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A SELECTIVE HPLC METHOD FOR THE DETERMINATION OF LOSARTAN POTASSIUM IN PURE AND PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

A reverse phase high performance liquid chromatographic (HPLC) method has been developed for the estimation of Losartan Potassium (LSP) in its pure and pharmaceutical dosage forms. The quantification was carried out using a RP Techsphere Silica column in isocratic mode, with mobile phase consisted of acetonitrile, methanol and water in the ratio of 30 : 30 : 40 (v/v). Beclomethasone dipropionate was used as an internal standard. The mobile phase was pumped at a rate of 0.5 mL/min and the detection was carried out at 254 nm and the linearity was found to be in the range of 2–10 µg/mL. The proposed method was found to be simple, precise, accurate, rapid and reproducible for the estimation of Losartan Potassium in pure and pharmaceutical dosage forms i.e. tablets.

Key words : HPLC, Losartan Potassium, Pharmaceutical dosage forms.

INTRODUCTION

Losartan potassium (LSP) is, the first of a new class of anti–hypertensives. It is an angiotensin II receptor antagonist. LSP and its principle active metabolites block the vasoconsrictor and aldosterone secreting effects of angiotensin II to the AT1 receptor found in many tissues, e.g. vascular smooth muscles, adrenal glands. Chemically, it is 2–buty1–4–chloro–1–[p–(o–1H–tetrazol–5–ylphenyl)–benzyl]imidazol–5–methanol monopotassium salt. Its empirical formula is C_{22} H_{22} Cl KN_6 O. Its molecular weight is 461.01. LSP is not official in IP, BP, USP, EP and JP. Literature survey reveals the presence of few analytical methods, such as HPLC [1–3], UV [6–8], GC[9] and HPTLC[10] in pharmaceutical formulations and in biological fluids. The present investigation has been undertaken to develop a simple method for the estimation of Losartan Potassium in tablet dosage forms.

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EXPERIMENTAL

Instrumentation

An isocratic high performance liquid chromatograph (Schimadzu) with two LC–10A pumps, variable wavelength programmable UV/Visible detector SPD–10A, Chromatopac integrator C R6 A, 20 µl Rheodyne 7125 loop injector and Techsphere silica column (250 mm x 4.6mm i.dl; particle size 10 µm) was used.

Chemicals and reagents

Losartan potassium and beclomethasone dipropionate were the gift samples from Aristo and Cipla Labs, respectively. HPLC grade methanol and HPLC grade acetonitrile are from Qualigens. Triple distilled water was used.

Chromatographic conditions

The chromatographic column used was a 250 x 4.6 mm Techsphere Silica with 10 µm particles. Both acetonitrile and methanol were filtered through 0.45 µm–membrane filter and sonicated before use. The HPLC equipment was operated at ambient temperature. The flow rate of the mobile phase was maintained at 0.5 mL $min.^{-1}$ Detection was carried out at 254 nm and the injection volume was 20 µL.

Internal standard solution

About 100.0 mg of beclomethasone dipropionate reference standard was dissolved in 100.0 mL of HPLC grade methanol. The solution was sonicated for 30 min and filtered. It was further diluted with mobile phase to prepare an internal standard solution of 100.0 µg mL^{-1}.

Procedure

About 100.0 mg of pure sample of LSP was weighed accurately and dissolved in 100.0 mL of HPLC grade water. The solution was sonicated for 30 min. It was further diluted to prepare a standard of 100.0 µg mL^{-1}. Subsequent dilutions of this solution was made after addition of beclomethasone dipropionate (100.0 µg mL^{-1}) as an internal standard (IS) to get concentration of 2–10 µg mL^{-1} of LSP and 10.0 µg mL^{-1} of IS in each dilution, respectively. The solutions prepared as above were filtered through 0.45 µm membrane filter and then 20.0 µL of filtrate was injected five times into the column at a flow rate of 0.5 mL min^{-1}. The ratio of drug peak area to that of internal standard for each of the drug concentration was calculated. The regression of the drug concentration over the ratio of drug peak area to that of internal standard was obtained. This regression equation was used to estimate the amount of LSP in tablet dosage forms.

Estimation of LSP in tablet dosage forms

Two commercial brands of tablets were chosen for testing suitability of the proposed method to estimate LSP in tablet dosage forms. About 20 tablets were pulverized and the powder equivalent of 100.0 mg of LSP was weighed, dissolved in 100.0 mL of HPLC grade water and sonicated for about 30 min. The insoluble portion was filtered through a 0.45 µm membrane filter. The filtrate was further diluted to prepare a solution of 100.0 µg mL^{-1}. From the filtrate, different aliquots (2–10 µg mL^{-1}) were taken in separate 10.0 mL volumetric flasks. These solutions were spiked with suitable volume of the internal standard solution, such that the concentration of the internal standard in each was 10.0 µg mL^{-1}. The contents of the flask were made up to the volume with the mobile phase and mixed well. Each of these solutions (20.0 µl) was then injected five times into the column. The mean peak area ratios of the drug to the internal standard of five such determinations were calculated and the drug content in the tablets was quantified using the regression equation obtained from the pure sample.

RESULTS AND DISCUSSION

The present study was carried out to develop a simple, rapid, accurate and precise HPLC method for the analysis of LSP in pharmaceutical dosage forms. A typical chromatogram is shown in Fig. 1. The retention times for LSP and internal standard (Beclomethasone dipropionate) were 3.84 min and 5.87 min, respectively. Each of the samples was injected five times and the same retention times were observed in all cases. The ratio of the peak area of the LSP to peak area of internal standard for different concentrations set up as above were calculated and the average values for five such determination are shown in Table 1. The peak areas of both the drug and internal standard were reproducible as indicated by low coefficient of variation (0.3440).

