ISSN: 0975-766X
CODEN: IJPTFI
Available Online through
Research Article
www.ijptonline.com

SIMULTANEOUS DETERMINATION OF IRBESARTAN AND HYDROCHLOROTHIAZIDE BY SPECTROPHOTOMETRY

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Received on 12-07-2016 *Accepted on 28-08-2016*

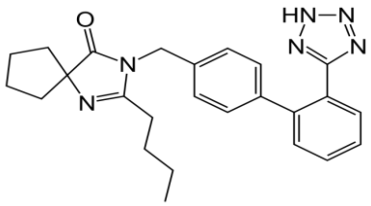
Abstract

Two new spectrophotometric methods have been developed and validated for the simultaneous determination of Irbesartan and Hydrochlorothiazide in pharmaceutical formulations using Hydrochloric acid. Both Irbesartan and Hydrochlorothiazide have shown linearity over the concentration range 1.0-35.0 µg/ml and 0.1-30 µg/ml in both Simultaneous equation method as well as absorbance ratio method (Q-analysis).

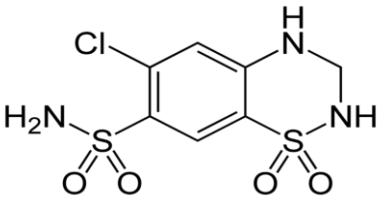
Keywords: Irbesartan, Hydrochlorothiazide, Spectrophotometric, Tablets, Validation.

Introduction

Irbesartan is mainly used for the treatment of hypertension. Irbesartan (Figure 1) is an angiotensin II receptor antagonist and also used for the reduction of renal disease progression in patients with type 2 diabetes[1]. Hydrochlorothiazide (HTZ) (Figure 2) is a diuretic drug used for the treatment of high blood pressure[2].



(A)



(B)

Figure 1: Chemical structures of Irbesartan (A) and Hydrochlorothiazide (B)

Literature survey reveals that LC-MS[3], UPLC[4], HPLC[5-10], Micro emulsion LC[11], HPTLC[12], spectrofluorimetric[13] and spectrophotometric[14-19] methods have been developed for the simultaneous determination of Irbesartan and Hydrochlorothiazide in biological fluids as well as pharmaceutical formulations. In the present study the authors have developed two spectrophotometric methods for the simultaneous determination of Irbesartan and Hydrochlorothiazide in tablets.

Materials and Methods

Chemicals and reagents

The combination of Irbesartan and Hydrochlorothiazide is available as film-coated tablets with brand names AVALIDE (Sanofi Aventis Pharma, India), XARB-H (Nicholas, India) containing 150 mg of Irbesartan and 12.5 mg of Hydrochlorothiazide. Methanol (MERCK), Conc. HCl were purchased and used as received. All the chemicals are of analytical grade.

Instrumentation

Spectral and absorbance measurements were made on an UV-1800 SHIMADZU double beam UV-Visible Spectrophotometer with 1cm matched quartz cells. SHIMADZU electronic balance was used for weighing the samples.

Preparation of stock solution

Stock solutions (1000 µg/ml) of Irbesartan and Hydrochlorothiazide were prepared by dissolving about 25 mg of each of Irbesartan and Hydrochlorothiazide in two separate 25 ml volumetric flasks in methanol and working standard solutions were prepared on dilution from the stock with 0.1N hydrochloric acid as per the requirement.

Procedure

A series of solutions of Irbesartan (1.0-35.0 µg/ml) and Hydrochlorothiazide (0.1-30.0 µg/ml) were prepared from their stock solutions and scanned (200- 400 nm) against the reagent blank i.e. HCl.

Method A: Simultaneous Equation Method

The absorption spectrum shows that Irbesartan has λ_{max} at 204 nm whereas Hydrochlorothiazide has at 272 nm respectively. For the simultaneous equation method, two wavelengths i.e. λ_{max} of the two drugs were selected and the absorbance as well as the absorptivity values were calculated from their individual spectra. Absorbance was noted against each concentration at 204 and 272 nm for both the drugs from their individual spectra and their absorptivity values were calculated.

Method B: Q Analysis (Absorbance ratio Method)

Irbesartan has shown λ_{max} at 204 nm and Hydrochlorothiazide at 272 nm respectively in their absorption spectra. Three isosbestic (iso-absorptive) points were observed at 214.25, 230.29, and 259.09 nm in the overlay spectra of Irbesartan and Hydrochlorothiazide. For the Q-analysis method, two wavelengths such as λ_{max} one of the drugs and the isosbestic point were selected and the absorbances as well as the absorptivity values were calculated from their individual spectra. By using the simultaneous equation method and absorbance ratio method Irbesartan and Hydrochlorothiazide

were determined in bulk and in its pharmaceutical formulations (Tablets) using 0.1N HCl and the proposed method was statistically validated.

