ANALYTICAL METHODS FOR ESTIMATION OF EPROSARTAN MESYLATE: A REVIEW


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ABSTRACT

Eprosartan mesylate is an angiotensin II receptor (AT1) antagonist. Eprosartan is an effective, well tolerated and potent pure competitive antagonist of the AT1 receptor and hence there has been significant research on broad range of analytical and detection techniques that could be useful in its estimation in formulations and biological matrices. Practical requirements for high-sensitivity analysis create challenges for routine analysis. Different existing analytical techniques, which offer rapid, sensitive and accurate methods of analysis, have been discussed in this manuscript. There are a number of methods used, but to our knowledge, high performance liquid chromatography with UV detection is more likely to be popular. This review manuscript discusses methods such as Ultraviolet (UV) spectrophotometry, High Performance Liquid Chromatography (HPLC), High Pressure Thin Layer Chromatography (HPTLC), Liquid Chromatography- Mass spectrophotometry (LC-MS) and Capillary Zone Electrophoresis (CE). This review explores the available analytical methods for estimation of eprosartan mesylate in various matrices for readers’ expediency.

Keywords: Eprosartan, estimation, bulk, formulation, biological matrices.

INTRODUCTION

Eprosartan mesylate is a non-biphenyl non-tetrazole angiotensin II receptor (AT1) antagonist. A selective non-peptide molecule, Eprosartan mesylate, is chemically described as the mono-methane sulfonate salt of (E)-2-butyl-1-(p-carboxybenzyl)-α-2-thienylmethylimidazole-5-acrylic acid[1].

Fig.1. Structure of Eprosartan mesylate.
Angiotensin II (formed from angiotensin I in a reaction catalyzed by angiotensin-converting enzyme [kininase II]), a potent vasoconstrictor, is the principal pressor agent of the renin-angiotensin system. Eprosartan mesylate blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor found in many tissues (e.g., vascular smooth muscle, adrenal gland). Eprosartan mesylate does not exhibit any partial agonist activity at the AT1 receptor. Its affinity for the AT1 receptor is 1,000 times greater than for the AT2 receptor. Unlike most other Angiotensin II Receptor Antagonists, which show noncompetitive kinetics, eprosartan is a potent pure competitive antagonist of the AT1 receptor.\(^2\) Blockade of the AT1 receptor removes the negative feedback of angiotensin II on renin secretion, but the resulting increased plasma renin activity and circulating angiotensin II does not overcome the effect of eprosartan mesylate on blood pressure. Importantly, eprosartan crosses the blood-brain barrier, which probably contributes to its antihypertensive efficacy.\(^3\)

Eprosartan which not only is an effective and well tolerated antihypertensive agent, but also lowers the activities of the renin-angiotensin system and sympathetic nervous system.\(^4\) Eprosartan has also been shown to affect the sympathetic nervous system, to alter vascular and endothelial function and to be protective of renal function.\(^5,6,7\) Eprosartan favorably alters platelet function, endothelial function, fibrinolytic capacity and haemostatic markers – all potent risk factors for cardiovascular disease. In hypertensive patients with a history of cerebrovascular events, eprosartan reduces the risk of stroke recurrence.

Eprosartan has a low absolute bioavailability\(^8\) due to its poor absorption after oral administration\(^9\) resulting in a bioavailability after a single 300 mg oral dose of 13%\(^10\). Eprosartan mesylate is eliminated by biliary and renal excretion, primarily as unchanged compound. Less than 2% of an oral dose is excreted in the urine as a glucuronide. Plasma protein binding of eprosartan mesylate is high (approximately 98%) and constant over the concentration range achieved with therapeutic doses. Eprosartan mesylate did not inhibit human cytochrome P450 enzymes CYP1A, 2A6, 2C9/8, 2C19, 2D6, 2E and 3A in vitro. Eprosartan mesylate is not metabolized by the cytochrome P450 system so is likely to have a lower potential for drug interactions.\(^11,12\) No gender differences were observed in
pharmacokinetics of eprosartan. There was around two fold absorption observed in elderly as compared to young men, due to increased bioavailability in the elderly. There was “lack of effect” of hepatic disease on the pharmacokinetics of eprosartan.\cite{13}

Eprosartan mesylate may be used alone or in combination with other antihypertensives such as diuretics and calcium channel blockers. Eprosartan–hydrochlorothiazide combination is well tolerated in both the short and long term, with negligible adverse events.\cite{14} Eprosartan mesylate has been shown to have no effect on the pharmacokinetics of digoxin and the pharmacodynamics of warfarin and glyburide.

