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Research Article

Development and Validation of Spectrophotometric Method for the Simultaneous Estimation of Valsartan and Hydrochlorothiazide

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Abstract

A combination of Valsartan and Hydrochlorothiazide is used to treat angina and hypertension. A new simple, sensitive, accurate and economical spectrophotometric method (simultaneous equation method) has been developed for the estimation of Valsartan and Hydrochlorothiazide in bulk drug and pharmaceutical formulations (Tablets) in phosphate buffer (pH 7.5). The λmax of Valsartan and Hydrochlorothiazide were observed at 250 nm and 272 nm respectively. Valsartan and Hydrochlorothiazide obey Beer-Lambert's law over the concentration range 5-60µg/ml and 0.5-50 µg/ml respectively. The method was validated and is suitable for the routine quality control applications in pharmaceutical formulation.

Keywords: Valsartan; Hydrochlorothiazide; Simultaneous Equation Method; Phosphate Buffer; Validation; ICH guidelines

Introduction

Valsartan (VAL) is an angiotensin II receptor antagonist [1], that is selective for the type I angiotensin receptor and is used in treatment of high blood pressure (Figure 1A). It is chemically, N-(1-oxopentyl)-N- [[2 '-(1H-tetrazol-5-yl) [1,1 '-biphenyl]-4-yl] methyl]-L-Valine ($C_{24}H_{29}N_5O_3$; 435.5 gm/mole). Hydrochlorothiazide (HCTZ) comes to the thiazide class of diuretics (Figure 1B). It is chemically, 6-chloro-3, 4-dihydro-2H-1, 2, 4-benzothiadiazine-7-sulfonamide 1, 1-dioxide ($C_7H_8ClN_3O_4S_2$; 297.73 gm/mole) [2]. The combination of Valsartan and Hydrochlorothiazide is used in treatment of angina and hypertension. The combination of Valsartan and Hydrochlorothiazide was estimated by various analytical techniques and out of which few spectral techniques include absorbance ratio method, first derivative method, ratio spectra derivative and inverse least square methods [3-12]. In the present study the authors have developed a simple and economical method for the simultaneous determination of Valsartan and Hydrochlorothiazide tablets and the method was validated as per ICH guidelines [13].

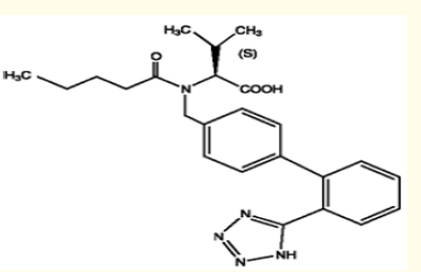

Figure 1A: Structure of Valsartan (VAL).

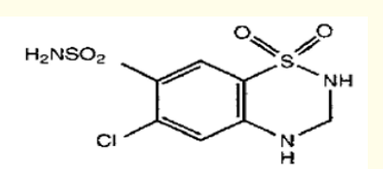

Figure 1B: Structure of Hydrochlorothiazide (HCTZ).

Materials and Methods

Model No. UV-1800 double beam UV-VIS spectrophotometer (Shimadzu) with quartz cells is used for the study and the solutions were scanned (200-400 nm). The combination of Valsartan and Hydrochlorothiazide is available as tables with brand names CO-DIOVAN (Novartis India Ltd.) and VALZAAR-H (Torrent Pharmaceuticals Ltd.) (Labelled claim: Valsartan 80 mg and Hydrochlorothiazide 12.5 mg).

Preparation of solutions

Preparation of phosphate buffer (pH 7.5)

27.218 gm of potassium dihydrogen phosphate was dissolved in water and the pH was adjusted to 7.5 with 0.2 M sodium hydroxide (about 29.1ml) and diluted with water in a 1000ml volumetric flask.

Preparation of stock and working standard solution

Accurately 10 mg of each of Valsartan and Hydrochlorothiazide were weighed and transferred to clean and dry 10 ml volumetric

flasks separately and dissolved in methanol (1000µg/mL) and working standard solutions were prepared on dilution with phosphate buffer pH 7.5. (100 µg/mL) from the stock solutions.

