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Research Article

# IDENTIFICATION AND DETERMINATION OF EPROSARTAN MESYLATE BY HPLC METHOD

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**Abstract**

**Objective:** A simple, specific, accurate and precise Rp-high-performance liquid chromatography method was developed and validated for determination of Eprosartan Mesylate in pharmaceutical preparations. Eprosartan Mesylate the Angiotensin II receptor antagonists, were analyzed in bulk substances and in tablets: Teveten tablets 600 mg. The conditions for identification by HPLC method in a gradient system and for determination of those compounds in isocratic systems were developed. **Materials and Methods:** The determination was carried out using: reverse phase $C_{18}$ (150x4.6mm, 5µm.) column with UV-VIS detector set at 233 nm and the following mobile phases: 0.1 mol/L sodium acetate (pH = 5.5) n acetonitrile n methanol in 35:9:6 v/v/v ratios for Eprosartan Mesylate. The recovery from simulated tablets was determined and amounted to: for Eprosartan Mesylate 99.04%. The method was validated as per ICH guidelines for precision, recovery, ruggedness and robustness. The specificity of the method was investigated under different stress conditions including acidic, basic, photochemical and thermal as recommended by ICH guidelines. The method was validated and successfully used for determination of the drugs in tablets. **Conclusions:** The developed HPLC technique is precise, specific, accurate and stability indicating. Statistical analysis proves that the method is reproducible and selective for the analysis of Eprosartan in pharmaceutical dosage form. The method can be used to determine the purity of the drug available from various sources. As the method separates the drug from its degradation products, it can be employed as a stability indicating one.

**Keywords:** Eprosartan Mesylate, Teveten, HPLC, Determination.

## Introduction

Angiotensin II (A-II) receptor antagonists are a relatively new useful class of antihypertensive agent [1] that block A-II Type 1 (AT1) receptors, and reduce the pressor effects of A-II in the vasculature. [3] The rennin-angiotensin system has an important role in the pathophysiology of hypertension and heart failure via the vasoconstricting effects of angiotensin II, which sustain elevated, blood pressure levels in hypertension and increase afterload in chronic heart failure. [2] Angiotensin II may stimulate the SNS on various levels. [1] Angiotensin II receptor antagonists are commonly prescribed antihypertensive drugs. [8] The POWER (Physicians' Observational Work on Patient Education According to their Vascular Risk) study, a large post-marketing survey of Eprosartan, an angiotensin II receptor blocker, created opportunities to evaluate both the effectiveness and safety of Eprosartan-based therapy in the treatment of high arterial blood pressure in a large population recruited in countries with varying degrees of baseline cardiovascular risk and the effect of Eprosartan-based therapy on total cardiovascular risk. [4] Eprosartan Mesylate (EPM) is chemically monomethane sulfonate of (E)-2-butyl-1-(p-carboxybenzyl)-a-2-thienylmethylimida zole-5-acrylicacid [13] (Fig. 1) is a new antihypertensive agent as an angiotension II receptor antagonist that is highly selective to elicit a higher reduction in systolic blood pressure than other antihypertensive drugs. [5,6] Antihypertensive agents may have differential effects on systolic blood pressure (SBP) and that home BP monitoring (HBPM) may enhance the

antihypertensive effects. [14] The drug acts on the rennin angiotension system in two ways to decrease total peripheral resistance. First, it blocks the binding of angiotension II to AT1 receptors in vascular smooth muscle, causing vascular dilatation. Second, it inhibits sympathetic nor epinephrine production, further reducing blood pressure. [1,3] Eprosartan Mesylate is not significantly metabolized and approximately 70% of its systemic clearance being hepatic and the remainder of its systemic clearance are renal in origin. [7, 8] Eprosartan Mesylate reduces BP by selectively blocking the AT1 receptor as well as by blockade of the pre synaptic AT1 receptors with a resultant diminution in sympathetic nerve activity.[9] Eprosartan Mesylate (Fig.1) is a novel Angiotensin receptor antangonist with chemical name IUPAC: (E)-2-Butyl – (1-Pcarboxy benzyl)-α-2-thenylimidazole-5-acrylic acid methane sulfonate. Its molecular weight is 520.61832 [g/mol] with molecular formula $C_{24}H_{28}N_2O_7S_2$. [10] Eprosartan has been determined by HPLC method with C18 column and DAD after the solid state extraction from urine. [11] It has also been determined in plasma by HPLC using an MS detector and C18 column. [12]

