Academic Sciences Asian Journal of Pharmaceutical and Clinical Research
Vol 5, Issue 1, 2012 ISSN - 0974-2441

Research Article

EXTRACTIVE VISIBLE SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF TELMISATAN AND IRBESARTAN IN BULK AND PHARMACEUTICAL FORMULATIONS

G.TULJA RANI*, D.GOWRI SANKAR[1], MADHAVI .L , B. SATYANARAYANA[2]

*Department of Pharmaceutical Analysis, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Exhibition Grounds, Nampally, HYDERABAD-500001, (A.P.) INDIA , [1]Department of Pharmaceutical Analysis and Quality Assurance, University college of Pharmaceutical sciences, Andhra University, VISAKHAPATNAM- 530003, (A.P.) INDIA , [2]Neosun Biotech (India) Pvt. Ltd, HYDERABAD-500007, (A.P.) INDIA

Received: 29 August 2011, Revised and Accepted: 4 October 2011

ABSTRACT

Simple, accurate, rapid and sensitive method has been developed for the estimation of telmisartan and irbesartan in bulk and pharmaceutical formulations. The method is based on the formation of ion association complex of the drug with eriochrome black-T in acidic buffer of pH 3.5 followed by extraction into chloroform. The linearity range of telmisartan and irbesartan with eriochrome black-T was found to be 50 – 250 µg/mL. The developed method was found to be precise and accurate from the statistical validation of the analytical data. The proposed method has been successfully applied for analysis of dosage formulations.

Keywords: Telmisartan, Irbesartan, Eriochrome black-T and Spectrophotometric method.

INTRODUCTION

Telmisartan chemically is 2-[4-[4- methyl-6- (1-ethylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl] phenyl] benzoic acid (Fig 1b), is an angiotensin II receptor antagonist, used in the management of hypertension.

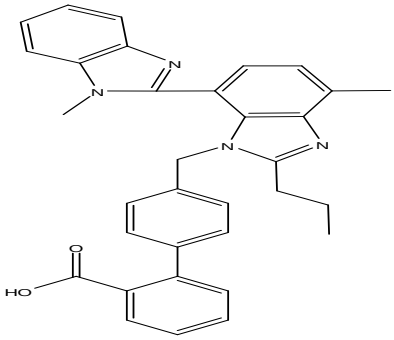

Fig 1a Telmisartan

Irbesartan chemically is 2-butyl-3-({4-[2- (2H-1, 2, 3, 4-tetrazol-5-yl) phenyl] phenyl) methyl)-1, 3-diazaspiro [4, 4] non-1-en-4-one, is an angiotensin II receptor antagonist, used mainly for the treatment of hypertension.

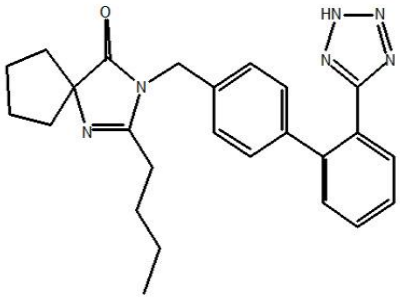

Fig 1b Irbesartan

Literature survey revealed a few analytical methods for quantitative determination of telmisartan [1-6] and irbesartan [7-10] in biological fluids and pharmaceutical formulations.

The main aim of the present study is to develop a relatively simple, sensitive, validated and inexpensive extractive visible spectrophotometric method for the estimation of telmisartan and irbesartan in pure and in pharmaceutical formulations. Since most of the previous methods involve tedious sample preparation, critical reaction conditions and expensive instruments, so the authors have made an humble attempt to develop a simple method which does not involve any heating to produce the color and also cost effective. The proposed method has been extended for the routine quality control analysis of pharmaceutical formulations of telmisartan and irbesartan.

EXPERIMENTAL

MATERIALS AND METHODS

Instrument

A Shimadzu uv-1800 spectrophotometer with 10 mm matched quartz cells was used for spectral and absorbance measurements .Telmisartan and irbesartan were obtained as gift samples from Aurobindo Pharmaceuticals Ltd., Hyderabad. Tablet formulation IROVEL (Sun Pharma) with 150 mg of irbesartan and TELMA containing 20 mg of telmisartan were procured from local pharmacy. All the chemicals used were of analytical grade and the solutions were freshly prepared with double distilled water.

