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Development and validation of combined dosage form of Torsemide and Spironolactone in Ultra-violet spectroscopy by simultaneous equation method

V.C.Rajeshwari* and S. Ravichandran

Department of Pharmaceutical Analysis, PSG College of Pharmacy, Coimbatore,Tamilnadu, India.

Abstract : A simple, accurate and precise spectrophotometric method has been developed for simultaneous estimation of Torsemide (TOR) and Spironolactone (SPI) in combined dosage form. Simultaneous equation method (**Vierordt's method**) was employed for determination of TOR and SPI from combined dosage forms. In this method, the absorbance was measured at 288 nm for TOR and SPI from combined dosage forms. In range of 1-5µg/ml and 5-25µg/ml for TOR and SPI respectively. Recovery studies confirmed the accuracy of proposed method and results were validated as per ICH guidelines. The method can be used for routine quality control of pharmaceutical formulation containing Torsemide and Spironolactone.
Keywords : λmax, Simultaneous equation method, Spironolactone, Torsemide.

Introduction

Hypertension (HT) or high blood pressure is a major contributor to the growing global cardiovascular disease. Its control is essential in reducing death from stroke[1]. Diuretic based Anti Hypertensive Drug Therapy (AHDT) is considered to be first line treatment in control of HT. Diuretics are the classes of drugs which helps the body to get rid of excess of water and salt by promoting the excretion of urine, which in turn reduces the HT and helps the heart to pump efficiently[2].

Torsemide (TOR) is a sulfonyl urea derivative and chemically known as 3-[4-[(3-methylphenyl)amino]pyridine-3-yl] sulfonyl-1-propan-2-ylurea[3]. It belongs to the class of loop diuretic, acts with in the lumen of the thick ascending portion of the loop of Henle, where its inhibits the Na+/K+/2Cl carrier system[4].

Spironolactone (SPI) is a steroidal derivative and chemically known as 7- Acetylthio-3-oxo-17-pregn-4-ene-21,17-carbolactone[3]. It belongs to the class of potassium sparing diuretic, competitively inhibit binding of Aldosterone to the mineralocorticoid receptor (MR). The MR- SPI complex is not able to induce the synthesis of multiple gene products called aldosterone induced proteins (APIs).Since SPI blocks the biological effects of aldosterone, referred as aldosterone antagonist[4].

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Literature survey revealed that several analytical methods are developed for TOR and SPI individually and combined dosage forms. HPLC[7-12],HPTLC[13,] and UV[14] method have been developed for TOR and SPI in pharmaceutical dosage form. To best of our knowledge UV simultaneous equation method have been reported for estimation of TOR and SPI in combined dosage form. Hence, an attempt has been made to develop new UV simultaneous equation method for its estimation in pharmaceutical dosage formulations with good accuracy, simplicity and sensitivity.

Materials and Methods

Instrument:

A Shimadzu UV-1650PC UV/VIS Spectrophotometer was used with 1 cm matches quartz cell.

Materials:

Gift samples of TOR and SPI were procured from shangrila industries (P), Sikkim respectively. Tablets containing both drugs i.e. Torsemide (TOR)and Spironolactone(SPI) were purchased from local pharmacy of commercial brand Dytor plus (Cipla pharmaceuticals).

Solvent used:

0.1N Sodium hydroxide, Methanol.

Preparation of stock Solution:

TOR (10mg) and SPI (10mg) were accurately weighed and transferred to two separate 10 ml volumetric flask, dissolved in Methanol to obtained stock solution of 1000 µg/ml. The stock solutions of both the drugs were further diluted separately with solvent to obtain 100 µg/ml solution each and scanned in spectrum mode from 400-200 nm. The overlain spectra of both the drug obtained (Fig No.1) to determine the λmax. TOR has λmax 288 nm while SPI has λmax 238 nm.

From the stock solution, working standard solution of drugs were prepared by appropriate dilution with 0.1N NaOH and were scanned in the entire UV range. Two wavelengths selected for the method are 288nm and 238nm that are absorption maximas of TOR and SPI respectively in 0.1N NaOH.A series dilution were prepared of standard solutions TOR and SPI 1-5µg/ml and 5-25µg/ml respectively. The absorptivity coefficients of TOR within concentration range of 1-5µg/ml and SPI within concentration range of 5-25µg/ml were determined at 288 nm and 238nm by calibration curve.

