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Spectrophotometric Methods for Simultaneous Estimation of Hydrochlorthiazide and Valsartan

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Two simple, rapid, accurate and precise spectrophotometric methods have been developed for simultaneous estimation of hydrochlorthi-azide and valsartan from tablet dosage form. Method **I** involves, formation of Q-absorbance equation at 264 nm (isoabsorptive point) and 270.5 (λ_{max} of hydrochlorthiazide); while method **II** multicomponent mode of analysis involves the measurement of absorbances at two wavelengths 270.5 (λ_{max} of hydrochlorthiazide) and 248.5 (λ_{max} of valsartan) in methanol. The linearity lies between 2-30 µg/mL for hydrochlorthiazide and 2-80 µg/mL for valsartan, respectively. The accuracy and precision of the method was determined and validated statistically. The method showed good reproducibility and recovery with RSD % less than 1. The method was found to be rapid, economical, specific, precise and accurate and can be successfully applied for the routine analysis of hydrochlorthiazide and valsartan in bulk and combined dosage form.

Key Words: Hydrochlorthiazide, Valsartan, Q-Absorbance ratio method, Multicomponent mode of analysis.

INTRODUCTION

Chemically, valsartan[1] is N-(1-oxopentyl)-N-{[2'-(1*H*-tetrazol-5-yl)[1,1-biphenyl]-4yl] methyl}-L-valine. It is second class of drugs known as angiotensis receptor blockers (ARB's) that is used for treating high blood pressure. Literature survey revealed that derivative spectrophotometry[2] and HPLC[3] methods are reported for its estimation in pharmaceutical formulation and human plasma, respectively.

Chemically, hydrochlorthiazide[4] is 6-chloro-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide. It is an orally effective diuretic and anti-hypertensive drug. Hydrochlorothiazide alone or in combination with other drugs is reported to be estimated by spectrophotometry[5], HPLC[6,7], LC-MS[8] and GLC[9].

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Only derivative spectrophotometric method[10] is reported so far for simultaneous estimation of both these drugs from in pharmaceutical formulation. Therefore, it was thought worthwhile to develop a simple spectrophotometric method for estimation of hydrochlorthiazide and valsartan from tablet formulations. In the present work, a successful attempt has been made to estimate both these drugs simultaneously by two simple UV-spectrophotometric methods (absorbance ratio method and multicomponent mode of analysis).

EXPERIMENTAL

Instrument used is UV-Visible double beam spectrophotometer, Make: Shimadzu, Model No.1700 with spectral bandwidth of 2 nm and a pair of 10 mm matched quartz cells. Pure drug samples of valsartan and hydrochlorothiazide were procured as gift sample from Lupin Pharmaceuticals Ltd., Pune. Combined dose tablet formulation (Valent-H) was procured from local medicine shop. Methanol (AR Grade) was used as solvent.

Preparation of stock solution: Accurately weighed quantity of hydrochlorthiazide (5 mg) and valsartan (5 mg) was transferred to two separate 50 mL volumetric flask, dissolved in 30 mL methanol and diluted to the mark with the same solvent (stock solution: 100 µg/mL).

Q-Absorbance ratio method (Method I): Q-Absorbance method uses the ratio of absorbances at two selected wavelengths, one at isoabsorptive point and other being the λ_{max} of one of the two compounds. From the stock solutions, working standard solutions of hydrochlorthiazide (5 µg/mL) and valsartan (32 µg/mL) were prepared by appropriate dilution and were scanned in the entire UV range to determine the wavelength of maximum absorbance (λ_{max}) and isoabsorptive point. Hydrochlorthiazide and valsartan have λ_{max} at 270.5 nm and at 248.5 nm, respectively. Both the drugs were found to have same absorbance at 264 nm (iso-absorptive point). The wavelengths selected for analysis were 264 and 270.5, nm respectively. A series of standard solutions ranging from 5-30 µg/mL for hydrochlorthiazide and 5-80 µg/mL for valsartan were prepared and the absorbance of solutions was recorded at 264 and 270.5 nm to plot a calibration curve of absorbance *versus* concentration. The calibration curves were found to be linear in the concentration range under study. Optical characteristic of both the drugs are presented in Table-1. Absorptivity values of hydrochlorthiazide and valsartan were determined at selected wavelengths and are presented in Table-2.