Preparation of reagents:

Preparation of standard solution (1mg/mL): 100 mg of each drug was accurately weighed and transferred to separate 100 mL volumetric flasks. To dissolve the drug 5 mL of methanol was added to each flask and the volume was made up to the mark with distilled water.

Eriochrome black-T solution (0. 1%): 100 mg of eriochrome black-T was dissolved in 100 mL of distilled water and washed with chloroform to remove chloroform soluble impurities.

Acetate buffer (pH 3.5): 0.4 gm of anhydrous sodium acetate in 84 mL of distilled water and sufficient amount of glacial acetic acid to adjust pH to 3.5 (about 15 mL) and the volume was made up to 100 mL with distilled water.

Selection of wavelength

In order to select the wavelength of maximum absorbance, telmisartan and irbesartan solutions were scanned in the range from 400-600 nm against the respective reagent blank to record the absorption spectra. The resulting spectra's were shown in Fig 2a and 2b and the absorption curve showed characteristic absorption maxima at 510 nm for both the drugs.

Procedure for calibration curve

Aliquots of standard solution of telmisartan and irbesartan ranging from 50 – 250 µg/mL were delivered in to a series of 60 mL separating funnels. To each separating funnel 2.5 mL of pH 3.5 buffer

(for both the drugs) and 1.0 mL of 0.1% eriochrome solution for telmisartan and 3.0 mL for irbesartan was added and the total volume of aqueous phase in each funnel was adjusted to 10 mL. Then 10 mL of chloroform was added and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the separated chloroform layer was measured at 510 nm for both the drugs against the reagent blank prepared similarly. Calibration curves were constructed by plotting the absorbance against the concentration of the respective drug. The optimum conditions are presented in Table-1.

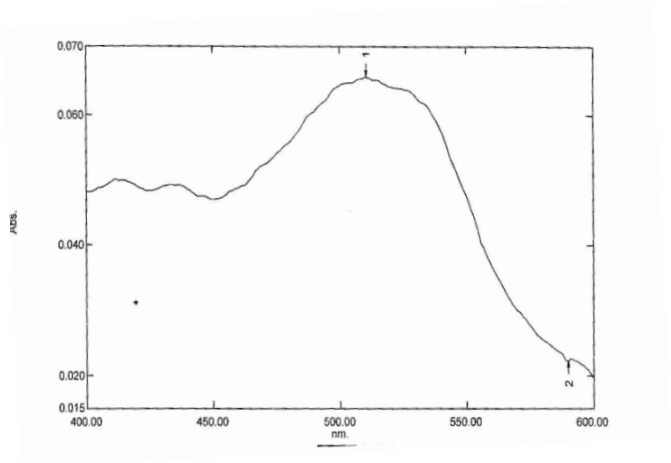

Fig.2a spectrum of telmisartan with eriochrome Black – T.

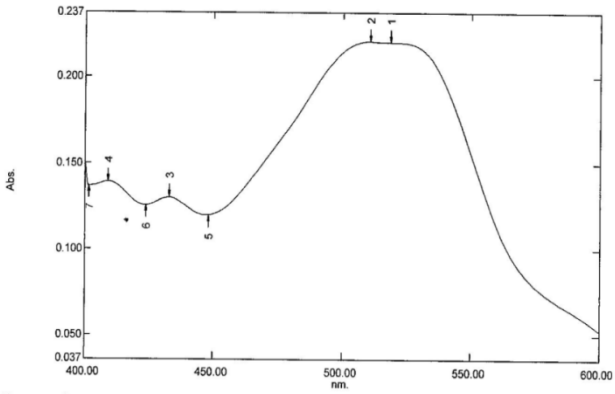

Fig. 2b Spectrum of irbesartan with eriochrome Black –T.

Table-1: Optimum conditions of the proposed method.