Many cardiotropic agents are currently used today that have broader therapeutic application and margins of safety. While these drug concentrations in human serum or plasma are generally not routinely monitored, there are certainly clinical situations (patient noncompliance, suboptimal clinical response, underlying renal or hepatic disease that alters clearance, bioavailability or metabolism, and signs and symptoms of toxicity) where laboratory analysis may be warranted and will prove to be beneficial for patient management and safety. The objective of therapeutic drug monitoring is to optimize pharmacological responses of a drug therapy. Therapeutic drug monitoring is not limited to measuring the concentration of a drug in a biological matrix but it also involves the proper interpretation of the drug concentration in serum or plasma using pharmacokinetic parameters so that appropriate conclusion can be reached regarding the progress of therapy and dose adjustment.\cite{15} Eprosartan mesylate, in certain clinical situations, may require monitoring of serum or plasma levels to ensure better clinical outcome.

**ANALYTICAL METHODS FOR ESTIMATION OF EPROSARTAN MESYLATE**

About twenty seven analytical methods are available for estimation of eprosartan mesylate in different matrices from either single drug, combined dosage form or from biological matrices. There are several spectrophotometric and chromatographic methods reported in the literature that are capable of analyzing multiple cardiotropic drugs using one protocol. One advantage of these methods is that multiple sample preparation and chromatographic runs are not required for therapeutic drug monitoring purpose in patients receiving multiple drugs.

1. **FOR ESTIMATION IN BULK AND DOSAGE FORMS.**

   A. **SPECTROPHOTOMETRIC METHOD.**
Kamila M. et al.\textsuperscript{[16]} developed and validated a method for estimation of Eprosartan mesylate in bulk and pharmaceutical formulations. Absorbance of the drug solution in methanol was measured at 232 nm. The method showed acceptable linearity, accuracy and precision in concentration range of 2-30 µg/ml.

Pattanaik A K and coworkers\textsuperscript{[17]} developed two simple, precise and accurate methods for estimation of Eprosartan mesylate. In one method, absorbance of drug was measured at 233 nm in methanol. In second method, derivative spectroscopy method was employed, wherein first order spectra was measured and the dA/dλ values of the corresponding maxima and minima at 222 (max) nm were plotted against concentration. The method was accurate, precise and linear over the concentration range of 1-70 µg/ml.

Anandkumar K. et. al.\textsuperscript{[18]} developed and validated an accurate and precise absorption ratio method for the estimation of eprosartan mesylate (EPR) and hydrochlorothiazide (HCT) in pure and fixed dose combination. The overlay of UV spectra of Eprosartan mesylate and hydrochlorothiazide showed isobestic point at 249.1 nm. The Q-absorbance equation was formed at 249.1 and 274.5 nm, wavelength of maximum absorbance. Both the drugs conform with Beer’s law in concentration range of 6-36 µg/ml and 1-10 µg/ml for eprosartan mesylate and hydrochlorothiazide, respectively.

Fatma Hacıoğlu and Armagan Onal\textsuperscript{[19]} developed a method for estimation of eprosartan mesylate and hydrochlorothiazide in pharmaceutical formulations. The method is based on first-derivative ultraviolet spectrophotometry with zerocrossing measurements at 246 and 279 nm for EPR and HCT, respectively. Overlaid first-derivative spectra of eprosartan mesylate and hydrochlorothiazide in acetonitrile –water (50:50) were used. The assay was linear over the concentration ranges 3.0–14.0 mg/ml for EPR and 1.0–12.0 mg/ml for HCT. This method showed good accuracy, reproducibility and recovery and can be used for routine analysis of eprosartan mesylate and hydrochlorothiazide in pure and in fixed dose combination.

