLME and HCTZ were prepared individually (1 mg/ml) by dissolving 25 mg of each in 25.0 ml volumetric flask using methanol. Further dilution was made with methanol to get a final concentration of 20 mcg/ml for both drugs.

PROCEDURE

Method-I Vierodt's Method (Simultaneous Equation Method)

The Simultaneous equation method was used because both the drugs absorb at the λ_{max} of each other. From the overlain spectra of the two drugs (As shown in figure: - 1) 256.5 nm and 271.0 nm were selected as sampling wavelengths of OLME and HCTZ, respectively. For linearity studies individual standard solution of 1mg/ml of OLME and HCTZ were serially diluted with methanol to different concentration in range of 8-40 mcg/ml for both the drugs. The data of absorbance versus drug concentration were treated by linear least square regression analysis to

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obtain calibration graph as shown in figure 2 and 3 respectively. Spectral data thus obtained was processed to obtain the absoptivity for these two drugs OLME and HCTZ at wavelengths 256.5 (λ_{max} of OLME) and 271.0 nm (λ_{max} of HCTZ).

The formula used for Simultaneous equation method for determination of OLME and HCTZ is as following,

$$C_x = A_2.ay_1 - A_1.ay_2 / ax_2.ay_1 - ax_1.ay_2$$

$$C_y = A_1.ax_2 - A_2.ax_1 / ax_2.ay_1 - ax_1.ay_2$$

Where C_x and C_y be the concentration of OLME and HCTZ respectively in the diluted sample. A_1 and A_2 are the absorbance of the diluted sample at wavelength 256.5 nm and 271.0 nm. The absorptivity ax_1 and ax_2 are 35.62 and 22.89 of OLME at 256.5 nm and 271.0 nm. a_{y1} and a_{y2} are 23.4 and 56.65, the absoptivity value of HCTZ at 256.5 nm and 271.0 nm.

Figure:-1 Overlay spectra of olmesartan medoximil and HCTZ

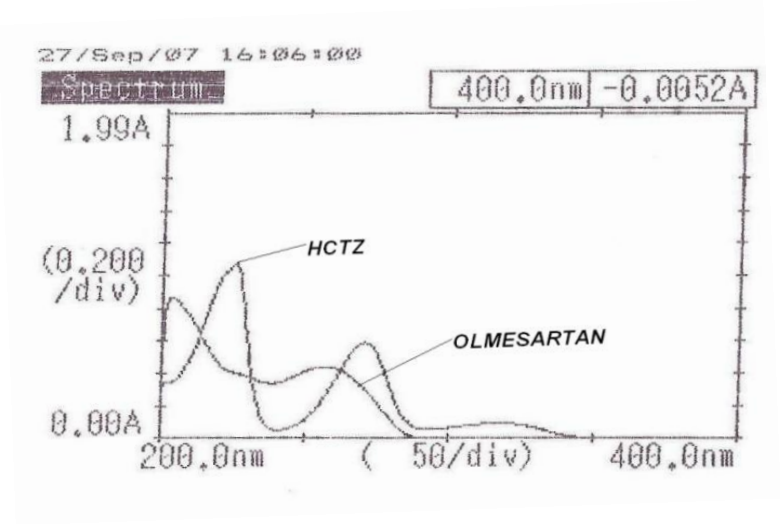
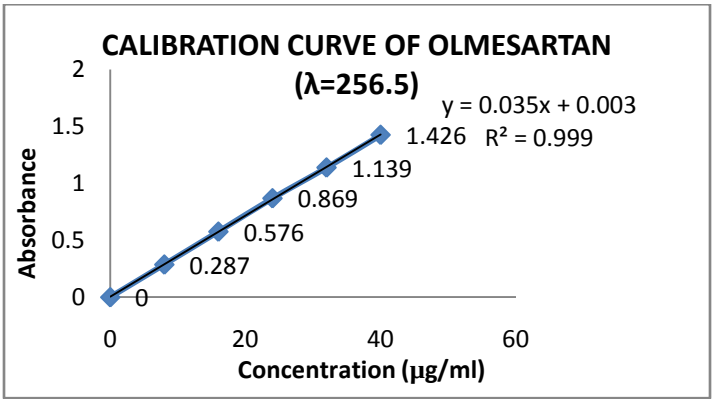


Figure: 2 Calibration curve of Olmesartan medoximil



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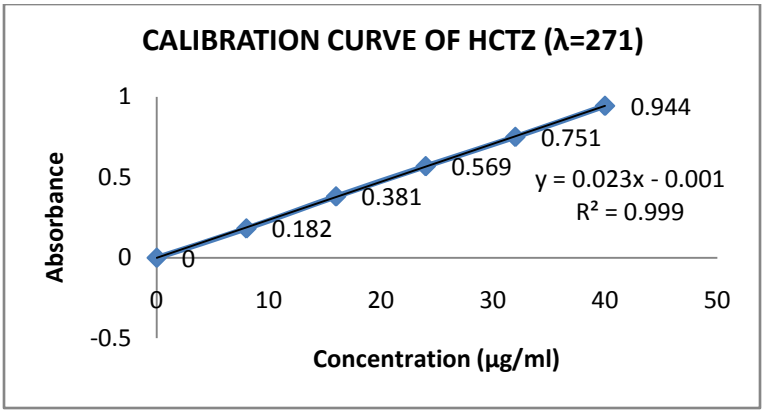

Figure: 3 Calibration curve of Hydrochlorothiazde

Procedure for the Analysis of Tablet Formulation

Twenty tablets were weighed and powdered in a glass mortar. Accurately weighed quantity of tablet powder equivalent to about 12.5 mg of HCTZ was transferred to 50.0 ml volumetric flask, added 30 ml of methanol and sonicated for 10 mins, volume was then made up to the mark with methanol. The solution was mixed and filtered through Whatman Grade I filter paper. From the filtrate, 5.0 ml of the solution was diluted to 25.0 ml with methanol. Further diluted 2.0 ml of this solution to 10.0 ml with methanol. Absorbance of the diluted solution was measured at the selected wavelengths and the amount of the drugs present in the sample solution was calculated by using the above mentioned formula. Results of tablet analysis are presented in Table 1.