The concentration of two drugs in the mixture was calculated by using following equations:

$$C_{Hydrochlorthiazide} = \frac{Qm - Qy}{Qx - Qy} \times \frac{A_1}{ax_1} \quad (1)$$

TABLE-1
OPTICAL CHARACTERISTICS AND STATISTICAL DATA OF THE REGRESSION EQUATIONS

Parameters	Hydrochlorthiazide	Valsartan
Absorption maxima (nm)	270.5	248.5
Beers law limit (mcg/mL)	5-30	5-80
Absorptivity	702.58	353.98
Coefficient of correlation	0.9981	0.9991
Regression equation	Y= 0.0070x	Y = 0.0322x
Intercept (A)		
Slope (B)	0.0070	0.0322

TABLE-2
ABSORPTIVITY VALUES (E 1 %, 1 cm) OF HYDROCHLORTHIAZIDE (HTCZ) AND VALSARTAN (VT) AT 264 nm (ISOABSORPTIVE POINT) AND 270.5 nm (METHOD **I**)

S. No.	Absorptivity at 264.0 nm		Absorptivity at 270.5 nm	
	HCTZ	VT	HCTZ	VT
1	559.0	210.370	710.2	141.180
2	557.9	209.470	708.9	142.600
3	558.0	211.270	709.5	141.500
4	558.0	209.000	710.0	141.500
5	559.0	211.520	709.1	141.560
Mean	558.3	210.351	709.5	141.093
SD	± 0.670	± 1.099	± 0.559	± 0.542
RSD (%)	0.120	0.522	0.078	0.371

$$C_{Valsartan} = \frac{Qm - Qx}{Qy - Qx} \times \frac{A_2}{ay_1} \quad (2)$$

where A_1 and A_2 are the absorbances of mixture at 264 and 270.5 nm and ax_1 (558.3), ax_1 (709.5) and ay_1 (210.351), ay_2 (141.093) are absorptivites E (1 %, 1 cm) of hydrochlorthiazide and valsartan at 264 and 270.5 nm, respectively and $Qm = A_2/A_1$, $Qy = ay_2/ay_1$ and $Qx = ax_2/ax_1$.

Multicomponent mode of analysis (Method II): 6 Mixed standard solutions with concentration of hydrochlorthiazide and valsartan in the ratio of 4:25.6, 6:38.4, 8:51.2, 10:64 and 12:76.8 (µg/mL) were prepared in methanol. All the standard solutions were scanned over the range of 400-200 nm, in the multicomponent mode, using two sampling wavelength 248.5 nm (λ_{max} of valsartan) and 270.5 nm (λ_{max} of hydrochlorthiazide). The data from these scans was used to determine the concentrations of two drugs in tablet sample solutions.

Assay of tablet formulation by Method I & II: 20 Tablets were weighed and crushed to obtain fine powder. An accurately weighed quantity of tablet powder equivalent to about 12.5 mg of hydrochlorthiazide and 80 mg of valsartan was transferred to 100.0 mL volumetric flask, dissolved in 20 mL methanol and sonicated for 10 min. The volume was then made up to the mark using same solvent. The resulting solution was filtered through Whatmann grade I filter paper and filtrate was appropriately diluted to get approximate concentration of 5 µg/mL of hydrochlorthiazide and 32 µg/mL of valsartan. Absorbances of sample solutions were recorded at 264 and 270.5 nm and the concentration of two drugs in the sample were determined by using eqns. 1 and 2 (**method I**).