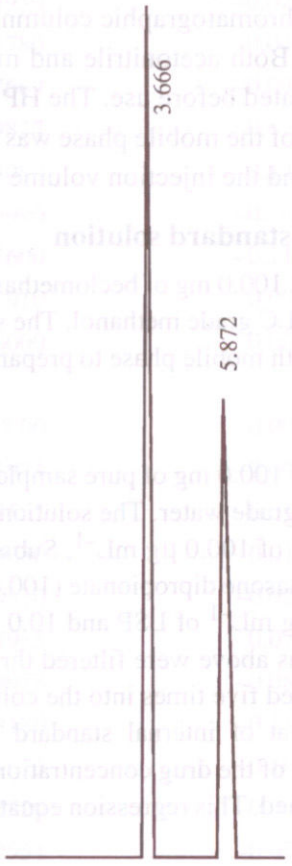

Figure 1 Model Chromatogram of Losartan

Table 1. Calibration of the proposed method

Drug concentration (μg mL^{-1})	Mean peak area ratio (n = 5)	Coefficient of variance (%) (CV)
2.0	0.301	1.23
4.0	0.602	0.96
6.0	0.904	0.68
8.0	1.201	0.28
10.0	1.501	1.03

Regression equation (from 2.0 to 10.0 μg mL^{-1}); Y = 0.1499X + 0.0023 (r = 0.9999)

Table 2. Precision of the proposed method

Concentration of LSP (μg mL^{-1})	Observed concentration of LSP (μg mL^{-1})			
	Intra–day		Inter–day	
	Mean (n = 5)	% CV	Mean (n = 5)	% CV
4.0	4.02	0.38	4.04	0.53
6.0	5.99	0.27	6.01	1.22
8.0	8.04	0.64	8.05	0.32

Table 3. Results of recovery study

Amount of drug added (μg)	Recovery from drug solution		Recovery from tablet formulation	
	Mean amount found (n = 5)	Mean % recovery	Mean amount found (n = 5)	Mean % recovery
2.0	2.01	100.5	1.99	99.5
6.0	6.01	100.16	6.02	100.33
10.0	9.98	99.8	10.01	100.1

Table 4. Assay of LSP in tablet dosage forms

S.No.	Labeled amount of drug (mg)	Mean (± s.d.) Amount (mg) found by the proposed method (n = 5)	Mean (± s.d.) % labeled amount (n = 5)
Table I	25	24.93 ± 0.08	99.72 ± 0.37
Table II	25	24.88 ± 0.16	99.52 ± 0.37

A good linear relationship (r = 0.9999) was observed between the concentration of the LSP and the respective ratio of peak areas. The calibration equation was found to be Y = 0.1499X + 0.0023 (where Y is the ratio of peak area of drug to that of internal standard, X = concentration of LSP). The intra–day and inter–day variations of the method were determined using five replicate injections of three different concentrations, which were prepared and analyzed on the

same day and three different days over a period of two weeks, a low coefficient of variation was observed (Table 2). This shows that the present HPLC method is highly precise.

To ensure the reliability and accuracy of the method, recovery studies was carried out by mixing a known quantity of drug with preanalyzed sample and contents were reanalyzed by the proposed method. The values are shown in Table 3. About 99.9% of LSP could be recovered from the preanalyzed samples indicating the high accuracy of the proposed HPLC method.

The drug content in the tablets was quantified using the proposed analytical method. The mean amount of LSP in two different brands of tablets dosage forms is shown in Table 4. The absence of additional peaks in the chromatogram indicates the non–interference of the common excepients used in the tablets. The tablets were found to contain 99.72 and 99.52% of labeled amount of the drug. It can be concluded that the proposed HPLC method is sufficiently sensitive and reproducible for the analysis of LSP in pharmaceutical dosage forms within a short analysis time.

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REFERENCES

1. N. Erk., J.Pharm. Biomed. Anal., **24**, 603 (2001).
2. L. Gongalez, R. M. Alonaso and R. M. Jimenez, Chromatographia, **52**, 735 (2000).
3. P. K. F. Yeung, A. Jamieson, G. J. Smith, D. Fice, and P. T. Pollock, Int. J. Pharm., **204**, 17 (2000).
4. G. Carlucci, G. Palumo, P. Mazzco, and M. Q. Giovanna, J. Pharm. Biomed. Anal., **23**, 185 (2000).
5. G. V. Kanumula, and B. Raman, Indian Drugs, **37**, 38 (2000).
6. M. N. Reddy, J. M. Krishna, V. R. Kumar, K. V. K. Rao and D. K. Sankar, Acta. Cienca. Indica, Chem., **26**, 31 (2000).
7. N. R. Lande, B. M. Shetkar, S. S. Kadem, and S. R. Dheneshwar, Indian Drugs, **37**, 577 (2000).
8. H. K. Jain, A. K. Singhai, and R. K. Agarwal, Indian Drugs, **37**, 239 (2000).
9. H. H. Maurer, T. Kraemer and J. W. Arlt, Ther. Drug Monit., **20**, 706 (1998).
10. K. E. Mc Carthy, Q. Wang, E. W. Tsai, R. E. Gilbert, D. P. Ip and M. A. Brooks, J. Pharm. Biomed. Anal., **17**, 671 (1998).

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