Reagent	Telmisartan	Irbesartan
Drug solution taken (µg/mL)	50 - 250	50- 250
Volume of pH 3.5 buffer (mL)	2.5	2.5
Volume of reagent employed (mL)	1.0	3.0
λmax (nm)	510	510

ASSAY

Twenty tablets of each drug were weighed accurately, finely powdered and powder equivalent to 100 mg of each drug was transferred to 100 mL volumetric flask extracted with 10 mL of methanol and made up to volume with distilled water. The sample solution of each drug was filtered through whatmann filter paper and from the filtrate required aliquots of the each drug solution was transferred to two 60 mL separating funnel and the same procedure was followed. The concentration of unknown was calculated from the regression equation.

METHOD VALIDATION

Linearity and range

Aliquots of standard stock solutions of telmisartan and irbesartan were taken in to 60 mL separating funnel and required amount of buffer and reagent was added to each separating funnel and 10 mL of chloroform was added to extract the colored complex. The absorbance of colored complex was measured at 510 nm and calibration curves were constructed in the range 50 250 µg/mL for both the drug Fig 3a and 3b. Linearity range of telmisartan and irbesartan is shown in Table 2a and 2b.

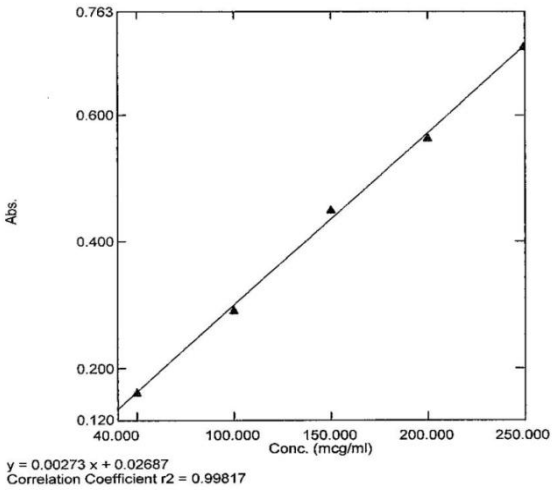

Fig 3a: Calibration curve of telmisartan with eriochrome Black-T.

Table 2a: Linearity range of telmisartan with eriochrome Black-T.

	Sample ID	Type	Ex	Conc	WL510.0
1	Tel eri1	Standard		50.000	0.164
2	Tel eri2	Standard		100.000	0.292
3	Tel eri4	Standard		200.000	0.564
4	Tel eri5	Standard		250.000	0.709
5	Tel eri3	Standard		150.000	0.451

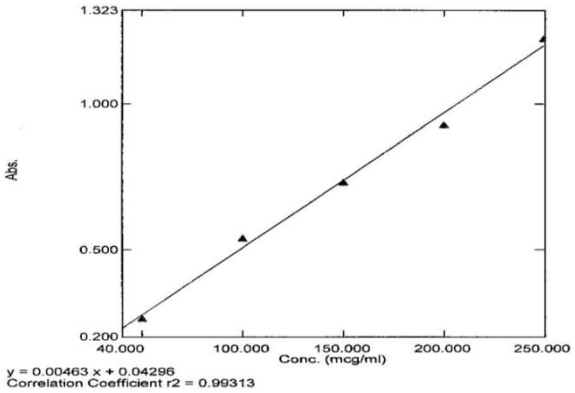

Fig. 3b Calibration curve of irbesartan with eriochrome Black-T

Table. 2b Linearity range of irbesartan with eriochrome Black-T

	Sample ID	Type	Ex	Conc	WL510.0
1	irbe eri 1	Standard		50.000	0.262
2	irbe eri 2	Standard		100.000	0.540
3	irbe eri 4	Standard		200.000	0.928
4	irbe eri 5	Standard		250.000	1.227
5	irbe eri 3	Standard		150.000	0.732

Precision

The intraday and interday precision was carried out for three different concentrations of telmisartan and irbesartan by measuring the corresponding absorbance six times on the same day and for three different days. The results are reported in terms of % relative standard deviation (%RSD) and presented in Table 3.

Table-3: Optical characteristics of the proposed method.