Method-2 Absorbance Corrected for Interference Method

The standard solution were diluted with methanol individually so as to get the concentration of 20 mcg / ml for both the drugs this solution were scanned separately in the UV range of 400 nm to 200 nm. Spectral data thus obtained was processed to obtain the absoptivity for these two drugs OLME and HCTZ at wavelengths 256.5 (λ_{max} of OLME) and 318.5 (λ_{max} of HCTZ where absorbance OLME is zero). The A (1%, 1 cm) of Olmesartan medoximil was found 35.62 at 256.5 nm and 0.0 at 318.5 nm (since absorbance of OLME at 318.5 is zero). The A (1%, 1 cm) of HCTZ was found 23.4 at 256.5 nm and 5.19 at 318.5 nm. Content of HCTZ in tablet formulation was calculated by using absoptivity value of HCTZ at 318.5 nm. Content of OLME in tablet was calculated by absorbance corrected for interference method. Absorbance of tablet sample solution at 256.5 nm minus absorbance of HCTZ at 256.5 nm which is calculated by using absoptivity value of HCTZ at 256.5 nm, and concentration of HCTZ in tablet sample which in turn is calculated by dividing absorbance of tablet sample at 318.5 nm with absoptivity value of HCTZ at 318.5 nm. The results are shown in Table - 1.

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Table 1 Results of Tablet Analysis

Tablet	Label claim mg/tab		METHOD I Simultaneous equation method				METHOD II Absorbance corrected for interference			
			Amount of drug estimated* (mg/tab)		% label claim* SD,CV		Amount of drug estimated* (mg/tab)		% label claim* SD,CV	
	OLME	HCTZ	OLME	HCTZ	OLME	HCTZ	OLME	HCTZ	OLME	HCTZ
Tablet-1	20	12.5	19.88	12.41	99.44 ±0.97, 0.97	99.35 ±0.58, 0.56	20.35	12.47	101.75 ±0.87, 0.86	99.83±0 .98,0.97
Tablet-2	40	12.5	39.84	12.46	99.62 ±0.94, 0.94	99.69 ±0.42, 0.42	39.91	12.51	99.79 ±0.97, 0.98	100.1±0 .37, 0.38

*Average of 6 determinations

Procedure for the Analysis of Tablet Formulation

As described under simultaneous equation method.

Validation

The results in (table -2) revealed excellent accuracy and high precision of the assay method. The proposed method when used for subsequent estimation of the drug combination from pharmaceutical dosage forms after spiking with 80%, 100% and 120 % of additional drug afforded recovery of 99 to 101% (table -3). The minimum detectable amount based on the standard deviation of the response and the slope, were found to be 0.85 mcg for OLME and 0.82 mcg for HCTZ. The limit of quantitation based on the standard deviation of response and slope were found to be 2.6 mcg for OLME and 2.52 mcg for HCTZ.

Table: -2 Validations of spectrophotometric methods developed for analysis of tablets

Parameters	Simultaneous equation method		Absorbance corrected for interference method	
	OLME	HCTZ	OLME	HCTZ
Accuracy				
% Mean ±SD	99.44 ±0.97	99.35 ±0.57	101.11 ±0.87	100.89 ±0.98
% RSD	0.9754	0.5737	0.8604	0.9713
Intraday Precision				
% Mean ±SD	101.54 ±0.514	99.98 ±0.746	100.84 ±0.4921	100.05 ±0.4930
% RSD	0.5062	0.7461	0.4880	0.4927
Interday Precision				
% Mean ±SD	99.96 ±0.6869)	100.58 ±0.4163	100.28 ±0.6038	100.12 ±0.6281
% RSD	0.6871	0.4138	0.6021	0.6273

SD: - Standard deviation, RSD: - Relative standard deviation

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Table-3 Recovery Study

Drug	Excess drug added to the analyte (%)	Theoretical content (mg)	Recovery (%) ± SD
OLME	80	36	100.31 ± 1.03
	100	40	100.25 ± 0.89
	120	44	99.72 ± 0.74
HCTZ	80	22.5	100.58 ± 1.33
	100	25	99.86 ± 1.17
	120	27.5	100.52 ± 0.53

SUMMARY AND CONCLUSION

The proposed spectrophotometric methods were found to be simple and rapid. Percent label claim for both the drugs in tablets by proposed methods was in the range of 98 to 101% for OLME and 99-101% for HCTZ. Percent recovery for both the method was nearly 100 %, indicating that there is no interference by excipients in the analysis by proposed methods. Standard deviation for tablet analysis and recovery studies is well below 2 % expressing the precision of the proposed methods. Based on the results obtained it can be concluded that both the method are simple, accurate, precise, economical and less time consuming and can be used for routine quality control of OLME and HCTZ combined dose tablet formulation.

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