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The estimation of eprosartan mesylate in pharmaceutical dosage forms by RP-HPLC

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ABSTRACT

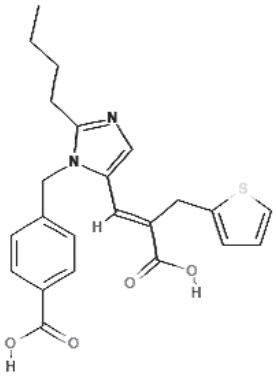
A simple, precise, rapid and accurate reverse phase HPLC method developed for the estimation of Eprosartan mesylate in tablet dosage form. An Xterra KP18 150x4.6 mm, 5 µm partical size, with mobile phase consisting of acetonitrile and 0.03 M potassium dihydrogen phosphate (pH adjusted to 3.0±0.05 with orthophosphoric acid) in the ratio of 35:65 v/v was used. The flow rate was 1 ml/min and the effluents were monitored at 215 nm. The retention time was 5.549 min. The detector response was linear in the concentration of 1-25 mcg/ml. The respective linear regression equation being Y= 6669.355x+892.3405. The limit of detection and limit of quantification was 0.1 and 0.5 mcg/ml respectively. The percentage assay of Eprosartan mesylate was 99.77 %. The method was validated by determining its accuracy, precision and system suitability. The results of the study showed that the proposed RP-HPLC method is simple, rapid, precise and accurate, which is useful for the routine determination of Eprosartan mesylate in bulk drug and in its pharmaceutical dosage form.

Key words: Eprosartan mesylate, RP-HPLC, Estimation, and Tablets.

INTRODUCTION

Eprosartan mesylate[1] is a novel angiotensin receptor antangonist with chemical name IUPAC: (E)-2-Butyl –(1-P-carboxy benzyl)-α-2- thenylimidazole-5-acrylic acid methane sulfonate. Its molecular weight is 520.61832 [g/mol] with molecular formula $C_{24}H_{28}N_2O_7S_2$.

It is used in the management of hypertension[2,6]. Literature survey reveals few Chromatographic methods[3-5] for the determination of Eprosartan mesylate in biological fluids were reported. So far, no assay procedure has been reported for the estimation of Eprosartan mesylate in pharmaceutical dosage forms. The availability of an HPLC method with high sensitivity and selectivity will be very useful for the determination of Eprosartan mesylate in pharmaceutical formulations. The aim of the study was to develop a simple, precise and accurate reversed-phase HPLC method for the estimation of Eprosartan mesylate in bulk drug samples and in pharmaceutical dosage form.



Structure of Eprosartan mesylate

EXPERIMENTAL

Materials and Methods

Eprosartan mesylate was obtained as a gift sample from Dr. Reddy's Laboratories Ltd, Hyderabad. Potassium dihydrogen orthophosphate was of analytical grade, and supplied by M/s S.D. Fine Chem. Limited, Mumbai. Acetonitrile and water used were of HPLC grade (Qualigens). Commercially available Eprosartan mesylate tablets were procured from local market.

Instrument

Quantitative HPLC was performed on liquid Chromatograph, Waters separation 2996, PDA detector module equipped with automatic injector with injection volume 10 µl, and 2693 pump. An Xterra KP18 (150x4.6 mm, 5 µm partical size) cololum was used. The HPLC system was equipped with Empower Software.

HPLC Conditions

The contents of the mobile phase were Acetonitrile and 0.03 M potassium dihydrogen phosphate (pH adjusted to 3.0±0.05 with orthophosphoric acid) in the ratio of 35:65 v/v. They were filtered before use through a 0.45 µm membrane filter, and pumped from the respective solvent reservoirs to the column at a flow rate of 1.0 ml/min. The run time was set at 8.0 min and the column temperature was ambient. Prior to the injection of the drug solution, the column was equilibrated for at least 30 min with the mobile phase flowing through the system. The effluents were monitored at 215 nm.

Preparation of Standard Stock solution

A standard stock solution of the drug was prepared by dissolving 50 mg of Eprosartan mesylate in 50 ml volumetric flask containing 30 ml of methanol, sonicated for about 15 min and then made up to 50 ml with methanol to get a 1mg/ml standard stock solution.

Working Standard solution

5 ml of the above stock solution was taken in 100 ml volumetric flask and made up to 500 ml with methanol to get a concentration of10 µg/ml.

Preparation of Sample solution

Twenty tablets were (Teveten 400mg, Solvey Pharmaceuticals, Netherlands) weighed accurately and finely powdered and mix thoroughly. Powder equivalent to 50 mg of the active ingredient, was mixed with 25 ml of methanol. The mixture was allowed to stand for 1 hr with intermittent sonication to ensure complete solubility of the drug, and then filtered through a 0.45 µm membrane filter, followed by adding methanol to obtain a stock solution of 1.0 mg/ml. Transfer 5ml of this solution to 500 ml volumetric flask and made up to sufficient volume with mobile phase to give an concentration of 10 mcg/ml.

Linearity

Aliquots of standard Eprosartan mesylate stock solution were taken in different 10 ml volumetric flasks and diluted up to the mark with the methanol such that the final concentrations of Eprosartan mesylate are in the range of 1-25 mcg/ml. Each of these drug solutions (10 ìL) were injected three time into the column, and the peak areas and retention times were recorded. Evaluation was performed with PDA detector at 215 nm and a Calibration graph was obtained by plotting peak area versus concentration of Eprosartan mesylate (Fig 2).