Validation[20]

Calibration curve (Linearity)

The series of solutions of Irbesartan (1.0-35.0 µg/ml) and Hydrochlorothiazide (0.1-30 µg/ml) prepared were scanned in the UV region (as the solutions were colourless) against the reagent blank i.e. 0.1N HCl and the absorbance was note that their selected wavelength for the two methods i.e. simultaneous equation method and absorbance ratio method (Q-analysis). A graph was drawn by taking the concentration on the x- axis and the corresponding absorbance values on the y-axis for the two drugs at the selected wavelength.

Accuracy:

Recovery studies were carried out by the standard addition method for the determination of accuracy of the proposed methods A and B. 80%, 100%, and 120% of pure bulk samples of Irbesartan and Hydrochlorothiazide were added to that of the pre-analyzed formulation and the % recovery as well as the % RSD were calculated

Precision:

The intra-day and inter-day precision studies of the method was performed at three different concentration levels (15, 20 and 30 µg/mL) at three different intervals on the same day (Intra-day) and on three different days (Inter-day) respectively and the %RSD was calculated.

Assay of Irbesartan and Hydrochlorothiazide combined dosage forms (Tablets)

The combined dosage forms of Irbesartan and Hydrochlorothiazide (Tablets) are available with brand names AVALIDE, XARB-H containing 150 mg of Irbesartan and 12.5 mg of Hydrochlorothiazide and were procured from the local pharmacy store. 20 tablets of each brand were weighed and powdered and powder equivalent w.r.t. 12.5 mg of Hydrochlorothiazide was taken and dissolved in a 100 ml volumetric flasks containing methanol and sonicated for 30 minutes. The volume was made up to the mark with methanol and filtered. These solutions were further diluted with 0.1N HCl as per the requirement for the two methods and the percentage purity was determined.

Results and Discussion

The authors have developed two spectrophotometric methods, simultaneous equation method (Method A) and absorbance ratio method (Method B) for the simultaneous determination of Irbesartan and Hydrochlorothiazide in 0.1N HCl.

Method A: Simultaneous Equation Method

For the simultaneous determination of two drugs by simultaneous equation method, specific absorptive values of the two drugs at the selected wavelengths were determined. The overlay absorption spectrum of Irbesartan and Hydrochlorothiazide was shown in Figure 3. The absorption spectrum Irbesartan has shown λ_{max} at 204 nm and that of Hydrochlorothiazide at 272 nm respectively.

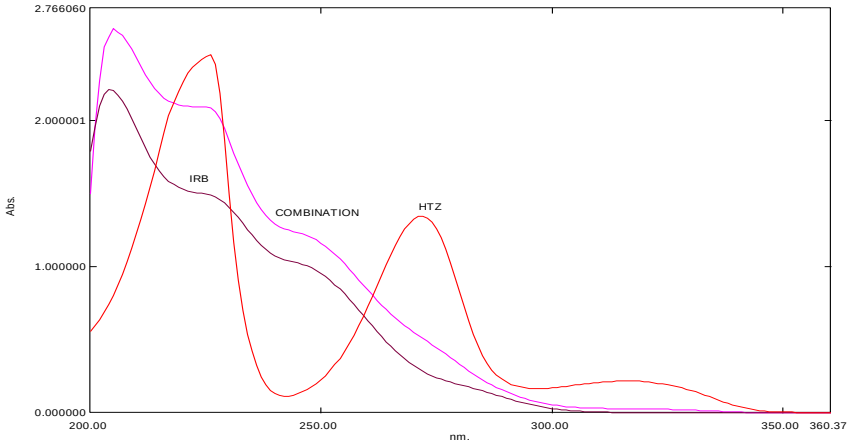


Figure 2: Overlay absorption Spectrum of IRB (25 µg/ml), HTZ (20 µg/ml) and mixture (IRB+HTZ) (Tablets) in Hydrochloric acid.

The specific absorptivity value of a drug is the absorbance of the drug shown by a 1%, i.e. g/100ml solution and the absorptivity values obtained were incorporated in the simultaneous equations.

At 204 nm, $A_1 = 869.2\ C_{IRB} + 332.14\ C_{HTZ}$

At 272 nm, $A_2 = 113.532\ C_{IRB} + 648.19\ C_{HTZ}$

where A_1 and A_2 are absorbance's of the mixture solution at 204 nm and 272 nm, respectively; 869.20 and 113.532 are the absorptivity's of Irbesartan at 204nm and 272 nm, respectively and 332.14 and 648.19 are the absorptivity's of Hydrochlorothiazide at 204 nm and 272 nm, respectively; C_{IRB} and C_{HTZ} are the concentrations of Irbesartan and Hydrochlorothiazide, respectively in g/100ml.

