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Original Article

SIMULTANEOUS ESTIMATION OF IRBESARTAN AND HYDROCHLOROTHIAZIDE BY UV SPECTROSCOPY

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ABSTRACT

Objective: The literature survey revealed that various methods are reported for determination of Irbesartan and Hydrochlorothiazide alone or in combination with other drugs So, the main objective of our study was to develop simple, accurate and reproducible methods for the simultaneous estimation of Irbesartan and Hydrochlorothiazide in a combined dosage form.

Methods: The method for the simultaneous determination of Irbesartan and Hydrochlorothiazide by spectroscopy has been developed. The simple, accurate and precise method includes Area Under the Curve (AUC) method. On response to the effect of solvent on spectral behaviors of Irbesartan and Hydrochlorothiazide, methanol was selected as solvent. Irbesartan shows maximum absorbance at 224 nm and Hydrochlorothiazide shows maximum absorbance at 271 nm. For the AUC method, the wavelength ranges between 225-230 nm and 258-265 nm respectively were selected with reference to the absorbance curves plotted between the wavelengths of 200-400 nm. This method allows rapid analysis of two drug combinations.

Results: The result of analysis was validated statistically by recovery study following ICH method validation guideline. Tablet containing both drugs was assayed using the method developed, showing a good accuracy and precision.

Conclusion: It can therefore be concluded that use of this method can save more time and money and it can be used in small laboratories with accuracy

Keywords: Spectroscopy, Irbesartan, Hydrochlorothiazide, Area Under Curve Method.

INTRODUCTION

Irbesartan (fig. 1) and Hydrochlorothiazide (fig. 2) are the combination angiotensin II receptor blocker and diuretic. The angiotensin II receptor blocker works by relaxing the blood vessels. The effect of diuretics on lowering the blood pressure is still unknown, but it helps the kidneys to eliminate fluid and sodium from the body.

Irbesartan (Irb) is a non-peptide compound, chemically described as a 2-butyl-3-[*p*-(*o*-1*H*-tetrazol-5-ylphenyl) benzyl]-1,3-diazaspiro[4.4] non-1-en-4-one. Its empirical formula is $C_{25}H_{28}N_6O$, and its structural formula (15) is in fig.

A hydrochlorthiazide (HCTZ; fig. 2) diuretic often considered as the prototypical member of this class. It reduces the re-absorption of electrolytes from the renal tubules. Thus results in increased excretion of water and electrolytes, including sodium, potassium, chloride, and magnesium. It has been used in the treatment of several disorders including edema, hypertension, diabetes insipidus, and hypoparathyroidism. (14)

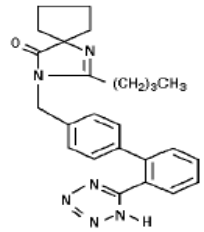

Fig. 1: chemical structure of Irbesartan

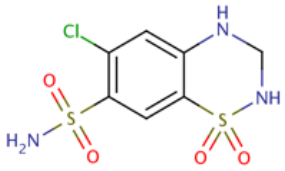

Fig. 2: Chemical structure of Hydrochlorthiazide

Many analytical methods like HPLC, capillary electrophoresis and UV spectroscopy (7-10) were reported for determination of Irb and HCTZ (11-13) in combination. However, no area under curve spectro photometric method is reported for simultaneous determination of these drugs. In this communication, we report a new UV spectro photometric method using area under curve spectroscopy.

MATERIALS AND METHODS

Instruments

A UV Probe type UV-VIS double beam spectrophotometer (shimadzu 1800) with 1 cm Quartz cells was used in this experiment. Analysis was performed using direct mode over a wavelength range from 200-400 nm. The instrument settings were zero order and first derivative mode and band width of 2 nm in the range of 200-400 nm. All weights were taken on an electronic balance.

Reagents and chemicals

Irbesartan, working standard was obtained as a gift sample from Sanofi Aventis (Goa) and Hydrochlorothiazide, as a gift sample from CTX Life Sciences Pvt Ltd. Methanol (Spectrochem Chemicals) and Irbesartan and Hydrochlorothiazide combination tablet (Irovel-H, Sun pharma) were purchased from local market.

Preparation of standard stock solutions

10 mg each of standard Irbesartan and Hydrochlorothiazide were weighed and transferred to two separate 100 ml volumetric flasks and

dissolved in methanol (98 % v/v) and further diluted with the methanol to get the standard solutions Irb and HCTZ of 100.0 µg ml^{-1}each.

Method: Area under curve method

In the simultaneous equation using AUC method, the area under curves of the spectrums were measured at the selected wavelength ranges, 225-230 nm and 258-265 nm and calibration curves were plotted by taking concentration on x-axis and AUC at 225-230 nm and 258-265 nm on Y-axis. The 'X' values were determined as, X= Area under curve of component (from 225-230 nm and 258-265). A set of two simultaneous equations of Irbesartan and Hydrochlorothiazide using these 'X' values as follows,

A_1=0.0010C_{irbi}+0.0442C_{hctz}----- (at λ 225.0-230.0 nm)-(1)

A_2=0.0004 C_{irbe}+0.0011 C_{hctz}---------- (at λ 258.0-265.0 nm)-(2)

Where, C_{Irb} and C_{HCTZ} are the concentrations of Irb and HCTZ measured in µg/ml, in the sample solutions. A_1 and A_2 are the area under curve of sample solutions at the wavelength ranges from 225-230 nm and 258-265 nm, respectively.

