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Journal of Pharmaceutical and Biomedical Analysis
27 (2002) 861–866

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

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A rapid colorimetric method for the determination of Losartan potassium in bulk and in synthetic mixture for solid dosage form

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Received 16 March 2001; received in revised form 5 June 2001; accepted 4 July 2001

Abstract

Two new rapid reproducible and economical spectrophotometric methods are described for the determination of Losartan potassium in bulk and in synthetic mixture for solid dosage forms. Both methods are based on the formation of an orange-red and orange ion-pair complex due to the action of Calmagite (CT) and Orange-II (O-II) on Losartan potassium in acidic medium (pH 1.2). Under optimised conditions, they show an absorption maxima at 491 nm (CT) and 486 nm (O-II), with molar absorptivities of 1.74×10^3 and 1.75×10^3 l mol^{-1} cm^{-1} and Sandell's sensitivities of 0.2649 and 0.2637 per 0.001 absorbance unit for CT and O-II, respectively. The colour is stable for 5 min after extraction. In both cases Beer's law is obeyed between 10 and 100 μg ml^{-1}. The proposed method was successfully extended to synthetic mixture for solid dosage forms.

Keywords: Losartan potassium; Spectrophotometry; Calmagite (CT); Orange-II (O-II); Synthetic mixture for solid dosage forms

1. Introduction

Losartan potassium, 2-Butyl-4-chloro-1 [[2′-(1H-tetrazol-5-yl)[1, 1′-biphenyl]-4-yl]methyl]-1H-imidazole-5-methanol, is a recent non-peptide angiotensin-II receptor (type AT_1) antagonist [1]. It is an excellent antihypertensive drug, which is used in CHF [2]. It is the prototype of a new class of antihypertensive agents, the angiotensin receptor antagonists.

Losartan has the potential to offer the advantage of increased selectivity, specificity and consistent blockade of circulating and tissue renin–angiotensin at AT_1 receptor level without some of the shortcomings associated with the use of ACE inhibitors [3,4]. The drug is not official in any pharmacopoeia as yet. The different analytical methods that are reported for its estimation include High performance thin layer chromatography [5], Radio receptor assay [6], normal and reverse phase High performance liquid chromatography [7–14] and one UV-spectrophotometric method [15]. No simple colorimetric method has been reported till date for the estima-

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0731-7085/02/$ - see front matter
PII: S0731-7085(01)00536-2

tion of Losartan potassium. Hence, it was thought worth while to develop spectrophotometric methods for the same.

In the present study, two colorimetric methods for the determination of Losartan in bulk and in synthetic mixture for solid dosage forms are described. The methods are based on the orange-red and orange coloured ion-pair formation of Losartan with CT and O-II (at pH 1.2), respectively. The absorbance measurements were made at λ_{max} 491 nm with CT and 486 nm with O-II after extraction of the colour complex with chloroform.

These methods are simple, rapid, and easy to apply in routine usage and do not need costly instrumentation.

2. Experimental

2.1. Apparatus

Absorbance measurements were made on Hitachi U-2000 UV-visible spectrophotometer (German make) with 10 mm matched quartz cells.

2.2. Reagents and solutions

All chemicals were of analytical reagent grade and solutions were prepared with purified water of I.P. [16] grade.

2.2.1. Losartan potassium

Pharmaceutical grade of Losartan potassium was kindly gifted by Alembic Chemical Works, Baroda, India and certified to contain 99.5% of Losartan potassium. It was used without further purification.

2.2.2. Calmagite (CT) standard solution (0.1% w/v)

A standard solution was prepared by dissolving 0.1 g of CT (S. D. Fine, Mumbai) in purified water and diluted to 100 ml with purified water.

2.2.3. Orange-II (O-II) standard solution (0.1% w/v)

A standard solution was prepared by dissolving 0.1 g of O-II (S. D. Fine, Mumbai) in purified water and diluted to 100 ml with purified water.

2.2.4. Losartan potassium stock solution (2.169×10^{-3} M)

A stock solution was prepared by dissolving 0.1 g of Losartan potassium in purified water and diluting to 100 ml with purified water.

2.2.5. Hydrochloric acid buffer solution (pH 1.2)

Hydrochloric acid buffer solution of pH 1.2 was prepared by adding 85 ml of 0.2 M hydrochloric acid solution to 50 ml of 0.2 M potassium chloride solution in a 200 ml volumetric flask and made to volume with purified water.

2.2.6. Chloroform (S. D. Fine, Mumbai)

Chloroform was purified as described by Vogel [17] and used.