Veerreddy K. et. al.\textsuperscript{[20]} developed and validated a spectroscopic method estimation of eprosartan mesylate and hydrochlorothiazide in bulk and fixed dose combination. In the present work, wavelength (λmax) of EPR, 292 nm, and isoabsorptive point, 246 nm, for both drugs were selected to simultaneously estimate eprosartan mesylate and hydrochlorothiazide. Absorbance of the drugs in 0.1 N NaOH solution was taken. Beer-
Lambert’s law is obeyed at the concentration range of 5-35 g/ml for Eprosartan mesylate and 0.5-10 g/ml for Hydrochlorothiazide. The results of analysis have been validated statistically and by recovery studies confirmed the accuracy of the proposed method.

Emad M Hussien et al.\(^ {21}\) developed two spectrophotometric methods for the direct determination of eprosartan mesylate and hydrochlorothiazide in bulk powder and combined dosage form, without prior separation. The first method was a first derivative spectrophotometry using a zerocrossing technique of measurement wherein the two series solutions were scanned within the range 220-330 nm against methanol as a blank. The absorbance at 240.7 nm (zerocrossing of HCT) was measured for the determination of EPR, while the amplitudes at 233.4 nm (zero-crossing of EPR) were recorded for the determination of HCT. The calibration curves were linear in the range 1.0-18.0 for EPR and 1.0-9.0 for HCT. The second method is the first derivative of ratio spectrophotometry. The ratio of absorption spectra of EPR and HCT was measured. The first derivative of the ratio spectra was calculated with \( \lambda = 21 \) nm and scaling factor (SF) =20. The absorbencies were measured at 237.0 nm and the values were plotted against the corresponding concentration. The calibration curves were linear in the range 2.0-18.0 g/ml for EPR and 1.0-9.0 g/ml for HCT.

B. CHROMATOGRAPHIC METHODS.

High Performance Liquid Chromatography methods, developed for the quantitation of most commonly prescribed cardioactive drugs, show acceptable analytical and clinical performance in most instances. There is no doubt on the fact that the spectroscopic methods mentioned in the above texts are rapid and far more economical than chromatographic methods but their non-selective nature and lack of sensitivity is a huge disadvantage for its application in biological fluids and impurities determination. LC/MS methods require more upfront equipment investment and operational support, but they yield lower specimen requirements, faster throughput and enhanced sensitivity desired in many laboratories. Thin-layer chromatography is defined by its attributes: a disposable stationary phase; simultaneous parallel separations; static detection, free of time constraints; storage device for chromatographic information; all sample components are observed in the chromatogram.
i. High Performance Liquid Chromatography.

Kiran Kumar V. et al.[22] developed and validated a reverse phase HPLC method for the estimation of Eprosartan mesylate in tablet dosage form. The separation was achieved on Xterra KP18 column (150x4.6 ID mm, 5 µm) 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 µg/ml. The method is useful for the routine determination of eprosartan mesylate in bulk drug and in its pharmaceutical dosage form.

G. Anantha Ram et al.[23] developed a reverse phase High performance liquid chromatographic method for the estimation of Eprosartan mesylate in bulk. In this method, separation was achieved by a C18 Oyster column (250 x 4.6 ID mm, 5µm) with mobile phase Sodium acetate buffer pH 3.0: Acetonitrile (70 : 30). The detection wavelength is 235 nm and the flow rate is 1.0ml/min. The linearity of eprosartan mesylate over the concentration range 25- 75µg/ml shows regression coefficient of 0.9999. The method was found sufficiently selective to distinguish the parent drug and the degradation products after hydrolysis photolysis or chemical oxidation.