Method B: Absorbance ratio Method (Q Analysis)

Irbesartan and Hydrochlorothiazide shows λ_{max} at 204 nm 272 nm respectively. Three isosbestic (iso-absorptive) points were observed at 214.25, 230.29 and 259.09 nm in the overlay absorption spectrum of Irbesartan and Hydrochlorothiazide (Figure 3)

The absorptivity values obtained at the selected wavelengths were incorporated in the following equation.

$$Cx = Qm-Qy/Qx-Qy \times A_1/ax_1$$

$$Cy = Qm-Qx/Qy-Qx \times A_2/ay_1$$

'Cx' = the concentration of Irbesartan

'Cy' = the concentration of Hydrochlorothiazide.

'A_1' = the absorbance at iso-absorptive wavelength 259.09 nm.

'A_2' = the absorbance at wavelength 272 nm.

'ax_1 = the mean absorptivity of Irbesartan at 259.09 nm.

'ay_1' = the mean absorptivity of Hydrochlorothiazide at 272 nm.

Qm = the ratio of absorbance of sample solution at 259.09 & 272 nm.

Qx = the ratio of absorptivity of Irbesartan at 259.09 & 272 nm.

Qy = ratio of absorptivity of Hydrochlorothiazide at 259.09 & 272 nm.

Validation

Linearity

Irbesartan and Hydrochlorothiazide have shown linearity over the concentration range 1-35 µg/ml and 0.1-30 µg/ml in 0.1N HCl in both simultaneous equation method and absorbance ratio method.

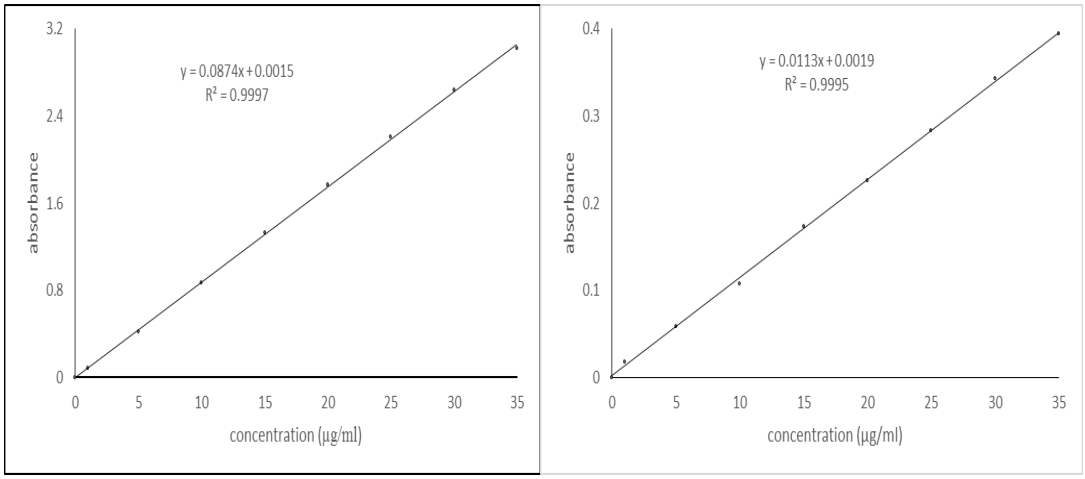


Figure 3: Calibration curve of Irbesartan at A) 204 nm B) 272 nm.