## Materials and Methods

### Chemicals

Eprosartan reference substance was obtained from Life care Laboratories Pvt. Ltd. Hyderabad (India). The solvent used for the experiment was methanol (SD Fine Chem. Ltd. Mumbai). All chemicals were used as obtained without further purification.

### Instrument

The analysis of drug was carried out on a Shimadzu HPLC system equipped with a reverse phase $C_{18}$ column (150x4.6mm, 5µm in particle size), a 20 µl injection loop and double beam UV-VIS spectrophotometer (Systronics India Limited UV-VIS Spectrometer-2203) was employed for spectrophotometric measurements (Fig.2).

### Experimental

**Standards:** Eprosartan Mesylate Ref. Standards by S.D. Fine Limited Mumbai.

**Test substances:** Eprosartan Mesylate – by Life care Laboratories Pvt. Ltd. Hyderabad (India) s0002.

**Test formulations:** Teveten-tablets 600 mg s.308192 (Eprosartan Mesylate) - by Ogene Systems (I) Pvt. Ltd., Hyderabad, (600 mg Eprosartan, as 735.795 mg Eprosartan Mesylate).

**Reagents and apparatus:** Analytically pure reagents and pure reagents for HPLC were from Lab Scan. Chromatograph: Shimadzu LC with SPD-M10ATVP photo-diode array detector, SPD-10 AVVP UV-VIS detector, SCL-10 AFP controller, DGU n 14A degasser and LC-10 AT VP pumps. Solvent: 0.1 mol/L sodium acetate (pH 5.5) n acetonitrile n methanol (10:9:6, v/v/v).

**Separation of sartans in gradient system:** A standard mixture of Eprosartan Mesylate (0.1 mg in 1 mL of the solvent) was prepared. Ten µl of the solution was injected onto the column and the chromatograms were acquired. After testing several columns and mobile phases, the following system was finally selected for the separation and identification: Column - reverse phase $C_{18}$ (150 × 4.6 mm, 5µm) Mobile phase flow - 1 mL/min. Detection - UV-VIS detector at 233 nm. Column temperature =25$^{o}$C. Injection - 10 µL. Mobile phase A: 0.1 mol/L sodium acetate at pH 5, 5 (glacial acetic acid). Mobile phase B: acetonitrile - methanol (3:2, v/v) (Table 6).

**Quantitative analysis:** The test samples were prepared in the solvent. Based on the gradient analysis, three isocratic systems were selected for the determination of compounds in pharmaceutical substances and formulations. The details of the isocratic systems were: column- C18 Column (150x4.6mm, 5µm.), column temperature 25$^{O}$C, UV-VIS detection at λ = 233 nm, mobile phase flow rate 1 mL/min, injection 10 µL. Mobile phases: System I for Eprosartan Mesylate: 0.1 mol/L sodium acetate (pH = 5.5) n acetonitrile n methanol (35:9:6, v/v/v).

**Determination of calibration graphs:** Relations between the peak surface area and the concentration of a tested substance were determined. The solutions of standards at concentrations of: 0.005 mg/ml, 0.025 mg/ml, 0.05 mg/ml, 0.1 mg/ml, 0.2 mg/ml, 0.5 mg/ml, 0.7 mg/ml and 1 mg/ml, were prepared in the solvent, as well as solutions of the same concentration from the tablets. The samples were shaken for 15 min in an ultrasonic bath and in a mechanical shaker for another 30 min. The solutions were passed through filters with a pore size of 0.45 µm. Linearity within the range of 0.005n1 mg was observed for all analyzed compounds. The correlation coefficients R2 with satisfactory values (0.9998n1.0) were determined for the regression lines.

