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RESEARCH ARTICLE

SIMULTANEOUS ESTIMATION OF VALSARTAN AND HYDROCHLOROTHIAZIDE IN SOLID DOSAGE FORM USING UV SPECTROSCOPY

Sunil Singh*, Ajit Kumar Yadav and Hemendra Gautam

Department of Pharmaceutical Chemistry, Invertis Institute of Pharmacy, Invertis University, Bareilly-243 123, Uttar Pradesh, India

**E-mails*: rssunil29@rediffmail.com, ajit.y@invertis.org
Tel.: +91-8859120888, +91-7409933383

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Simple, accurate, sensitive and precise ultraviolet spectrophotometric method for simultaneous estimation of Valsartan (VAL) and Hydrochlorothiazide (HTZ) in combined tablet dosage form have been developed and validated. Beer's law was obeyed in the concentration range of 0.5-3.5 mg/ml and 0.2-1.4 mg/ml in methanol at 248.5 and 271 nm for VAL and HTZ respectively. The recoveries were in the range of 99.00±0.12 and 99.34±0.03 for VAL and HTZ for simultaneous equation method. The method has been successfully applied for the analysis of VAL and HTZ in pharmaceutical formulations. The results of analysis were validated statistically that included parameters such as linearity, accuracy, precision, LOD, LOQ, recovery and robustness.

Key words: Absorptivity, Validation, Simultaneous equation, Robustness.

INTRODUCTION

Valsartan, chemically known as (S)-3-methyl-2-(N-{[2'- (2*H*-1, 2, 3, 4-tetrazol-5-yl) biphenyl-4-yl]methyl}pentanamido)butanoic acid, is an angiotensin II receptor antagonist and is used in the treatment of high blood pressure, congestive heart failure (CHF) or post-myocardial infarction (MI) (Saydam and Takka, 2007). It is official in United State Pharmacopoeia. Hydrochlorothiazide, chemically known as 6-chloro-1, 1-dioxo-3, 4-dihydro-2*H*-1, 2, 4-benzothiadiazine-7-sulfonamide, is a first-line diuretic (Real *et al* 2010) which is official in British Pharmacopoeia (**Figure 1**). A combination of VAL and HTZ in form of a tablet or capsule formulations is widely used for moderate to severe antihypertensive, not controlled by single agent (Siddiqui *et al* 2011). The official monographs describe the procedure for individual assay of VAL and HTZ.

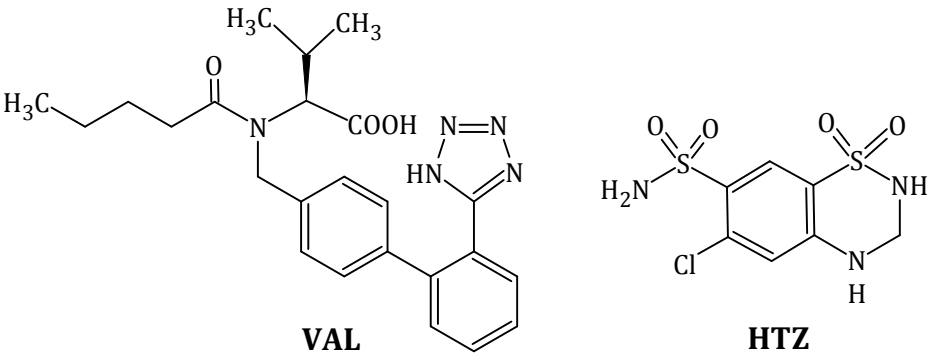

Fig. 1. Structures of Valsartan (VAL) and Hydrochlorothiazide (HTZ)

RP-HPLC, HPTLC and UV spectroscopic methods have been reported for quantitative simultaneous determination of VAL and HTZ in singly and with other combinations (Tian *et al* 2008; Thanusha *et al* 2010; Varghese and Ravi, 2011). But, no spectrophotometric method has been yet reported for the quantitative determination of VAL and HTZ in combined dosage form. In recent years, simultaneous equation method has been reported to be a useful method in resolving overlapping spectra of multiple components. The method is also reported for successful determination of active ingredients in presence of matrix. In the present work, simultaneous equation method (Goyal and Singhvi, 2008; Shukla *et al* 2011) has been exploited for quantitative determination of VAL and HTZ in combined dosage form.