Syeda Kulsum and co-workers[24] developed a sensitive reverse phase high performance liquid chromatographic method for the quantitation of Eprosartan mesylate in both bulk and pharmaceutical dosage forms. Successful separation was obtained from an Phenomenex Luna 100A column (250 x 4.6 ID mm, 5µm) with mobile phase containing Acetonitrile : 1% Diethyl amine : 1% Glacial acetic Acid (13 : 3 : 4 v/v/v). The flow rate was 0.6 ml/min and the effluents were monitored at 242 nm. The linearity was in the range of 5-20 µg/ml.

Devika G S et al.[25] developed and subsequently validated a reverse phase high performance liquid chromatographic for the simultaneous determination of Eprosartan mesylate and hydrochlorothiazide, in combination. Chromatographic separation of the two drugs was performed on a Purospher BDS C18 column (150× 4.6 ID mm, 5 µm). The mobile phase comprising of acetonitrile: methanol: 10mM potassium dihydrogen phosphate buffer (40:40:10) was delivered at a flow rate of 1.0 mL/min. The pH of the
The mobile phase was adjusted to 4 with orthophosphoric acid. Detection was performed at 270nm. The method was found to be linear over a concentration range of 216-576 µg/ml and 9-24 µg/ml, respectively. The excipients present in the formulations did not interfere with the assay procedure. The developed method was successfully applied to determine eprosartan mesylate and hydrochlorothiazide in pharmaceutical formulations.

A.B.N. Nageswara Rao and associates\textsuperscript{[26]} developed and validated anisocratic RP-HPLC method for the simultaneous analysis of Hydrochlorothiazide and Eprosartan mesylate in bulk and tablet dosage forms. Method development was carried out on Agilent Eclipse XBD-C18 (150 × 4.6ID mm, 5 μ) column. The mobile phase was a mixture of buffer (20mM potassium dihydrogen phosphate) and methanol in the ratio of 80:20 v/v. The flow rate was set at 1.0 ml/min and UV detection at 225nm. The linearity for HPLC method was determined at concentration levels ranging from 5-30 g/ml for Hydrochlorothiazide and 20-100 g/ml for Eprosartan mesylate.

Satheesh et. al\textsuperscript{[27]} developed and validated a stability indicating UPLC method for simultaneous determination of eprosartan mesylate, hydrochlorothiazide and their impurities in tablets. The chromatographic separation was performed on Acquity HSS C18 column (150 x 2.1 mm, 1.7 μ) by adopting gradient elution using acetonitrile and 10mM disodium hydrogen phosphate buffer (pH 5.5 adjusted with phosphoric acid) at flow rate of 0.3 ml/min. UV detection was performed at 274nm. Total run time was 20 min for performing the analysis in which two main compounds and ten other known, unknown impurities were separated. The calibration curves obtained for the ten impurities were linear over the range 0.017 to 3.79 g/ml. The relative standard deviations of intra- and inter-day experiments were less than 1.0%. The detection limits ranged from 0.005 to 0.15 g/ml of Eprosartan mesylate depending on the concentration of impurity.

Fatma Hacıoğlu and ArmaganOnal\textsuperscript{[19]} developed a reverse phase high performance chromatography method for estimation of eprosartan mesylate and hydrochlorothiazide from tablets. Chromatographic separation was achieved isocratically at a temperature of 30°C on an ACE 5 CN column (200 × 4.6 ID mm, 5 μ). The mobile phase was composed of acetonitrile–10mM phosphoric acid (pH 2.5; 40:60, v/v) with a flow rate of 1.0 ml/min. Olmesartan was used as internal standard and the substances were detected at

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272 nm. The linearity ranges were found to be 0.5–30 and 0.3–15.0 mg/ml for Eprosartan and Hydrochlorthiazide, respectively.

Piyush Trivedi et al. [28] developed a stability-indicating reverse phase ultra-performance liquid chromatographic assay method for estimation of eprosartan mesylate from bulk. Separation of the drug and the degradation products was successfully achieved on a BEH (bridged ethylene hybrid) C18 column (150 x 2.1 ID mm, 1.7 μm) with gradient elution of water–acetonitrile as mobile phase. The flow rate was 0.1 ml/min and detection wavelength was 232 nm. The method was found to be linear in the drug concentration range 5–25 g/ml. The drug was subjected to acidic, alkaline, hydrolytic, photolytic, thermal and oxidative degradation. Degradation of the drug was found to occur under alkaline, acidic and neutral hydrolytic conditions. The method was specific to the drug, selective to degradation products, and robust. PDA purity test also confirmed the specificity of the method.