Parameters	Telmisartan	Irbesartan
λmax (nm)	510	510
Beer's law limit (μg/ml)	50 - 250	50 - 250
Sandel sensitivity (mcg/cm^2/0.001 A.U)	0.1282	0.047058
Molar absorptivity mL/mol^{-1} cm^{-1}	4.014×10^4	2.090×10^5
Regression equation Y=b+ax	0.00273x + 0.02687	0.00463x + 0.04296
Slope (a)	0.02687	0.04296
Intercept (b)	0.00273	0.00463
Correlation coefficient (r^2)	0.9981	0.9931
Range of errors*		
Confidence limit with 0.05level	0.3652	0.3198
Confidence limit with 0.01level	0.5403	0.2283
%RSD	0.4368	0.4738

***Average of six determination**

Table 4a: Determination of ruggedness of the proposed method for Telmisartan

Sample number	% labeled amount obtained by the proposed method					
	Analyst 1		Analyst 2			
	Intraday	Interday	Intraday	Interday	Instrument 1	Instrument 2
1	99.98	99.97	99.89	99.99	99.89	100.16
2	99.97	99.98	99.96	99.98	99.95	100.02
3	100.05	99.94	99.99	99.97	99.97	99.98
4	100.12	99.98	100.14	100.03	100.02	99.94
5	99.97	99.89	100.11	100.10	100.16	99.96
6	99.84	99.94	99.97	100.16	99.99	99.89
Mean	99.98	99.95	100.01	100.16	99.99	99.99
%RSD	0.0858	0.3163	0.0872	0.0968	0.0833	0.0850

Table 4b: Determination of ruggedness of the proposed method for Irbesartan

Sample number	% labeled amount obtained by the proposed method					
	Analyst 1		Analyst 2			
	Intraday	Interday	Intraday	Interday	Instrument 1	Instrument 2
1	99.90	100.2	99.89	99.92	99.99	100.12
2	99.97	100.03	99.87	99.96	99.89	100.03
3	100.06	99.95	99.89	99.98	99.89	99.95
4	100.12	99.99	99.54	100.13	100.13	99.99
5	99.99	99.96	100.2	100.12	100.14	99.97
6	99.97	99.93	100.1	100.07	99.99	99.93
Mean	100.00	100.01	99.91	100.03	99.99	99.99
%RSD	0.0508	0.0909	0.2081	0.0818	0.1106	0.0631

Specificity

Commonly used excipients were spiked into pre weighed quantity of the drugs. The absorbance was measured after appropriate dilutions and the quantities were determined. No interference of placebo was observed with absorbance hence the method is specific for these drugs.

Stability

No changes in the assay values were observed after 24 hrs indicating stability of the drugs in the solvent and the color obtained was stable up to 45 min after extraction. However a decrease in absorbance was measured thereafter.

Recovery studies

To study the accuracy of the proposed method, recovery studies were carried by standard addition method at three different levels. A known amount of drug was added to preanalysed tablet powder and percentage recoveries were calculated.

Ruggedness

The data of ruggedness obtained for different analysts with two different instruments for telmisartan and irbesartan is presented in Table 4a and 4b.

RESULTS AND DISCUSSION

The color product is due to ion pair formation of the drug with the dye in acidic medium. The optimum conditions were established by varying one parameter at a time and keeping other parameters fixed by observing the effect produced on the absorbance of the colored species. Investigations were carried out to establish most favorable conditions for the formation of colored product. The influence of buffer pH (pH ranging from 1.2-6.8) and different amounts of pH3.5 buffer on the reaction has been studied. It was observed that the absorbance started decreasing above 2.5 mL of pH 3.5 for both the drugs, so 2.5 mL of buffer was used for further study. The effect of changing the concentration of eriochrome black T over the range 0.5 mL to 4.0 mL was examined and it was observed that the absorbance started decreasing above 1.0 mL for telmisartan and 3.0 mL for irbesartan. Hence 1.0 mL of 0.1% w/v eriochrome dye solution for telmisartan and 3.0 mL for irbesartan was used for further studies. The optimum conditions such as λ max, volume of drug used, volume of reagent and buffer used were presented in Table-1. The optical characteristics and regression analysis are summarized in Table-3.To study accuracy, reproducibility, reliability and the interference from excipients used in the formulation, recovery experiment was carried out by standard addition method. From the total amount of drug found, the percentage recovery was calculated. The results of recovery analysis were presented in Table-5.

