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Simultaneous Estimation of Irbesartan and Hydrochlorothiazide in Combined Pharmaceutical Dosage Form by UV Spectroscopy using Multi-component Mode of Analysis

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ABSTRACT: A simple, accurate, precise and economical procedure for simultaneous estimation of irbesartan and hydrochlorothiazide in combined tablet dosage form has been developed utilizing concept of standard addition. The method is based upon determination of irbesartan at 234nm and hydrochlorothiazide at 272nm, in aqueous ethanol (30%v/v). Different analytical performance parameters such as linearity, precision, accuracy and ruggedness were determined according to ICH guidelines. Irbesartan and hydrochlorothiazide at their respective λmax shows linearity in the concentration range of 10-26µg/mL and 5-13µg/mL respectively. The method was validated statistically. The results of analysis formulation given as percentage of label claim were found to be 99.32±0.631 and 100.15±0.762 for irbesartan and hydrochlorothiazide respectively. Therefore, the proposed methods can be used for the routine analysis of both drugs in quality control laboratories.

Keywords*: Irbesartan, Hydrochlorothiazide, multi-component mode of analysis.*

INTRODUCTION

The combination of irbesartan and hydrochlorothiazide is used in hypertension. Irbesartan is an angiotensin receptor antagonist[1], and it is chemically 2-butyl -3[(29-(1H-tetrazol-5yl) [1, 19-biphenyl]-4-yl] methyl] 1, 3-diazaspirol [4, 4] non-1-en-4-one[2]. Hydrochlorothiazide is chemically known as 6-chloro,-3, 4-dihydro-7-sulfamoyl-2H-1, 2, 4-benzothiadiazine 1,1-dioxide[3]. It inhibits the absorption of sodium and chloride at the beginning of distal convoluted tubule. In this combination, hydrochlorothiazide is official in IP, BP and USP and also many analytical methods[3] are reported for it. Irbesartan is not official in any pharmacopoeia but derivative spectrophotometric methods[4, 5, 6] one fluorimetric method and qualitative kinetic spectrophotometric methods are reported for it. There is, however, no work reported on combination of these drugs by multi-component mode of analysis. The significant feature of these combinations lies in the fact that hydrochlorothiazide is present in minute amount compared to irbesartan which makes its analysis more complicated and tedious. Hence, in the present communication we propose fast, simple, and accurate spectrophotometric method, without tedious extraction procedure, was developed by applying standard addition method, for the simultaneous estimation of both the drugs in tablet dosage form by multi-component mode of analysis.

EXPERIMENTAL

Apparatus

A shimadzu UV-1700 double beam UV-Visible spectrophotometer (Japan) equipped with 100mm matched quartz cells was used in the present study. A shimadzu AX-220 single pan balance was used.

Chemicals and reagents.

Ethanol (AR grade, Merck Ltd, Mumbai) and double distilled water was used in the present study. Pure irbesartan and hydrochlorothiazide were obtained as gift sample from Orchid Health Care Pvt. Ltd.,

Chennai; the tablet dosage form IROVEL-H (claim: 150mg irbesartan and 12.5 hydrochlorothiazide) was procured from the local market.

Preparation of standard stock solutions

Standard stock solution containing irbesartan and hydrochlorothiazide was prepared by dissolving 100mg of irbesartan and hydrochlorothiazide separately in 30mL of Ethanol; and then final volume of both the solutions was made up to 100mL with double distilled water.

The aliquot portions of stock solutions of irbesartan and hydrochlorothiazide were diluted appropriately with aqueous ethanol (30% v/v) to obtain concentration of 15µg/mL of irbesartan and 7.5µg/mL of hydrochlorothiazide. These solutions were scanned in the range of 200-400nm in 1cm cell against blank. From the overlain spectra shown in Fig-1, the wavelength selected for the estimation are 234nm and 272nm for irbesartan and hydrochlorothiazide respectively.

Preparation of synthetic mixture of irbesartan and hydrochlorothiazide

The six mixed standard solutions with concentration of irbesartan and hydrochlorothiazide in the ratio of 10:5, 12:6, 14:7, 16:8, 18:9, and 20:10 (µg/mL) were prepared in 30%v/v aqueous ethanol. All the mixed standard solutions were scanned over the range of 200-400nm, in multi-component mode; using two sampling wavelengths 234 and 272nm. The spectral data from these scans were used to determine the concentration of these drugs in tablet formulation.

Procedure for analysis of tablet formulation

Marketed tablet formulation (IROVEL-H) containing 150mg of irbesartan and 12.5mg of hydrochlorothiazide were analyzed by this method. From the triturated powder of 20 tablets, an amount equivalent to an average weight of the tablet was accurately weighed, and following standard addition method, 62.5mg of pure hydrochlorothiazide was added to achieve 2:1 ratio and shaken vigorously with ethanol for 15minutes and filtered through Whatman filter paper No.42. Necessary dilutions are made with aqueous ethanol to give final concentration of 15µg/mL and 7.5µg/mL of irbesartan and hydrochlorothiazide respectively. The sample was analyzed in triplicate by multi-component mode of analysis. 30%v/v aqueous ethanol was used as blank. The concentration of each component was obtained by the spectral data of the sample solution with reference to that of the mixed standard. Results of analysis of tablet formulation are shown in table-1.