Belal et al. [29] developed a specific and sensitive RP-HPLC method for simultaneous determination of eprosartan and hydrochlorothiazide. Good chromatographic separation was achieved using a Symmetry C18 column (250 x 4.6 ID mm, 5 μm). The mobile phase acetonitrile-0.1 M phosphate buffer (35: 65, v/v), pH 4.5, was pumped at a flow rate of 1 mL/min, with UV detection at 275 nm. The method showed good linearity in the ranges of 0.5-50 and 0.1-10 μg/mL, with LOD of 0.06 and 0.02 μg/mL and LOQ of 0.20 and 0.08 μg/mL for EPR and HCT, respectively. The proposed method was successfully applied for the analysis of the studied drugs in their synthetic mixture and co-formulated tablets.

ii. HIGH PERFORMANCE THIN LAYER GHROMATOGRAPHY.

The focal attributes of modern TLC are the use of fine particle layers for fast and efficient separations; sorbents with a wide range of sorption properties to optimize selectivity; the use of instrumentation for convenient (automated) sample application, development and detection; and the accurate and precise in situ recording and quantitation of chromatograms. Its uses have flourished because of its simple instrumentation and low operation costs [30].

Patel H.U.et.al. [31] developed a high-performance thin-layer chromatographic (HPTLC) method has been established for simultaneous analysis of eprosartan mesylate and
hydrochlorothiazide in tablet formulations. Standard and sample solutions of eprosartan mesylate and hydrochlorothiazide were applied to precoated silica gel G 60 F_{254} HPTLC plates by means of Desaga AS30Win sample applicator equipped with 100-μL applicator syringe and were developed with benzene–methanol–formic acid 7:3:0.1 (v/v/v) as mobile phase. Detection and evaluation of chromatograms was performed densitometrically at 272 nm. The linear range was 4.8–43.2 μg/spot for EPR and 0.15–1.35 μg/spot for HCT.

Emad M Hussien et al.\textsuperscript{21} developed a method based on TLC separation of eprosartan mesylate and hydrochlorothiazide followed by densitometric measurements of their spots at 290 and 270 nm for EPR and HCT, respectively. The separation was carried out on silica gel 60 F_{254} using n-butyl acetate: ethanol: water: 33% ammonia (40:40:10:1, v/v/v/v) as mobile phase. The calibration curves were linear in the range 2.0–20.0 μg/spot for EPR and 2.0–9.0 μg/spot for HCT. The suggested method was successfully applied for the analysis of pharmaceutical preparations.

iii. CAPILLARY ZONE ELECTROPHORESIS.

The individual detection of closely related angiotensin-II-receptor antagonists (ARA-IIs) requires sophisticated separation technique in addition to high sensitivity. The effective and fast separation of components by capillary electrophoresis is based upon charge and mass dependent migration in an electrical field.

