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Research Article

SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF ANGIOTENSIN –ll RECEPTOR ANTAGONIST IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

Simple, sensitive, rapid and accurate spectrophotometric method has been developed for the determination of losartan and irbesartan in pure and pharmaceutical preparation. The method is based on the formation of ion-association complex of drug with orange-G in acidic buffer followed by its extraction into organic solvent (chloroform). The absorbance of organic layer was measured at their respective wavelength of maximum absorbance against the reagent blank. Beer's law is obeyed in the concentration range of 25-150 µg/mL for losartan and 20-100 µg/mL for irbesartan at the selected wavelengths. The results of analysis validated statistically and by recovery studies. The proposed method is simple, economical and useful in the estimation of these drugs in pharmaceutical formulations.

Keywords: Losartan, Irbesartan, Orange-G, Spectrophotometric method.

INTRODUCTION

Losartan chemically is (2-butyl-4-chloro-1-{[2[1]-(1H-tetrazol-5-yl) biphenyl-4-yl] methyl} - 1H-imidazol-5-yl) methanol (Fig 1a), is an angiotensin II receptor antagonist, used mainly to treat high blood pressure.

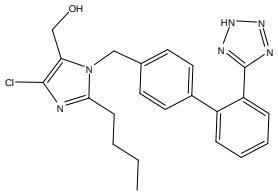

Fig 1a. Losartan

Irbesartan (Fig 1b) 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.

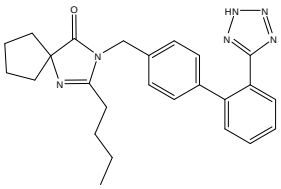

Fig 1b Irbesartan

Only a few methods appeared in the literature for the determination of losartan[1-6] and irbesartan[7-10] in bulk and pharmaceutical formulations. But there is no simple extractive spectrophotometric method[(11-12)] for determination of these drugs in the literature. The present paper describes a simple, accurate, specific and precise method for estimation of these drugs. The proposed method is optimized, validated and applied for the determination of these drugs in pharmaceutical formulations.

MATERIALS AND METHODS

Instrument

All the measurements were made using spectrophotometer Shimadzu uv-1800 with 10 mm matched quartz cells. Losartan and irbesartan were obtained as gift samples from Aurobindo Pharmaceuticals Ltd., Hyderabad. All the chemicals used were of analytical grade and procured from Qualigens India Ltd. All the solutions were freshly prepared with double distilled water and tablet formulation labeled to contain 25 mg of losartan (LOSCAR - ZY-Medica) and IROVEL (Sun Pharma) with 150 mg of irbesartan were purchased from local pharmacy.

Preparation of reagents

Orange-G solution (0.2%)

200 mg of orange-G was dissolved in 100 mL of distilled water and washed with chloroform to remove chloroform soluble impurities.

0.1M HCL solution

0.85 mL of HCL is diluted to 100 mL of distilled water.

Preparation of standard drug solution

100 mg of each drug was weighed and transferred into two different volumetric flasks. To each flask 10 mL of methanol was added to dissolve the drug and diluted to 100 mL with distilled water (1 mg/mL).

Selection of wavelength

In order to ascertain the wavelength of maximum absorbance losartan and irbesartan solutions were scanned in the range from 400-600 nm against the reagent blank. The resulting spectra's were shown in Fig 2a and 2b and the absorption curve showed characteristic absorption maxima at 485 for losartan and 481 for irbesartan.

General procedure

Into a series of 60 mL separating funnels, different volumes of the working standard solution of these drugs (losartan and irbesartan) were taken. To each of these funnel, dye solution (0.2% orange-G), buffer solution (0.1M HCL) and 10 mL of chloroform were added (as per optimized conditions mentioned in Table-1). The reagent blanks were also prepared. The ion-association complex was then extracted into chloroform layer by shaking these funnels. The separating funnels were allowed to stand for ten minutes to allow the two layers to separate. The organic layers of these drugs (losartan and irbesartan) were collected. The absorbance values of the resulting solutions were taken against the corresponding reagent blank at the respective λ max as mentioned in the Table-1. The Beer's law plot of absorbance against concentration was plotted. Linearity was observed between 25-150 µg/mL for losartan, 20-100 µg/mL for irbesartan.