2.3. Procedure for calibration curve

Into a series of separating funnels, appropriate aliquots of the standard drug solution (Table 1) were pipetted out. To each funnel was added

Table 1
Optimum conditions, optical characteristics and statistical data of the regression equation for ion-pair complex formation with Losartan potassium

Parameters	CT	O-II
Drug aliquot (ml)	0.1–1.0	0.1–1.0
pH of buffer	1.2	1.2
Amount of buffer (ml)	2.0	2.0
Amount of reagent (ml)	1.0	1.0
Absorption maxima (nm)	491	486
Beer's law limits (μg ml^{-1})	10–100	10–100
Molar absorptivity (l mol^{-1} cm^{-1})	1.74×10^3	1.75×10^3
Sandell's sensitivity (μg cm^{-2} per 0.001 AU)	0.2649	0.2637
Regression equation[a]	$Y = 0.00224 + 0.00296x$	$Y = -0.02162 + 0.00456x$
Intercept (a)	2.24×10^{-2}	-2.16×10^{-2}
Slope (b)	2.96×10^{-3}	4.56×10^{-3}
Correlation coefficient (r)	0.9998	0.9999

[a] $n = 25$ for CT; $n = 30$ for O-II.

buffer and dye solution as mentioned in Table 1. The solution was mixed thoroughly and successively extracted with chloroform. The combined chloroform extracts were dried over anhydrous sodium sulphate and the volume was made to 10 ml with chloroform. The absorbance was measured within 5 min of extraction against respective reagent blanks at the absorption maxima mentioned in Table 1. The determinations were repeated five times for each method. The linearity range for both the methods was found to be 10–100 μg ml^{-1}. Data are summarized in Table 2.

2.4. Procedure for the analysis of synthetic mixture for solid dosage forms

Synthetic mixture containing Losartan potassium was prepared with excipients commonly used in solid dosage forms and analysed to check the applicability of the proposed method. The following excipients were added to the drug to prepare a synthetic mixture for solid dosage forms.

Ingredients	Weight (g)
Losartan potassium	1.000
Lactose	0.850
Starch	0.090
Talc	0.040
Magnesium stearate	0.020

A portion of the synthetic mixture equivalent to 25 mg of Losartan potassium was transferred to a 50 ml conical flask. The drug in the mixture was dissolved in a small quantity of purified water by shaking the flask for 5 min. The solution was filtered into a 25 ml volumetric flask through Whatman filter paper No. 42 and the flask and the filter paper were rinsed thoroughly with purified water. The contents of the volumetric flask were then diluted to 25 ml with purified water. An appropriate aliquot was then taken in such a way that the final concentration in 10 ml flask lies within the range tested. The determination for Losartan potassium was done with CT and O-II as described in Section 2.3. The results are summarized in the Table 3.

3. Results and discussion

3.1. Optimization of parameters

Losartan potassium was found to yield a clear orange-red and orange colour with CT and O-II in acidic medium extractable with chloroform with absorption maxima of 491 and 480 nm, respectively. The coloured product is due to ion-pair complex formation of the drug with the dyes CT and O-II. Therefore, investigations were carried out to establish the most favorable conditions for the formation of the coloured product.

The influence of the different pH buffers (pH ranging from 1.2 to 10) on the reaction has been studied. It was observed that the absorbance

Table 2
Data for calibration curve

For CT		For O-II	
Concentration (μg ml^{-1})	Absorbance[a]	Concentration (μg ml^{-1})	Absorbance
10	0.050	10	0.025
25	0.100	20	0.070
50	0.168	40	0.158
75	0.254	60	0.250
100	0.318	80	0.345
–	–	100	0.435

[a] Average of five determinations.

Table 3
Analysis of Losartan potassium in synthetic mixture

Method Applied	Equivalent amount taken for estimation (mg)	Quantity of drug recovered (mg)[a]	Recovery (%)
CT	25	25.18	100.72
	50	50.32	100.64
O-II	25	25.15	100.60
	50	50.28	100.56

[a] Average of five determinations.

started decreasing above the pH 1.2 and between pH 4 and 10, there was no extraction of the coloured complex in chloroform layer in both the methods. Hence, a buffer of pH 1.2 was used in further studies.

The influence of different amounts of pH 1.2 buffer on the reaction has been studied. It was observed that the absorbance started decreasing above 2.0 ml of pH 1.2 buffer. Hence, 2.0 ml of pH 1.2 buffer was used in further studies.