Hillaert S. et al.\textsuperscript{32} illustrated the potential of the capillary zone electrophoretic method and micellar electrokinetic capillary chromatographic method to simultaneously separate candesartan, eprosartan mesylate, irbesartan, losartan potassium, telmisartan, valsartan and hydrochlorothiazide. Separation was achieved on a Crystal Thermo Capillary Electrophoresis system wherein a fused-silica capillary (85 cm x 50 μm ID) was applied with a constant voltage of 25 kV. UV absorbance was detected at 214 nm. In Capillary Zone Electrophoresis, 60 mM sodium phosphate buffer (pH 2.5) was used as mobile phase. With micellar electrokinetic capillary chromatography, separation is achieved by 55 mM sodium phosphate buffer solution containing 15 mM sodium dodecyl sulfate. These methods are suitable for the qualitative as well as quantitative determination of combined dosage forms of ARA-IIs and Hydrochlorothiazide.
Hillaert S. et al.\cite{33} optimized a capillary zone electrophoretic method for separation of six angiotensin-II-receptor antagonists (ARA-IIs): candesartan, eprosartan mesylate, irbesartan, losartan potassium, telmisartan and valsartan. A three-level, full-factorial design was applied to study the effect of the pH and molarity of the running buffer on separation. The separation was best carried out using 60 mM sodium phosphate buffer (pH 2.5) on a Crystal Thermo Capillary Electrophoresis system in which a fused-silica capillary (85 cm x 50µm ID) was applied with a constant voltage of 25kV. UV absorbance was detected at 214 nm. Thus, the aim of simultaneous quantification and identification of the active ingredient in the finished product was accomplished.

Hillaert S.et. al.\cite{34} also optimized a micellar electrokinetic capillary chromatographic method for the separation of six angiotensin-II receptor antagonists (ARA-IIs): candesartan, eprosartan mesylate, irbesartan, losartan potassium, telmisartan and valsartan. A face-centered central composite design was applied to study the effect of the pH, the molarity of the running buffer and the concentration of the micelle-forming agent on the separation properties. The separation of the six ARA-IIs was best carried out using a 55-mM sodium phosphate buffer solution (pH 6.5) containing 15 mM of sodium dodecyl sulfate. A fused-silica capillary (30 cm x 75µm ID) was applied with a constant voltage of 10kV. UV absorbance was detected at 214 nm. The same system was also applied for the quantitative determination of these compounds, but only for the more stable ARA-IIs (candesartan, eprosartan mesylate, losartan potassium and valsartan).

2. FOR ESTIMATION FROM BIOLOGICAL MATRICES

Eprosartan mesylate, in certain clinical situations, may require monitoring of serum or plasma levels to ensure better clinical outcome. Therapeutic drug monitoring involves the proper interpretation of the drug concentration in serum or plasma using pharmacokinetic parameters so that appropriate conclusion can be reached regarding the progress of therapy and dose adjustment. Both HPLC and LC/MS methods perform acceptably and equivalently for clinical measurement within the clinically relevant concentration ranges. HPLC-UV methods using fast and simple solid phase extraction have been most widely adopted and provide adequate analytical sensitivity.

Xue-Ning Li et. al.\cite{35} developed and validated a protein precipitation, liquid chromatography/tandem mass spectrometry (LC/MS/MS) method for the determination
of eprosartan mesylate in human plasma and urine. The solvent system also served as a protein precipitation reagent. The chromatographic separation was achieved on a Capcell Pak C18 column (50×2.0 ID mm, 5 µm). A mobile phase was consisted of 0.5% formic acid in water and 0.5% formic acid in acetonitrile (72:28 v/v). Detection was by positive ion electrospray tandem mass spectrometry on a Sciex API3000. The standard curves, which ranged from 5 to 2000 ng/ml in human plasma and from 0.25 to 50 µg/ml in urine, were fitted to a 1/x weighted quadratic regression model. The method proved to be accurate, specific and sensitive enough to be successfully applied to a pharmacokinetic study.

Alonso et. al.\textsuperscript{[36]} developed a solid phase extraction-reverse phase high performance liquid chromatographic (SPE-RP-HPLC) method with photometric detection for monitoring the antihypertensive drug eprosartan mesylate in order to assure good quantitation of eprosartan mesylate in plasma samples obtained from patients under cardiovascular treatment. This analytical method was developed by using experimental design and quantitation was accomplished with the internal standard method. The clean-up procedure consisted of a solid-phase extraction and was performed using Varian Bond Elut C8 cartridges non-end capped. A Waters Atlantis dC18 (100×3.9 ID mm, 3µm) 100°A column was used to perform separation. Prior to the analytical column, a Waters Bondapak C18 guard column 10 µm was placed to prevent column degradation. The mobile phase consisted of a mixture of water 0.031% TFA acetonitrile 0.026% TFA, low-pressure mixed and delivered in gradient mode at a flow rate of 1.25 mL/min. No interferences were observed from endogenous compounds of plasma and other drugs which are commonly co-administered in elderly patients. The recoveries of eprosartan mesylate from plasma samples, measured at three levels of the linear concentration range (150–4000 ng/ml) were found to be between 93.4 and 102.8%.