Method validation

Linearity

A series of Valsartan and Hydrochlorothiazide solutions were prepared in phosphate buffer pH 7.5 from the stock solution and scanned (200-400 nm) against reagent blank. Valsartan has shown maximum absorbance at 250 nm (λ_{max}) and that of Hydrochlorothiazide at 272 nm in phosphate buffer pH 7.5 respectively. The absorptivity values of these solutions were calculated from the absorbance values observed in the respective absorption spectra of these two drugs and substituted in the simultaneous equation. Calibration curve were drawn by taking the concentration of the drug on the x axis and the corresponding absorbance values on the y axis.

Precision and accuracy studies

The intra-day and inter-day precision studies were calculated at three different concentration levels and accuracy studies were carried out by standard addition method (50%, 100%, and 150%) and finally the percentage recovery was calculated.

Application of the method to the marketed formulations (Tablets)

Twenty tablets of two different brands containing Valsartan 80 mg and Hydrochlorothiazide 12.5 mg were weighed accurately, powdered and extracted with methanol separately in two different volumetric flasks> Dilutions were made using phosphate buffer pH 4.5 and the percentage recovery of each drug was calculated from the simultaneous equation developed.

Result and Discussion

Method validation

A new simultaneous spectrophotometric method has been developed for the simultaneous determination of Valsartan and Hydrochlorothiazide tablets. The overlay absorption spectra obtained for Valsartan and Hydrochlorothiazide was shown in Figure 2. Beer-Lambert's law was obeyed (Figure 3) over the concentration range 5-50 µg/ml for Valsartan (Table 1) and 1-50 µg/ml for Hydrochlorothiazide (Table 2) respectively. The percentage RSD in precision and accuracy studies was found to be less than 2 indicating that the proposed method is precise (Table 3) and accurate (Table 4).

A set of two simultaneous equations were framed from the absorptivity values and the simultaneous equations are

$A_1 = 333.5\ C_x + 116.9\ C_y$

$A^2 = 165.1\ C_x + 637.2\ C_y$

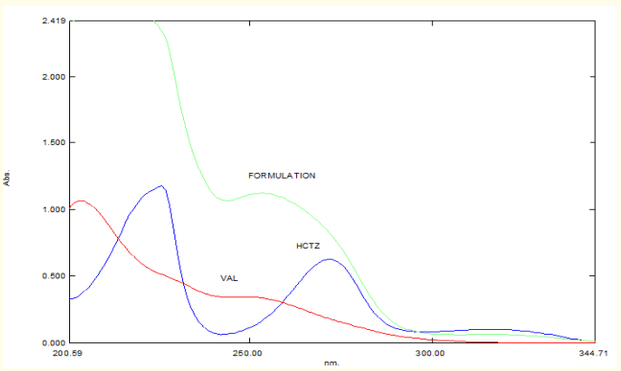

Figure 2: Overlay absorption spectrum of Valsartan (10 µg/mL), Hydrochlorothiazide (10 µg/mL) and tablet formulation.

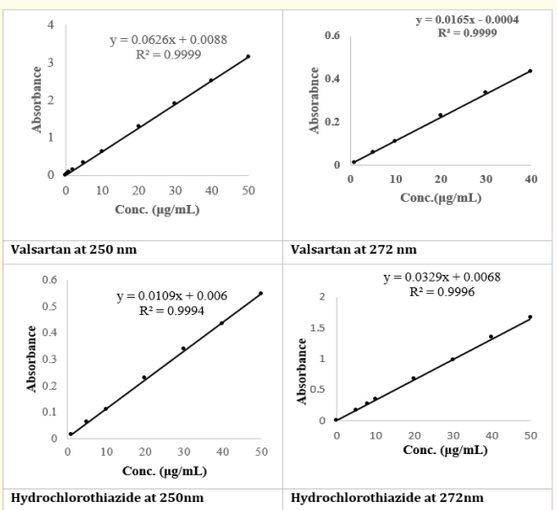

Figure 3: Calibration curves of Valsartan and Hydrochlorothiazide.