Preparation of sample solution:

For the estimation of drugs in the commercial formulations, ten tablets containing 10mg of TOR 50mg of SPI were weighed and average weight was calculated. The tablets were crushed and powdered. Quantity of powder equivalent to 1mg TOR and 5mg of SPI was transferred to 100ml volumetric flask, dissolved in sufficient quantity of Methanol, sonicated and volume was adjust up to mark with the solvent to obtain a stock solution 10µg/ml of TOR and 50µg/ml of SPI. This solution was then filtered through Whatmann filter paper. Further dilutions were made from this stock solution to get required concentration. Absorbances of these solutions were measured at appropriate wavelengths, and values were substituted in the respective formula to obtain their respective concentrations. Results of tablet analysis are shown in Table No. 2. The analysis procedure was repeated six times (n=6).

A set of two simultaneous equations as developed using these absorptivity coefficients as:

$$Cx = \left(\frac{A2\ ay1 - A1\ ay2}{ax2\ ay1 - ax1\ ay2}\right)$$

$$Cy = \left(\frac{A1\ ax2 - A2\ ax1}{ax2\ ay1 - ax1\ ay2}\right)$$

Where, C1and C2 are concentrations of TOR and SPI respectively in µg/ml in sample solution. A1 and A2 are absorbances of the sample solution measured at 288 and 238nm respectively.

The absorbances (A1 and A2) of the sample solutions were recorded at 288 and 238nm, respectively and concentration of both components were calculated using above mentioned equation (1 and 2)

Validation[15,16]:

The methods were validated with respect to accuracy, linearity, sensitivity, precision and repetability.

Accuracy (Recovery Test):

To ascertain the accuracy of proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). Percent recovery for TOR and SPI, by the method, was found in the range of 0.898(Table No.1)

Linearity:

The linearity of measurements was evaluated by analyzing different concentration of the standard solution of TOR and SPI. For both the method, the Beer-Lambert's concentration range was found to be 1-5µg/ml and 5-25µg/ml for TOR and SPI respectively.

Sensitivity:

The high molar absorptivity and low sandell's sensitivity for the respective method reveals that this methodwas highly sensitive. (Table No.1)

Table No:1 Optical Characteristics and Validation data of Torsemide and Spironolactone.

Parameters	**Torsemide**	**Spironolactone**
Working λ (in 0.1N NaoH)	288	238
Sandell's sensitivity (mcg/sq cm/0.001)	2.58×10^{-2}	2.09×10^{-2}
Accuracy (%RSD)	0.898	0.898
Precision(%RSD) Repeatability	0.455	0.092
Linearity	1-5µg/ml	5-25µg/ml
Regression coefficient($r^{2)}$	0.996 (at 288) 0.996 (at 238)	0.985 (at 288) 0.970 (at 238)

Precision:

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogenous sample under the prescribed conditions. Precision may be considered at three levels: Intermediate (Intraday) precision, reproducibility (Interday precision), repeatability.

1) Intraday Precision:

Solutions containing 2, 3, 4 µg/ml of Torsemide andSpironolactone were analyzed three times on the same day and %RSD was calculated.

2) Interday Precision:

Solution containing 2, 3, 4µg/ml of Torsemide and Spironolactone were analyzed different successive days and %RSD was calculated.

Repeatability:

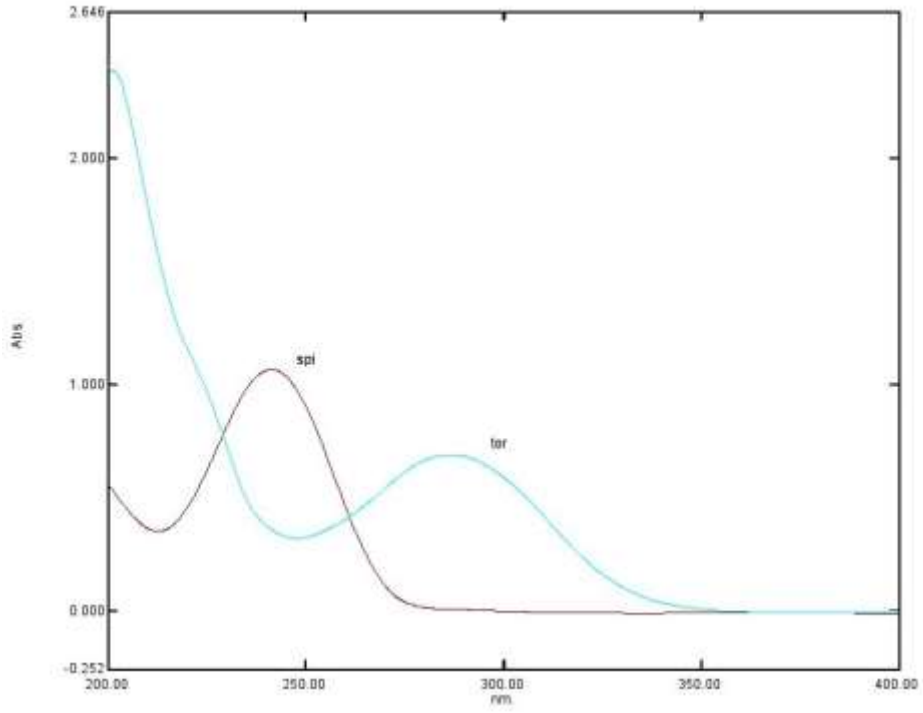
Solution containing 3 µg/ml of Torsemide and Spironolactone were analyzed for six times and %R.S.D was calculated. RSD was not more than 2%.