Alonso et.al.\textsuperscript{[37]} also applied a chemometric approach for the optimization of the extraction and separation of the antihypertensive drug eprosartan mesylate from human plasma samples. MultiSimplex program was used to optimize the HPLC-UV method due to the number of experimental and response variables to be studied. The measured responses were the corrected area, the separation of eprosartan chromatographic peak from plasma interference peaks and the retention time of the analyte. The extraction
procedure for spiked human plasma samples was carried out using C8 cartridges, phosphate buffer pH 2 as conditioning agent, washing with methanol–phosphate buffer (20:80, v/v) and methanol as eluent liquid. The use of an Atlantis dC18 (100 × 3.9 ID mm) chromatographic column for separation with a 0.026% trifluoroacetic acid (TFA) in the organic phase and 0.031% TFA in the aqueous phase, an initial composition of 80% aqueous phase in the mobile phase, a stepness of acetonitrile of 3% during the gradient elution mode with a flow rate of 1.25 mL/min and a column temperature of 35°C allowed the separation of eprosartan mesylate and irbesartan, used as internal standard from plasma endogenous compounds.

Cyronak M. and co-workers\textsuperscript{[38]} developed a sensitive, selective and rugged analytical method for the determination of Eprosartan mesylate in human plasma. The new method employed a simple solid-phase extraction procedure to isolate the drug and its internal standard from plasma samples. The SPE cartridges were conditioned with methanol, washed with ethyl acetate containing 0.1% triethylamine and elution with methanol-0.05 M acetic acid (90:10 v/v). Separation was achieved by BDS Hypersil C18 column (150 x 2 ID mm, 5µm) supported with BDS Hypersil C18 column (20x2 ID mm, 5µm). The mobile phase was optimized to 0.05 M citrate buffer (pH 3.5) tetrahydrofuran (34:16, v/v) and flow rate was set to 0.25 ml/min. The assay was based on analysis by reverse phase high performance liquid chromatography with UV absorbance detection. The dynamic range of the assay was 10 to 5000ng/ml.

Manish TR et. al.\textsuperscript{[39]} developed a simple, rapid, selective and sensitive HPLC method for the determination of eprosartan from human plasma. The drug was extracted with a mixture of 0.05M sodium hydroxide and ethyl acetate. Eprosartan was measured in plasma using a validated a HPLC method with UV detector at 235nm. Chromatographic peaks were separated on 5 m Intensil, C18 column (4.6 x 250 ID mm, 5 m) using phosphate buffer pH 4 and acetonitrile (60:40 v/v) as mobile phase at a flow rate of 1 ml/min. The method was linear over the concentration range of 300 to 20,000ng/ml. This method was successfully applied to pharmacokinetics studies.

**CONCLUSION**

A broad range of analytical techniques are available for separation and detection of eprosartan for practical analysis. This review highlighted some recent development and
new techniques that have been used in the analysis and detection of eprosartan mesylate. High Performance Liquid Chromatography with UV detector is the most widely employed technique for determination of eprosartan mesylate in formulation and biological matrices as well as for evaluation of its pharmacokinetics. Capillary Zone Electrophoresis is the commonly utilized method for simultaneous quantitative estimation of eprosartan mesylate along with other angiotensin-II receptor antagonists (ARA-IIs). As shown, although there have been several recent successes in its detection, new methods are still required to achieve higher sensitivity and address other challenges that are posed. The application of MS in conjunction with other tools for decreasing limits of detection has been of increased interest in the recent times. Future trend would be to concentrate on designing of more rapid and sensitive tool for the estimation purpose. The presented information would be useful for the researchers especially those involved in the formulation development and quality control of eprosartan mesylate.

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