Table-5: Assay and Recovery studies of proposed method

Name of the dosage form	Labeled amount (mg)	Content of the drug found mg [a] ± S.D		% Recovery by the proposed method
		Proposed method	*Reference method	
Telmisartan Tablet	20	19.99.±0.059 F=0.7828 T=0.6540	20.025±0.051	99.95
Irbesartan Tablet	150	150.02±0.0715 F=0.2990 T=0.4561	149.95±0.043	100.011

Average ± standard deviation of eight determinations, the t and F- values referred to comparison of proposed method with reference method. Theoretical values at 95% confidence limits t = 2.365 and F=4.88

***Methanol was used as solvent for reference UV methods for both the drugs.**

The analysis results of marketed formulation were in good agreement with the labeled claim. High percentage of recovery shows that this method is free from the interference of excipients used in formulation and can be used in routine quality control analysis of these drugs.

The proposed method for determination of telmisartan and irbesartan by using eriochrome black –T was applied to commercial tablets together with the reference method. These determinations were carried out on the same batches of samples. The results obtained were compared statistically by student T-test and variance ratio F-test. The experimental values did not exceed the theoretical values in either test which indicates that there was no significant difference between the methods compared.

CONCLUSION

The proposed method is simple, rapid, sensitive and can be successfully applied for estimation of these drugs in pharmaceutical dosage form. The proposed reagent is cheaper and easily available and the method does not need any heating for color development.

REFERENCES

1. Zonghui Qin, Weifen Niu and Rong Tan: Spectrophotometric method for the determination of telmisartan with congored. Journal of Analytical Chemistry. 2008; Vol. 64(5): 449-454.
2. U.P.Patil, S. V. Gandhi, M. R. Sengar and V. S. Rajmane: Simultaneous determination of atorvastatin calcium and telmisartan in tablet dosage form by spectrophotometer.Inter. J. of Chemtech Research., 2009; Vol. 1(4), 970-973.
3. Shen J Jiao Z, Li ZD, Shi XJ, Znong MK: HPLC determination of telmisartan in human plasma and its application to a pharmacokinetic study. Pharmazie., 2005; Vol. 60(6), 418-420.
4. Sun L: Determination of telmisartan by HPLC. Chinese Journal of New drugs. 2006; Vol. 15(14), 1210-1212.
5. SB. Wankhede, MR Jajne, KR Gupta and SG. Wadodkar: RP-HPLC method for simultaneous estimation of telmisartan and hydrochlorothiazide in tablet dosage form. Indian Journal of Pharmaceutical Sciences. 2007; Vol. 69(2), 298-300.
6. K.L.Lakshmi, Lakshmi Subramanian and Krishanu Pal: Stability indicating HPTLC method for simultaneous determination of telmisartan and ramipril in tablet. International Journal of Pharmacy and Pharmaceutical Sciences. 2010; Vol. 2(4), 127-129.
7. Isabel Albero, Vicente Rodenas, Soledad Garcia and Concepcion Sanchez Pedreno: Determination of irbesartan in the presence of hydrochlorothiazide by derivative spectrophotometry. Journal of pharmaceutical and Biomedical Analysis. 2004; Vol. 29(2), 299-305.
8. Bae SK, Kim MJ, Shim E J, Cho D Y, Shon J H, Liu KH, Kim E Y, Shin JG: HPLC determination of irbesartan in human plasma, its application to pharmacokinetic studies. Biomed chromatography. 2009; Vol. 23(6), 568-572.
9. Nevin Erk: Simultaneous determination of irbesartan and hydrochlorothiazide in human plasma by liquid chromatography. Journal of Chromatography., 2003;Vol. 784 (1), 195-201.
10. R.T. Saue, M. Francis and S.Pawar: Determination of irbesartan in pharmaceutical dosage forms by HPTLC. Indian Drugs. 2002; Vol.39 (1), 32-35.