The plot of peak area of each sample against respective concentration of Eprosartan mesylate was found to be linear in the range of 1-25 µg/ml with correlation coefficient of 0.9996. Linear regression least square fit data obtained from the measurements are given in table I. The respective linear regression equation being Y= 6669.355x+892.3405. The regression characteristics, such as slope, intercept, and %RSD were calculated for this method and given in Table 1.

Assay

10 µl of sample solution was injected into the injector of liquid chromatograph. The retention time was found to be 5.549 mins. The amount of drug present per tablet was calculated by comparing the peak areas of the sample solution with that of the standard solution. The data are presented in Table 2.

Recovery Studies

Accuracy was determined by recovery studies of Eprosartan mesylate, known amount of standard was added to the pre-analyzed sample and subjected to the proposed HPLC analysis. Results of recovery study are shown in Table II. The study was done at three different concentration levels.

RESULTS AND DISCUSSION

The system suitability tests were carried out on freshly prepared standard stock solution of Eprosartan mesylate. Parameters that were studied to evaluate the suitability of the system are given in Table 3.

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection (LOD) and limit of quantification (LOQ) for Eprosartan mesylate were found to be 0.1 and 0.5 µg/ml respectively. From the typical chromatogram of Eprosartan mesylate as shown in fig 1, it was found that the retention time was 5.549 min. A mixture of Acetonitrile and 0.03 M potassium dihydrogen phosphate (pH adjusted to 3.0±0.05 with orthophosphoric acid) in the ratio of 35:65 v/v was found to be most suitable to obtain a peak well defined and free from tailing. In the present developed HPLC method, the standard and sample preparation required less time and no tedious extraction were involved. A good linear relationship (r=0.9996) was observed between the concentration range of 1-25 mcg/ml. Low values of standard deviation are indicative of the high precision of the method. The assay of Eprosartan mesylate tablets ((Teveten 400mg, Solvey Pharmaceuticals, Netherlands) was found to be 99.7%. From the recovery studies it was found that about 101.5 % of Eprosartan mesylate was recovered which indicates high accuracy of the method. The absence of additional peaks in the chromatogram indicates non-interference of the common excipients used in the tablets. This demonstrates that the developed HPLC method is simple, linear, accurate, sensitive and reproducible. Thus, the developed method can be easily used for the routine quality control of bulk and tablet dosage form of Eprosartan mesylate within a short analysis time.

Table 1: Linear Regression Data for Calibration curves

Parameter	Eprosartan mesylate
Concentration range (mcg/ml)	1-25
Slope (m)	0.0015
Intercept (b)	0.11977
Correlation coefficie	0.9966
%RSD	0.4

Table 3: Validation Summary

Validation Parameter	Results
System Suitability	
Theoretical Plates (N)	6282
Tailing factor	1.2
Retention time in minutes	5.549
% of Peak Area	100
LOD (mcg/ml)	0.1
LOQ (mcg/ml)	0.5

Table 2: Results of HPLC assay and Recovery studies

Sample	Amount claim (mg/tablet)	% found by the proposed method	% Recovery*
1.	400	399.85	103.37
2.	400	400.52	102.00
3.	400	399.26	98.37

*Average of three different concentration levels.

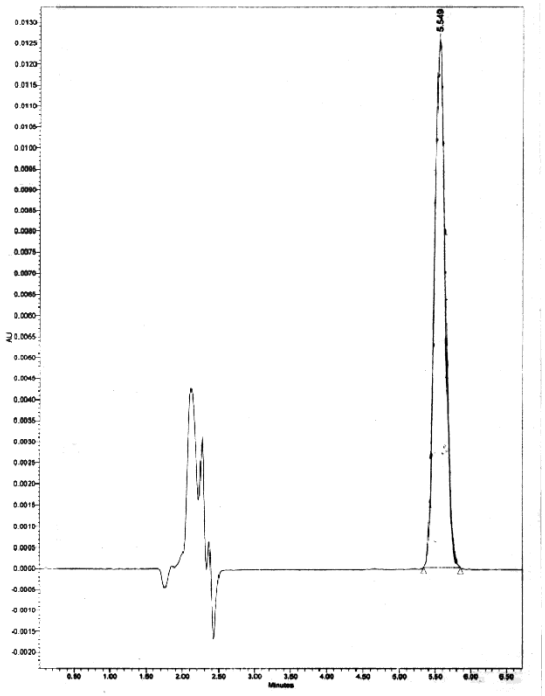


Fig 1: Typical Chromatogram of Eprosartan mesylate by HPLC.

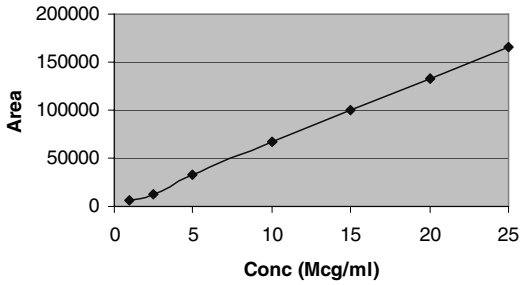


Fig 2: Calibration curve of Eprosartan mesylate by HPLC

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