**Quantification of analyzed bulk substances:** The solutions of standard and test samples were prepared in the solvent at a concentration of 0.1 mg/mL. Ten µL of the solutions were injected on the column and analyzed in I systems. The solutions of standards and extracts of the tablets were prepared and chromatographed as described above.

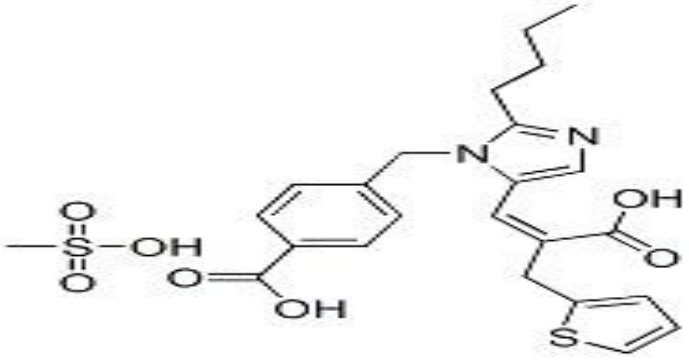


Fig.1: Eprosartan Mesylate

**Recovery analysis:** Preparation of model samples Portions of an active substance were added to the placebo mixture in quantities corresponding to 80, 100, and 120% of the declared content in the formulation. The samples were treated as described above to obtain solutions of the compound with a final concentration of 0.1 mg/mL.

## Results

Figure 2 shows chromatogram of sartans separated in gradient system and Table 1 reports values of the retention time, resolution between successive peaks and determined limits of detection. Table 2 shows the respective values for isocratic systems. Figure 3 shows chromatogram of Eprosartan Mesylate in isocratic system I. Table 3 reports statistical assessment for the results of Eprosartan Mesylate content determination in substances whereas Table 4 shows these results for tablets. The results of recovery analysis are shown in Table 5.