Results and Discussion:

The method discussed in the present work provides a convenient and accurate way for simultaneous analysis of TOR and SPI. In simultaneous equation method, wavelengths selected for analysis were 288nm for TOR and 238nm for SPI. The linearity was observed in the concentration range of 1-5 µg/ml and 5-25 µg/ml for TOR and SPI respectively. In this method concentration of individual drug present in the tablet sample solution was determined by solving the simultaneous equation at 288nm and 238nm using the respective absorptivity value. The label claim for TOR and SPI in tablet analysis, by this method, was found in the range of 94-96%. Accuracy of proposed method was ascertained by recovery studies. The results of validation parameters shown in Table no.1 are as per ICH guidelines for TOR and SPI. This method can be employed for routine analysis of these two drugs in combined tablet dosage form. The results obtained for tablets and recovery study is summarized in Table no. 2

Table No:2 Result of analysis of tablet Formulation:

Methods	Drugs	Label claim (mg)	Amount found	% label claim
I	TOR	10	9.86	98.15
	SPI	50	50.15	100.24



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References:

1. P. M. Kearney, M. Whelton, K. Reynolds, P. Muntner, P. K. Whelton, J. He, Lancet, 2005, 365, 217–223.
2. L. R. Krakoff, Circulation, 2005, 112, e127–e129.
3. Indian pharmacopoeia, Vol-III, The Indian pharmacopoeia commission, Ghaziabad,IndiaIndia, 2018, 3407.
4. L. R. Krakoff, Circulation, 2005, 112, e127–e129.
5. United state pharmacopoeia, United States pharmacopoeial convention, INC., 2005, 1952.
6. British pharmacopoeia, Vol-II, H.M. Stationary Office, London. India, 2012, 2189.
7. Venkatesan Subramanian, KannappanNagappan and SaiSandeep Mannemala, Optimization and Validation of a Sensitive Methodfor HPLC–PDA Simultaneous Determinationof Torasemide and Spironolactone in Human Plasmausing Central Composite DesignActaChim. Slov. 2015, 62, 633–641
8. R.Laxman, AcharyaAshish, Jain Bhardwaj and Jain Deepti*,Development and Validation of RP-HPLC and Ultraviolet Spectrophotometric Methods for Simultaneous Determination of Spironolactone and Torsemide in Pharmaceutical Dosage Form IJRAP 2010,1 (2) 459-467
9. Smita Sharma, M. C. Sharma a, D. V. Kohlib, S. C. Chaturvedic, Isocratic reverse phase HPLC estimation method of Torsemide and Spironolactone in pharmaceutical combined dosage form,rapid communications Vol. 4, No. 2, February 2010, p. 234 – 237
10. BhojaniMaulik, DadhaniaKetan, FalduShital, Development and Validation of RP-HPLC Method for Simultaneous Estimation ofFurosemide and Spironolactone in their Combined Tablet Dosage Form, JPSBR: Volume 2, Issue 3: May-Jun 2012 (144-147)
11. P.V.V.Satyanarayana, G.V.Adilakshmi2, RP-HPLC Method Development Validation and Forced Degradation Studies for Simultaneous Estimation of Torsemide and Spironolactone in Tablet Dosage Form, Am. J. PharmTech Res. 2015; 5(4)
12. Lin Zhang a, Rulin Wang a, Yuan Tiana,n, Zunjian Zhang a,b,nn, Determination of torasemide in human plasma and its bioequivalence study by high-performance liquid chromatography with electrospray ionization tandem mass spectrometry, Journal of Pharmaceutical Analysis 6 (2016) 95–102
13. PD Sethi, HPTLC quantitative analysis of pharmaceutical formulations, CBS publishers and Distributors, New Delhi, 1996, p.122
14. A Backett, H Stenlake and J Davidson Instrumental methods in the development and use of medicines, practical pharmaceutical chemistry , CBS Publishers and Distributors, , New Delhi,2002;vol.11,85-174.
15. ICH Topic Q2A, Validation of analytical procedures methodology, CPMP/ ICH/ 281/ 1995.
16. International Conference on Harmonization (ICH Q2B), Guidelines on Validation of Analytical procedures, Definitions and Terminology, Federal Register, 1996, 60, 27464

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