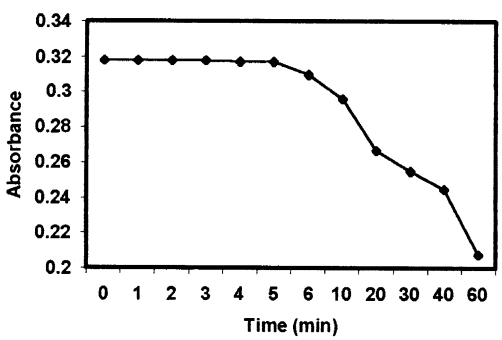

Fig. 1. Effect of time on stability of orange-red coloured complex.

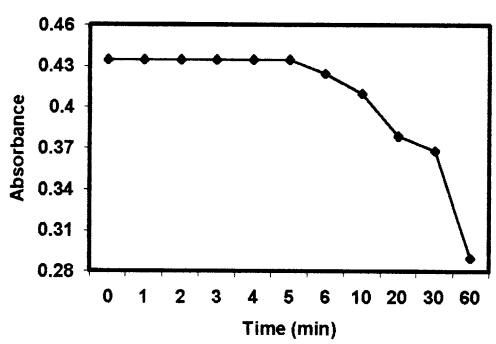

Fig. 2. Effect of time on stability of orange coloured complex.

The effect of changing the concentration of CT and O-II over the range of 0.5–4.0 ml was examined. It was observed that the absorbance started decreasing above 1.0 ml for both CT and O-II. Hence, 1.0 ml of CT and O-II was used in all studies.

There was no effect of time on the stability of the colour (in both the methods) up to 5 min after extraction. However, a decrease in the absorbance was noted after this period. Therefore, it is recommended that the absorbance be measured within this time period (Figs. 1 and 2).

3.2. Conformity to Beer's law

Beer's law is obeyed in the concentration (C, μg ml^{-1}) range 10–100 μg ml^{-1} of the drug with both CT and O-II. The optical characteristics such as Beer's law limits, molar absorptivities, Sandell's sensitivities [18] are recorded in Table 1. The regression analysis using the method of least square was made for the slope (b), intercept (a) and correlation coefficient (r) obtained from different concentrations. The results are summarized in Table 1.

3.3. Selectivity

The selectivity of the method was checked by monitoring a standard solution of Losartan potassium in the presence of other compounds of the tablet (excipients). The response was not different from that obtained in the calibration. The absorbance values of solution of the excipients alone were measured too, at 491 nm with CT and

Table 4
Evaluation of the accuracy and precision of the two proposed procedures

Method applied	Added (mg)	Found ± S.D.[a]	R.S.D. (%)	S.A.E.[b]	CL[c]
CT	10	10.08 ± 0.058	0.575	0.026	10.08 ± 0.0720
	25	25.21 ± 0.039	0.155	0.017	25.21 ± 0.0484
	50	50.35 ± 0.060	0.119	0.027	50.35 ± 0.0745
		Mean:	0.283	0.023	
O-II	25	25.13 ± 0.055	0.219	0.025	25.13 ± 0.0683
	50	50.27 ± 0.065	0.129	0.029	50.27 ± 0.0807
	75	75.36 ± 0.082	0.109	0.037	75.36 ± 0.1018
		Mean	0.152	0.030	

[a] Mean ± S.D. for five determinations.
[b] S.A.E., standard analytical error.
[c] Confidence limit at $P = 0.05$ and four degrees of freedom.

at 486 nm with O-II, showing no significant difference from the baseline. The excipients caused no effect upon the estimation of Losartan potassium (Table 3). Hence, the determination of the drug is considered to be free from interference due to excipients.

3.4. Precision and accuracy

In order to determine the precision and accuracy of the methods, solutions containing known amounts of drug were prepared and analysed in five replicates. The analytical results obtained from these investigations are summarized in Table 4. The mean relative standard deviation (R.S.D.) and the mean standard analytical error (S.A.E.) can be considered to be very satisfactory.

3.5. Application

The proposed methods for the determination of Losartan potassium were extended to synthetic mixture for solid dosage forms. The analytical results summarized in Table 3 indicate that the methods do not suffer interference from common excipients used in tablets viz., talc, starch, magnesium stearate, lactose, etc.

However, due to non-availability of the formulation the proposed methods could not be extended to pharmaceutical dosage forms.

4. Conclusion

The orange-red and orange coloured complexes formed under the above mentioned conditions can be regarded as ion-pair complex formation between the dye (CT, O-II) and the drug. The proposed methods have the advantage of simplicity, reproducibility and satisfy the need for a rapid procedure for the determination of Losartan potassium in bulk and in its dosage forms. Hence, the proposed methods should be useful for routine quality control purposes.

Acknowledgements

The financial assistance by M/s. Astral Pharmaceutical Industries, Baroda, India, is gratefully acknowledged.

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