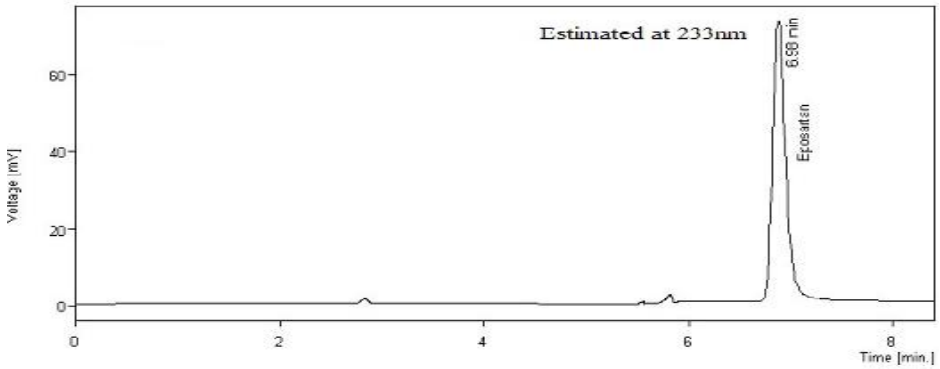


Fig.2: Chromatogram of Eprosartan Mesylate separated in gradient system

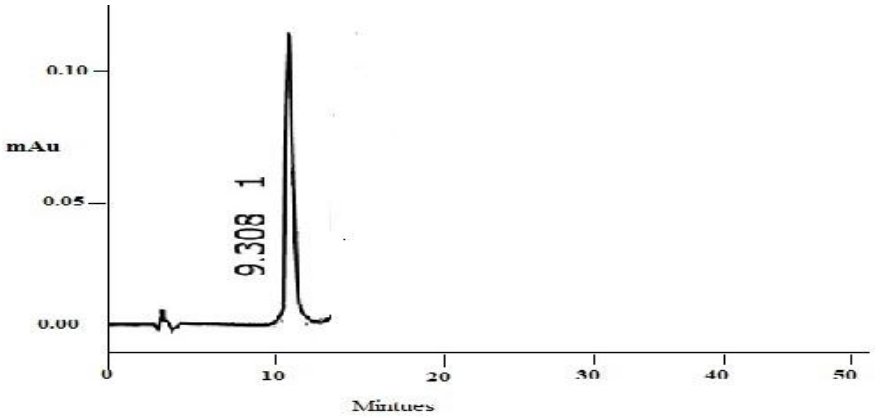


Fig.3: Chromatogram of Eprosartan Mesylate in isocratic System

Table1: Retention time, resolution and limits of detection in the gradient system

| Determined Compound | Retention Time (Min.) | Resolution between Subsequent Peaks | Limit of detection - injection 10µL (mg) |
|---|---|---|---|
| Eprosartan Mesylate | 6.02 | 3.02 | 01 |

Table 2: Retention time, Resolution and limits of detection in isocratic system

| Determined Compound | Mobile Phase | Retention Time (min.) | Resolution | Limit of Quantitation – injection 10µL (µg) | Limit of detection – injection 10µL (mg) |
|---|---|---|---|---|---|
| Eprosartan Mesylate | Phase1 | 9.31 | - | 0.05 | 1 |

Phase 1: 0.1 mol/L sodium acetate (pH 5.5) n acetonitrile n methanol (35:9:6, v/v/v).

Table 3: Statistical assessment for the result of Eprosartan Mesylate content determination in substances

| Tested Substances | Mobile Phase | Arithmetic mean for all measurements-X (%) | Confidence interval X±ΔX PU = 95% (%) | Coefficient of variation RSD (%) |
|---|---|---|---|---|
| Eprosartan Mesylate | Phase 1 | 98.65 | 98.65 ± 0.766 | 0.74 |

Table 4: Statistical assessment for the results of Eprosartan Mesylate content determination in tablets

| Tested Substances | Mobile Phase | Arithmetic mean for measurement | Confidence interval X±ΔX PU= 95% (%) | Coefficient of Variation RSD (%) |
|---|---|---|---|---|
| Teveten tablets 600 mg(Eprosartan Mesylate | Phase 1 | 601.05 | 601.05±4.75 | 0.75 |

Table 5: Recovery tests Eprosartan Mesylate from model table.

| Tested substances | Mobile Phase | Percent of weight substance (%) | Recovery (%) | X-Arithmetic Mean for all measurements (%) S-Standard Deviation X±ΔX - Confidence interval RSD - relative standard deviation |
|---|---|---|---|---|
| Eprosartan Mesylate | Phase 1 | 80 | 99.01 | X=99.04% S=0.24 X±ΔX = 99.04±0.25% Wz=0.24% |
| | | 100 | 98.98 | |
| | | 120 | 99.15 | |

Table 6: Mobile phase A & Mobile phase B Gradient

| Time (Min.) | Mobile Phase A (%v/v) | Mobile Phase B (%v/v) |
|---|---|---|
| 0-10 | 65 | 35 |
| 10-14 | 65—60 | 35-40 |
| 14-25 | 60 | 40 |
| 25-29 | 60—40 | 40-60 |
| 29-45 | 40 | 60 |
| 45-48 | 40—65 | 60-35 |
| 48-55 | 65 | 35 |

## Conclusion

The conditions for identification and separation of Eprosartan Mesylate by HPLC method in gradient system were developed. Identification and determination conditions were established for substances and tablets by HPLC in three isocratic systems. Statistical data for developed method shows a sufficient precision and accuracy. The method was used for a quantitative analysis of tested formulations.

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