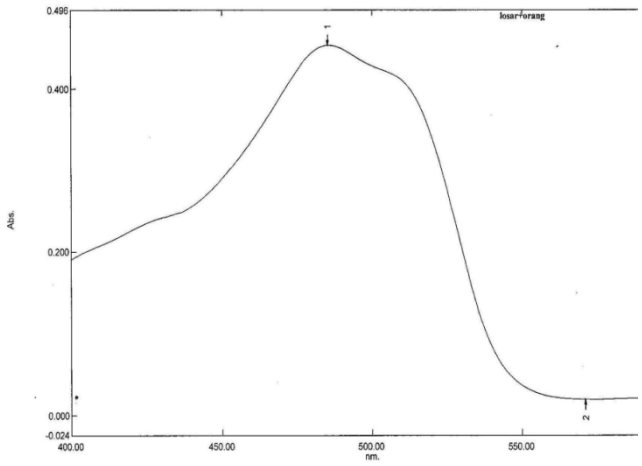

Fig. 2a: Spectrum of Losartan with Orange-G

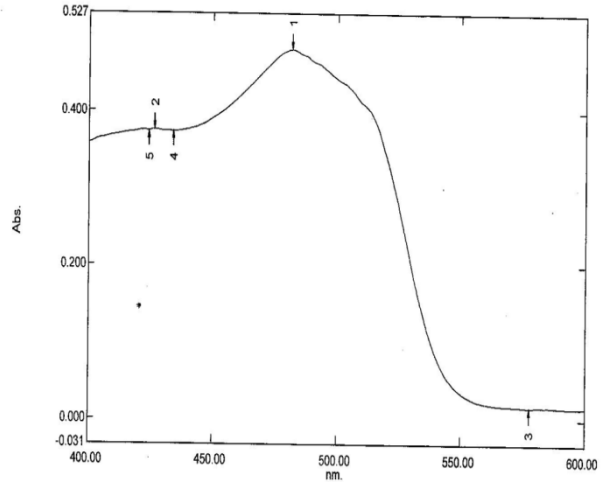

Fig. 2b: Spectrum of Irbesartan with orange-G

Table1: Optimum conditions of the proposed method

Reagent	Losartan	Irbesartan
Drug solution taken (µg/mL)	25 - 150	20 - 100
Volume of pH 9.8 buffer (mL)	2.0	1.5
Volume of reagent employed (mL)	1.5	2.0
λmax (nm)	485	481

Analysis of formulation

Twenty tablets (each drug) were weighed accurately and an average weight was calculated. The tablets were powdered and the tablet powder equivalent to 50 mg of each drug was weighed and transferred to two 50 mL volumetric flasks. Small amount of methanol was added to dissolve the drug and the volume was made up to the mark with distilled water. Both the solutions were filtered through Whatmann filter paper and from the filtrate 1.0 mL of losartan solution and 0.5 mL of irbesartan solution was transferred to two different 60 mL separating funnels for color development and the experiment was carried out as described above. The amount of the drug present in tablet was calculated from their respective calibration curves.

Recovery studies

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

Repeatability

Repeatability is given by intraday and inter day precision. The assay and recovery procedures were repeated for three times on the same day and for the three consecutive days for both the drugs.

Ruggedness

The data of ruggedness obtained from two different analysts and on two different instruments for losartan and irbesartan was presented in Table 4a and 4b.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation (calculated from the eight

measurements containing 3/4th of the amount of the upper Beer's law limits) and regression characteristics like slope (b), intercept (a), percentage range of error (0.05 and 0.01 confidence limits), all these parameters were calculated and summarized in Table 2. The results showed that the method has reasonable precision. The percent RSD was found to be less than 1% for both the drugs which indicates the method has good precision and the results are presented in Table 2.

Table 2: Optical characteristics of the proposed method

Parameters	Losartan	Irbesartan
λmax (nm)	485	481
Beer's law limit (µg/ml)	25 - 150	20 - 100
Sandel sensitivity (mcg/cm^2/0.001 A.U)	0.1282	0.047058
Molar absorptivity mL/mol^{-1} cm^{-1}	3.299×10^4	9.1×10^4
Regression equation Y=b+ax	0.00624x + 0.13483	0.01969x + 0.05253
Slope (b)	0.13483	0.01969
Intercept (a)	0.00624	0.05253
Correlation coefficient (r^2)	0.9935	0.9994
Range of errors	0.26903	0.15437
Confidence limit with 0.05level	0.3979	0.2283
Confidence limit with 0.01level	0.214	0.150
%RSD		

y=b+ax*, where y is the absorbance, x is concentration in µg/ml; %RSD - Percent relative standard deviation

The linearity range for losartan and irbesartan was found to be 25 – 150 µg/mL and 20 – 100 µg/mL respectively and presented in Table 3a and 3b (Fig. 3a and 3b).