MATERIALS AND METHODS

Materials

Analysis carried out on Shimadzu UV 1601 UV-Vis spectrophotometer, a double beam high speed scanning spectrophotometer with a photomultiplier tube detector and having spectral bandwidth of 1 nm (190-900 nm). VAL and HTZ were received as gratis sample by Torrent Pharmaceutical Industries Ltd., Ahmedabad. Methanol and all the chemicals used were of analytical grade (Merck, India).

Simultaneous equation method

Standard stock solution

To prepare stock solution of VAL, 100 mg of VAL was placed in 100 ml volumetric flask and dissolved in 75 ml of methanol and the volume was made up to the mark with methanol (1000 µg/ml). From this, 10 ml of the solution was diluted up to 100 ml with methanol to produce final stock solution of 100 µg/ml of VAL. Standard stock solution of HTZ was prepared similarly as that of VAL, the equimolar solution containing 100 µg/ml of solution and prepared appropriate dilutions

Sample preparation

The content of twenty tablets were taken and weighed. Powder weight equivalent to 80 mg of VAL (corresponding amount of HTZ - 10 mg) was accurately taken and transferred to a 50 ml of volumetric flask and 20 ml of methanol added to the same and flask and was sonicated for the 30 min. The flask was shaken and the volume was diluted to the mark with the same mixture. The above solution was filtered using Whatman filter paper no. 1. Appropriate volume of the aliquot was transferred to a 50 ml volumetric flask and the volume was made up to the mark with methanol. The first derivative spectra were recorded and then, measured at 248.5 and 271 nm for VAL and HTZ respectively.

RESULTS AND DISCUSSION

In UV-Spectroscopic method, the crossing points of spectra were utilized for developing the equations for simultaneous analysis. The overlain spectra are shown in **Figure 2** and analytical data is presented in **Table 1**. In contrast, the spectra of each pure drug was found to show crossing point and assisted in their simultaneous estimation. In this method, wavelengths were utilized 248.5 nm for VAL and 271 nm for HTZ. The percentage recovery value obtained was within standard limit of 98% to 101% for the method which confirmed that the method was accurate and free from any interference of excipients. The low value of standard deviation obtained confirmed precision of the method. The reproducibility, repeatability and accuracy of the proposed method were found to be satisfactory (**Table 2**) which was evidenced by low values of standard deviation, percent relative standard deviation and standard error.

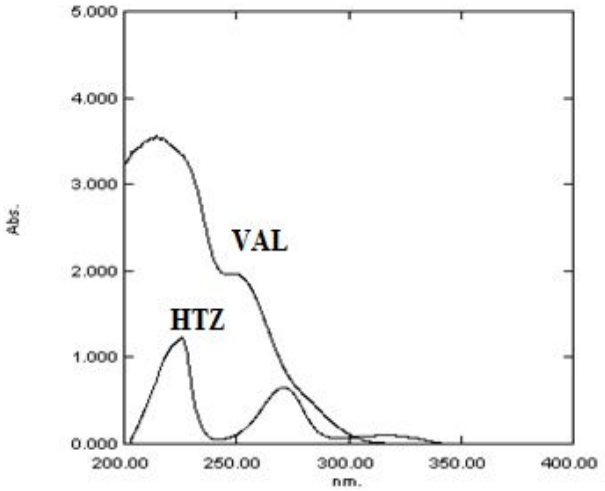

Fig. 2. Overlain spectra of Valsartan and Hydrochlorothiazide

Table 1. Statistical validation of dosage form by simultaneous equation method

Sr. No.	Drug	%Mean±SD
1	VAL	99.6±0.140
2	HTZ	99.81±0.11

Table 2. Validation parameters for UV-Spectroscopic methods

Sr. No.	Validation Parameter	Mean±SD	
		VAL	HTZ
1	Linearity (R square)	0.9991	0.9998
2	Accuracy	100.20±0.29	99.69±0.30
3	Precision		
	Interday	99.98±0.089	99.67±1.021
	Intraday	99.48±0.831	99.69±0.813
4	Recovery		
	80%	101±0.0.277	102±0.224
	100%	99.87±0.212	99.99±0.326
	120%	100.12±0.132	99.64±0.114
5	LOD (mg/ml)	0.69	0.13
6	LOQ (mg/ml)	1.83	0.42
7	Robustness	99.54±1.64	98.12±0.625
8	Ruggedness	98.31±1.2562	97.97±0.4212

CONCLUSION

The UV spectrophotometric method developed was found to be simple, accurate, sensitive and precise for simultaneous estimation of Valsartan and Hydrochlorothiazide in combined tablet dosage form and can be successfully applied for the routine quality control analysis.

ACKNOWLEDGEMENTS

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