Preparation of tablet sample solution

Twenty tablets of IROVEL-H each containing Irb (150 mg) and HCTZ (12.5 mg) were weighed and crushed to fine powder. An accurately weighed powder sample equivalent to 150 mg of Irb and 12.5 mg HCTZ was transferred to a 100 ml conical flask. These were extracted with methanol (4 x 20 ml) and the solution was sonicated for 30 min and volume was made up to the mark with methanol in a 100 ml calibrated volumetric flask, the solution was filtered through Whatman filter paper. 1.0 ml of this solution was pipetted out and transferred to 100 ml calibrated volumetric flask and volume was made up to the mark with methanol to obtain a concentration of 15 µg/ml for Irb and 1.25 µg/ml for HCTZ. After appropriate dilutions, the absorbances were measured and the concentration of each analyte was determined with the equations generated from the calibration curve for respective drugs. The developed method was validated by following ICH Q2B (R1) guidelines. The following parameter were studied for validation.

Validation of methods

Linearity

For all the methods, 6-point (2-20 µgml^{-1} Irb and 0.5-10 µgml^{-1} HCTZ to calculate the equation of the line by using the least-squares regression method.

Accuracy

Recovery study was performed by standard addition method at three levels i.e., 80%, 100% and 120%. Known amounts of pure Irbesartan and HCTZ were added to pre-analyzed sample of marketed formulation and they were subjected to analysis by the proposed method. A result of recovery study is shown in table 1.

Precision

Precision study was performed to find out intra-day and inter-day variations. The results of precision studies are reported in table 2 and values of standard deviation less than 2% indicates high degree of precision.

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The LOD and LOQ were separately determined based on the calibration curves. The standard deviation of the y-intercepts (σ) and slope of the regression lines (S) were used. These values were calculated using following formula

$$LOD = 3.3 \times \sigma/S \quad LOQ = 10 \times \sigma/S$$

Ruggedness

Ruggedness of the proposed methods was determined by analyzing aliquots from homogenous slot in different laboratories by different analyst using similar operational and environmental conditions.

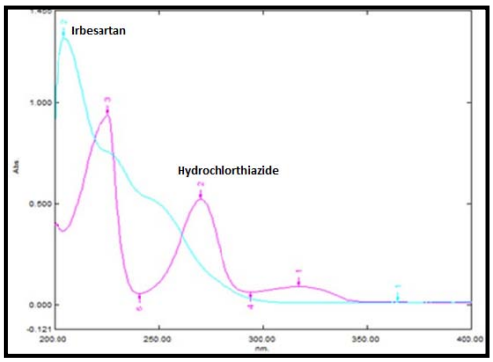

Fig. 3: Overlay spectra of Irbesartan and Hydrochlorothiazide.

Table 1: Results of recovery study

Drug	% added	Conc in µg/ml	Std added in µg/ml	Total	Amt recovered	SD	%RSD	%recovery	SD	%RSD
	80	6	4.8	10.8	10.7066	0.085	0.787	99.1352	0.3251	0.328
Irb	100	6	6	12	12.0100	0.0665	0.5536	100.083	0.5548	0.5536
	120	6	7.2	13.2	12.9866	0.1209	0.9365	98.3833	1.7637	1.7746
	80	4	3.2	7.2	7.1966	0.0757	1.0699	99.9528	1.0516	1.0521
HCTZ	100	4	4	8	7.9833	0.1209	1.5152	99.7913	1.5121	1.5152
	120	4	4.8	8.8	8.8036	0.0151	0.1723	100.041	0.1723	0.1722

Table 2: Precision study

Conc(µg/ml)	intraday		interday	
Irbe	mean conc±SD	%RSD	mean conc±SD	%RSD
4	3.99±.0503	1.2593	3.95±0.0608	1.5399
10	10.0933±.1096	1.0868	9.966±0.0611	0.6139
18	18.06±.1708	0.9461	17.96±0.13	0.7238
HCTZ				
1	0.9904±.0094	0.9507	0.9863±.0030	0.3045
4	3.9866±.0351	0.8809	3.9666±.0550	1.3884
10	10.01±.0200	0.1998	9.970±0.0624	0.6251

RESULTS AND DISCUSSION

The proposed method for simultaneous estimation using AUC of Irb and HCTZ in combined dosage form was found to be accurate, simple and rapid. Hence, it can be used for routine analysis of two drugs in the combined dosage forms. There was no interference from tablet excipients was observed in these methods. The values of % RSD for simultaneous determination (Tablet) were found to be

(0.274-1.25), (0.2214-1.11 %) for Irb and HCTZ and correlation coefficient was 0.999. The result of recovery studies for tablet was found to be in the range of 98.38-100.83, 99.740-100.04 % for Irb and HCTZ respectively. Values are reported in table 1. It indicates that there is no interference due to excipients present in the formulation. It can be easily and conveniently adopted for routine quality control analysis. This method is accurate, simple, rapid, precise, reliable, sensitive, reproducible, economic and validated as per ICH guidelines.

CONCLUSION

The results of above mentioned study indicate that the proposed UV spectroscopic method is simple, rapid, precise and accurate. The developed UV spectroscopic method was found suitable for determination of Irb and HCTZ as bulk drug and in marketed solid dosage formulation without any interference from the excipients. Statistical analysis proves that this method was repeatable and selective for the analysis of Irb and HCTZ. It can therefore be concluded that use of this method can save more time and money and it can be used in small laboratories with accuracy.

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CONFLICT OF INTERESTS

Declared None

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