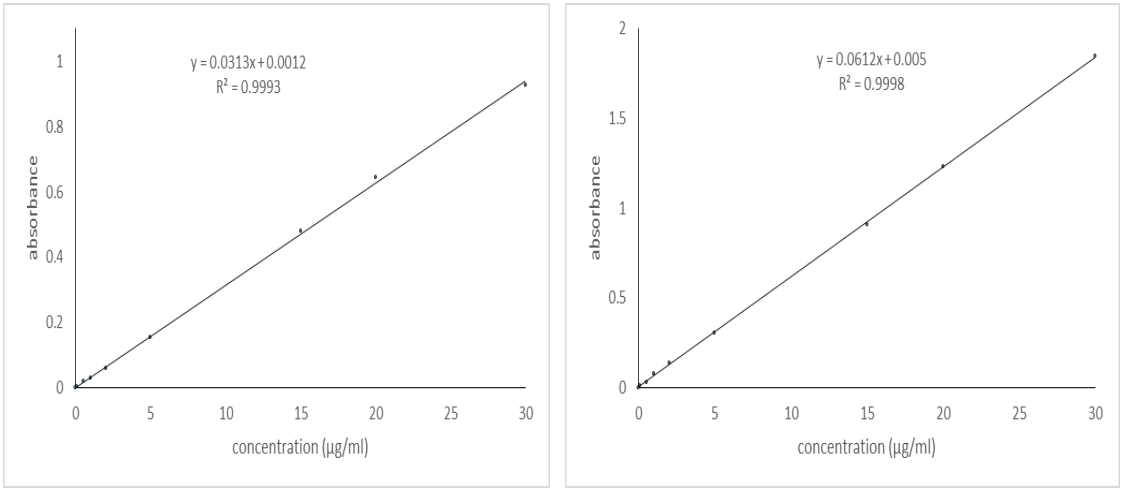


Figure. 4: Calibration curve of Hydrochlorothiazide at A) 204 nm B) 272 nm.

Accuracy

The percentage recovery of Irbesartan and Hydrochlorothiazide were found to be 99.25-99.87 and 98.31-99.88 for method A; 98.50-98.85 and 98.31-99.50 respectively for method B. The % RSD for Irbesartan and Hydrochlorothiazide by the two methods is found to be less than 2.0 indicating that the methods are accurate (Table 1).

Table 1: Accuracy study of Irbesartan and Hydrochlorothiazide.

Drugs	Spiked Conc (µg/ml)	Formulation Conc. (µg/ml)	Method A		Method B	
			%RSD	%*Recovery	%RSD	%*Recovery
IRB	12 (80%)	15	0.63	99.45	0.78	98.48
	15 (100%)	15	0.54	99.43	0.59	98.60
	18 (120%)	15	0.67	99.49	0.95	98.78
HTZ	1.00 (80%)	1.25	0.36	98.98	0.32	99.38
	1.25 (100%)	1.25	0.82	99.68	0.49	99.59
	1.50 (120%)	1.25	0.98	98.71	0.61	98.26

*Mean of three replicates

Precision

The intra-day and inter-day precision studies were performed by the two methods A and B and the results were shown in Table 3. The % RSD for Irbesartan and Hydrochlorothiazide by the two methods is found to be less than 2.0 indicating that the methods are precise (Table 2).

Table 2: Precision study of Irbesartan and Hydrochlorothiazide

Drug	Conc. µg/mL	Intra-day precision				Inter-day precision			
		Method A		Method B		Method A		Method B	
		*Conc. obtained (µg/ml) (RSD)	*% Recovery	*Conc. obtained (µg/ml) (RSD)	*% Recovery	*Conc. obtained (µg/ml) (RSD)	*% Recovery	*Conc. obtained (µg/ml) (RSD)	*% Recovery
IRB	10	9.98 (0.32)	99.80	9.96 (0.52)	99.6	9.90 (0.95)	99.0	9.82 (0.99)	98.2
	20	19.96 (0.65)	99.80	19.97 (0.29)	99.8	19.85 (0.98)	99.25	19.83(1.19)	99.15
	30	29.99 (0.87)	99.97	29.96 (0.76)	99.8	29.95 (1.21)	99.83	29.92 (1.31)	99.73
HTZ	10	9.97 (0.34)	99.70	9.99 (0.29)	99.9	9.93 (0.98)	99.3	9.96 (0.98)	99.6
	20	19.95 (0.63)	99.75	19.99 (0.39)	99.9	19.86 (1.15)	99.30	19.82 (1.04)	99.10
	30	29.97 (0.27)	99.90	29.93 (0.65)	99.7	29.92 (1.23)	99.73	29.95 (1.23)	99.83

*Mean of three replicates

Assay of Tablets

The combined dosage forms of Irbesartan and Hydrochlorothiazide (Tablets) were evaluated by the two methods and the results were incorporated in Table 3.

Table 3: Assay of Irbesartan and Hydrochlorothiazide Tablets.

Formulation Brand	Drug	Label claim(mg)	Method A		Method B	
			*Amount found	*Recovery (%)	*Amount found	*Recovery (%)
I	IRB	150	148.99	99.33	147.69	98.46
	HTZ	12.5	12.46	99.68	12.15	97.23
II	IRB	150	149.33	99.55	147.93	98.62
	HTZ	12.5	12.39	99.12	12.38	99.04

*Mean of three replicates

Conclusion

The proposed methods were validated and can be used for the determination of Hydrochlorothiazide and Irbesartan in tablets. The methods were found to be precise and accurate.

Acknowledgements

We are grateful to M/s GITAM University, Visakhapatnam, India for providing research facilities and to Sanofi Aventis Pharma, India for providing the gift samples of Hydrochlorothiazide and Irbesartan. The authors have no conflict of interest.

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