Validation of the Method

The following validation parameters; linearity, range, accuracy, precision and specificity were studied. The accuracy of the method was ascertained by carrying out recovery studies using standard addition method. The recovery study was performed to determine if there was any positive or negative interference from excipients present in the formulation. The precision of an analytical method is expressed as standard deviation or relative standard deviation of a series of measurements. It was ascertained by replicate estimation of drug by the proposed method. Test for ruggedness was carried out the repeating the procedure under difference conditions i.e. on different days, at different analysts.

RESULTS AND DISCUSSION

In 30% v/v ethanol, Irbesartan and hydrochlorothiazide, showed absorbance maxima at 234 and 372 nm, respectively. The proposed method for simultaneous estimation of irbesartan and hydrochlorothiazide was validated as per the ICH guidelines. The Linearity was observed in the concentration range 10-26µg/mL for Irbesartan and 5-13µg/mL for Hydrochlorothiazide with regression co-efficient of 0.9989 and 0.9991 respectively. Amount of drugs estimated by the proposed method was in good agreement with the label claim. The accuracy of the method was assessed by recovery experiments. Recovery experiment indicated the absenece of interference from commonly encountered pharmaceutical additives (Table 2). The precision of the method was studied as repeatability, intra-day and inter-day variations; the % RSD less than 2, indicates proposed method is precise. The results did not show any statistical difference between operators (%RSD less than 2) suggesting that method developed was rugged. Recovery was close to 100% for both the drugs.

CONCLUSION

The present study comprises a UV spectroscopic, multi-component mode of analysis for the simultaneous determination of Irbesartan and Hydrochlorothiazide in tablet dosage form. From the study of validation parameters, it was observed that the method is specific, accurate, precise, reproducible and rugged. The proposed method could be applied to routine analysis in quality control laboratories.

Table I: Results of analysis of tablet formulation and statistical data.

Sample	Label Claim (mg/Tablet)	Amount Found	%Label Claim	SD	%RSD
Brand I (Irovel-H)	Irbesartan 150	149.56	99.71	0.1845	0.1852
	Hydrochlorothiazide 12.5	12.45	99.67	0.1808	0.1815
Brand II (Xarb-H)	Irbesartan 150	149.73	99.82	0.1369	0.1372
	Hydrochlorothiazide 12.5	12.44	99.56	0.1827	0.1835

*Results are mean of five readings

Table 2: Results of Recovery Study

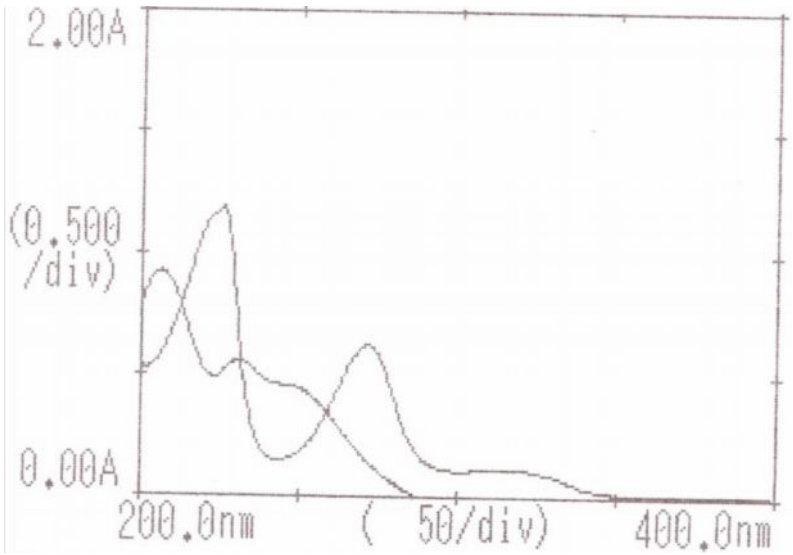
Brand Name	Label Claim mg/tablet	Amount added%	Total amount added (mg)	Amount received (mg) ±SD*	%Recovery ±SD
Brand I (Irovel-H)	**Irbesaratan 150mg**	**50**	**75**	**74.52±0.28**	**99.36±0.57**
		100	**150**	**149.62±0.34**	**99.74±0.49**
		150	**225**	**224.73±0.56**	**99.88±0.71**
	Hydrochlorothiazide 12.5mg	**50**	**6.25**	**6.27±0.23**	**100.32±0.62**
		100	**12.5**	**12.48±0.84**	**99.84±0.25**
		150	**18.75**	**18.69±0.47**	**99.68±0.46**
Brand II (Xarb-H)	**Irbesaratan 150mg**	**50**	**75**	**74.62±0.36**	**99.49±0.36**
		100	**150**	**149.56±0.39**	**99.66±0.48**
		150	**225**	**224.83±0.69**	**99.92±0.61**
	Hydrochlorothiazide 12.5mg	**50**	**6.25**	**6.24±0.15**	**99.84±0.25**
		100	**12.5**	**12.40±0.64**	**99.20±0.54**
		150	**18.75**	**18.34±0.94**	**97.81±0.75**

*Each Value is a Mean±Standard Deviation of three determinations

Table 3: Results of Ruggedness study

Conditions	% Label Claim		SD		%RSD	
	Irbe	HCTZ	Irbe	HCTZ	Irbe	HCTZ
Intraday Study	99.85	99.81	0.6521	0.5314	0.4268	0.5631
Interday Study	100.32	99.87	0.7570	0.3126	0.7012	0.2967
Different Analyst study	99.92	99.16	0.5514	0.4617	0.4327	0.3792

Figure 1: UV spectrum of Irbesartan and Hydrochlorothiazide.



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