Conc. (µg/mL)	Absorbance		Absorptivity		A (1% 1cm)	
	250 nm	272 nm	250 nm	272 nm	250 nm	272 nm
5	0.169	0.083	0.034	0.016	338.0	166.0
8	0.264	0.132	0.033	0.016	330.0	164.6
10	0.342	0.164	0.034	0.016	342.0	164.0
20	0.673	0.327	0.034	0.016	336.5	163.5
30	0.979	0.494	0.033	0.016	326.3	164.7
40	1.348	0.658	0.034	0.016	337.0	164.5
50	1.663	0.823	0.033	0.016	332.6	164.6
Average			0.033	0.016	333.6	165.1

Table 1: Linearity of Valsartan.

Conc. (µg/mL)	Absorbance		Absorptivity		A (1% 1cm)	
	250 nm	272 nm	250 nm	272 nm	250 nm	272 nm
1	0.014	0.065	0.014	0.065	140	650
5	0.061	0.33	0.012	0.066	122	660
10	0.111	0.626	0.011	0.062	111	626
20	0.229	1.29	0.011	0.064	114.5	645
30	0.338	1.883	0.011	0.062	112.6	627.6
40	0.434	2.493	0.010	0.062	108.5	623.2
50	0.548	3.145	0.011	0.062	109.6	629
Average			0.011	0.063	116.9	637.2

Table 2: Linearity of Hydrochlorothiazide.

where A_1 and A_2 are the absorbance of sample solution at 250 nm and 272 nm respectively. C_x and C_Y are the concentrations (µg/mL) of Valsartan and Hydrochlorothiazide respectively in sample solution. The absorbance [A_1 and A_2] of the sample solution obtained at 250 nm and 272 nm respectively and concentration of both the drugs were calculated individually using above mentioned equation.

Application of the method to the marketed formulations (Tablets)

The percentage of purity of Valsartan and Hydrochlorothiazide in tablets was found to be 98.18-98.90 for Valsartan and 98.72-99.12 for Hydrochlorothiazide respectively (Table 5).

Conc. (µg/mL)		Inter-Day Precision			Intra-Day Precision				
	*Assay		*Mean ± SD (%RSD)		*Assay		*Mean ± SD (%RSD)		
VAL	HCTZ	VAL	HCTZ	VAL	HCTZ	VAL	HCTZ	VAL	HCTZ
16	2.5	102.50	99.60	101.56 ± 1.62 (1.6)	99.73 ± 1.006 (0.10)	101.50	98.54	101.56 ± 1.62 (1.6)	98.58 ± 1.006 (0.10)
32	5	102.22	98.20	102.42 ± 1.57 (1.5)	98.33 ± 0.41 (0.42)	100.97	98.00	101.42 ± 1.57 (1.5)	98.13 ± 0.41 (0.42)
48	7.5	103.23	98.13	103.85 ± 0.35 (0.3)	98.35 ± 0.204 (0.21)	102.52	98.53	102.85 ± 0.35 (0.3)	98.65 ± 0.204 (0.21)

Table 3: Precision studies of Valsartan and Hydrochlorothiazide.

*Mean of three determinations

Level	Tablet (µg/mL)		Pure drug (µg/mL)		Recovery (%)		*Mean ± SD (%RSD)	
	VAL	HCTZ	VAL	HCTZ	VAL	HCTZ	VAL	HCTZ
80%	16	2.5	8	1.25	98.33	99.46	98.48 ± 0.145 (0.147)	99.19 ± 0.265,0.267
100%	16	2.5	16	2.5	98.65	99.1	98.82 ± 0.147 (0.149)	99.22 ± 0.104, 0.105
120%	16	2.5	24	3.75	98	98.56	98.25 ± 0.25 (0.254)	98.82 ± 0.244, 0.247

Table 4: Accuracy studies of Valsartan and Hydrochlorothiazide.

*Mean of three determinations.

Brand name	Drug	Label claim (mg)	Amount obtained (mg)	*Assay (%w/w)
Brand I	VAL	80	78.54	98.18
	HCTZ	12.5	12.39	99.12
Brand II	VAL	80	79.12	98.90
	HCTZ	12.5	12.34	98.72

Table 5: Assay of Valsartan and Hydrochlorothiazide tablets.

*Mean of three determinations

Conclusion

The proposed spectrophotometric technique was validated as per ICH guidelines and found to be simple, precise, accurate and economical for the routine analysis of Valsartan and Hydrochlorothiazide tablets.

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