Table 3a: Linearity table of Losartan with orange -G

S. No.	Concentration (µg/ml)	Absorbance at 481 nm
1	20	0.439
2	40	0.850
3	60	1.223
4	80	1.649
5	100	2.008

Table 3b: Linearity table of Irbesartan with orange –G

S. No.	Concentration (µg/ml)	Absorbance at 485 nm
1	25	0.268
2	50	0.476
3	75	0.585
4	100	0.789
5	125	0.907
6	150	1.061

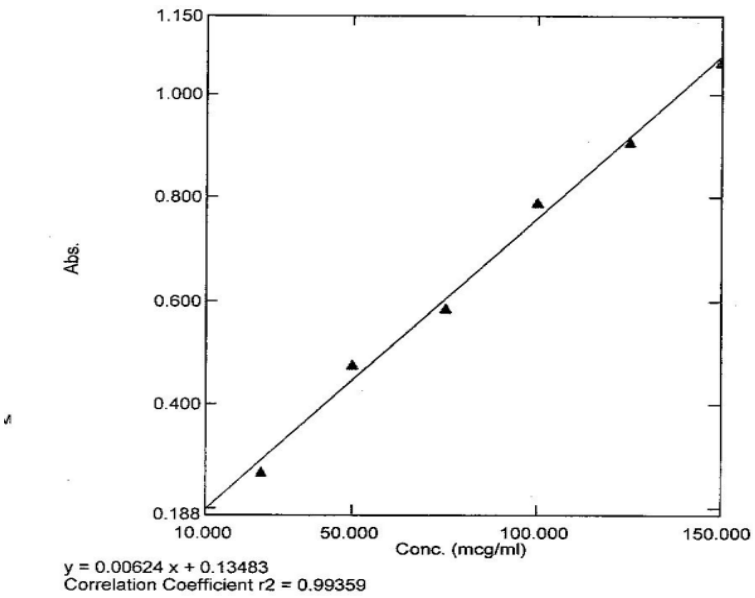

Fig. 3a: Calibration curve of Losartan with Orange -G

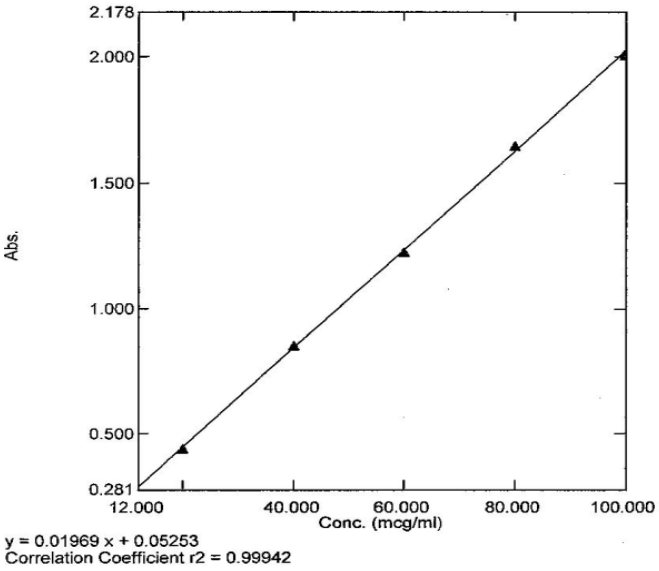

Fig. 3b: Calibration curve of Irbesartan with orange –G

Further the precision was confirmed by intra and inter day analysis for both the formulations which are presented in Table 4a and 4b. The results show good agreement with the label claim of the formulations. The method was validated for ruggedness and the results confirm the ruggedness of the method. The excipients usually present in formulations of these drugs did not interfere with proposed analytical method.

Commercial formulations (tablets) containing these drugs were successfully analyzed by the proposed method. The values obtained by the proposed and reference methods for formulations were compared statistically by the T test and F test and found not to differ significantly. As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the pre-analyzed formulations. These results were presented in Table-5.

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

Sample number	% labeled amount obtained by the proposed method					
	Analyst 1		Analyst 2			
	Intraday	Interday	Intraday	Interday	Instrument 1	Instrument 2
1	99.89	100.1	99.96	99.92	99.94	100.1
2	99.94	100.2	99.87	99.86	99.97	100.09
3	100.4	99.86	99.89	99.88	99.98	99.90
4	100.2	99.99	99.54	100.03	100.03	99.89
5	99.87	99.78	100.2	100.30	100.1	99.86
6	99.89	99.89	100.1	100.10	99.89	99.95
Mean	100.03	99.97	99.92	100.01	99.98	99.96
%RSD	0.1993	0.1442	0.2081	0.1527	0.0665	0.0956

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	99.99	99.98	99.87	99.89	99.99	100.06
2	99.91	99.92	99.98	99.96	99.99	100.12
3	100.14	99.79	99.95	99.98	99.87	99.88
4	100.03	98.99	100.04	100.13	100.12	99.91
5	99.99	99.82	100.01	100.20	100.06	99.86
6	99.78	99.91	99.87	100.04	99.79	99.99
Mean	99.97	99.88	99.95	100.03	99.97	99.97
%RSD	0.1105	0.3391	0.0649	0.1048	0.1109	0.0955

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	
Losartan Tablet	150	150.015±0.0157 F=0.231378 T=0.868449	150.006±0.04	100.001
Irbesartan Tablet	25	25.003±0.0217 F=0.2060 T=0.3374	24.99±0.036056	100.012

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.

CONCLUSION

The extractive colorimetric method for the estimation of these drugs is selective, economical, accurate, precise, and rapid and can be employed for the routine quality control analysis and quantitative determination of these drugs from their pharmaceutical preparation.

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