Also the tablet sample solution was subjected to analysis in the multicomponent mode of instrument. The solution was scanned over the wavelength range of 200-400 nm and the concentration of each drug was determined by analysis of spectral data of the sample solution with reference to the mixed standards.

The analysis procedure was repeated 6 times with tablet formulations. The result of analysis of tablet formulation is reported in Table-3.

TABLE-3
RESULTS OF SIMULTANEOUS ESTIMATION OF MARKETED FORMULATION FOR METHOD **I** & **II**

Brand	Tablet content	Label claim (mg/tab)	Label claim (%)	SD	RSD (%)
Method **I**					
Valent H	VT	80.0	101.6	± 0.1095	± 0.1077
(Lupin)	HCTZ	12.5	100.1	± 0.1095	± 0.1093
Method **II**					
Valent H	VT	80.0	100.01	± 0.7333	± 0.7332
(Lupin)	HCTZ	12.5	100.36	± 0.3223	± 0.3214

Mean of six estimations; HTCZ = Hydrochlorthiazide; VT = Valsartan.

Recovery studies: To study the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels. A known amount of drug was added to preanalyzed tablet powder and percentage recoveries were calculated. The results of recovery studies were satisfactory and results are presented in Table-4.

RESULTS AND DISCUSSION

The proposed methods were found to be simple, accurate, economical and rapid for the routine determination of hydrochlorthiazide and valsartan in tablet formulation. The accuracy of the method was determined by

calculating mean percentage recovery. Precision was calculated as repeatability (% RSD is less than 1) and inter and intra day variations (% RSD is less than 1) for both drugs. The repeatability data, ruggedness data are presented in Table-4. Both the methods were successfully used for simultaneous estimation of hydrochlorthiazide and valsartan in combined dosage form.

TABLE-4
RESULTS FOR RECOVERY STUDIES

Brand	Amount of drug added (mcg/mL)		Method **I** Recovery* (%) ± SD		Method **II** Recovery* (%) ± SD	
	HCTZ	VT	HCTZ	VT	HCTZ	VT
Valent-	2.5	16	100.76 ± 0.694	99.34 ± 0.779	99.84 ± 1.083	100.13 ± 0.928
H	5.0	32	100.48 ± 1.403	99.69 ± 0.748	99.53 ± 1.476	99.62 ± 0.610
(Lupin)	7.5	48	100.66 ± 0.650	99.58 ± 1.082	100.14 ± 0.700	99.57 ± 0.550

*Mean of six estimations; HTCZ = Hydrochlorthiazide; VT = Valsartan.

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REFERENCES

1. The Merck Index, Merck Research Lab., Division of Merck & Co., Inc., Whitehouse Station, NJ, edn. 13, p. 1767 (2001).
2. S. Tatar and S. Saglik, *J. Pharm. Biomed. Anal.*, **30**, 371 (2002).
3. N. Daneshtalab, R.Z. Lewanczuk and F. Jamali, *J. Chromatogr. B, Biomed. Sci. Appl.*, **766**, 345 (2002).
4. The Merck Index, Merck Research Lab., Division of Merck & Co., Inc., Whitehouse Station, NJ, edn. 13, p. 854 (2001)
5. D. Erdal and U. Ozgur, *IL Farmaco*, **58**, 1151 (2003)
6. I. Niopas and A.C. Daftsios, *J. Liq. Chromatogr. Rel. Technol.*, **25**, 487 (2002).
7. J. Ouyang, W.R.G. Baeyens, J. Delanghe, G. Van Der Weken, D. De Keukeleire and A.C. Calokerinos, *Biomed. Chromatogr.*, **12**, 162 (1998).
8. T. Takubo, H. Okada, M. Ishii, K. Hara and Y. Ishii, *J. Chromatogr. B*, **806**, 199 (2004).
9. W.J. Vandenheuvel, V.F. Gruber, R.W. Walker and F.J. Wolf, *J. Pharm. Sci.*, **64**, 1309 (1975).
10. N. Erk, *Anal. Lett.*, **35**, 283 (2002).

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