AMERICAN JOURNAL OF PHARMTECH RESEARCH
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# Development and Validation of RP- HPLC Method For The Simultaneous Estimation of Amlodipine Besylate and Valsartan In Solid Dosage Form

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## ABSTRACT

The objective of the present research work was to simultaneously separate the anti-hypertensive agents, Amlodipine and Valsartan and develop a validated analytical method for simultaneous quantitative determination of amlodipine and valsartan in tablet dosage form. A simple, rapid, precise and selective chromatographic method was developed and validated for separation and determination amlodipine and valsartan in tablet preparations. The anti-hypertensive agents were analyzed by Symmetry $C_{18}$, (150 × 3.4 mm, 5 µ), Shimadzu LC-2010CHT Prominence Liquid Chromatograph and a mobile phase constituted of 10 mM Buffer (pH 3.0): methanol (50:50, v/v). The flow rate was 1.0 mL/min and the analysis were performed using UV- Vis detector at 237nm. The anti-hypertensive agents, Amlodipine and Valsartan were separated within 10 min. Amlodipine and Valsartan showed retention time of 5.06 and 8.28 min respectively. The drugs were found to obey Beer's law in the concentration range of 100 ppm of amlodipine and 128 ppm of valsartan. The developed assay method is selective, precise and accurate. The method has been successfully applied for determination of Amlodipine and Valsartan in pharmaceutical combination tablet dosage form. This developed method is sensitive, fast and simple with excellent peak symmetry and high resolution.

**Keywords:** Amlodipine, Valsartan, Gradient RP-HPLC, UV detection, Validation.

*Corresponding Author Email: kakaniraja123@gmail.com
Received 14 October 2016, Accepted 16 November 2016

Please cite this article as: Rahul K *et al.*, Development and Validation of RP- HPLC Method For The Simultaneous Estimation of Amlodipine Besylate and Valsartan In Solid Dosage Form. American Journal of PharmTech Research 2016.

## INTRODUCTION

Valsartan (VAL) is a popular Angiotensin II antagonist and chemically it is N-(1-oxopentyl)-N-[[2′-(1H-tetrazol-5-yl)[1,1′-biphenyl]-4-yl]methyl]-L-valine[1]. Amlodipine (AML) is calcium-channel blocker (CCB), and is chemically (3-Ethyl-5-methyl (4RS)-2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-6-methyl-1, 4dihydropyridine-3, 5-dicarboxylate benzene sulphonate[1]. The combination of VAL and AML has been shown to be effective in the management of hypertension. The combination was generally more effective than individual drug therapy[2]. Stability testing is an important part of the process of drug product development. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors, such as temperature, humidity, and light, and enables recommendation of storage conditions, retest periods, and shelf lives to be established. The two main aspects of a drug product that play an important role in shelf life determination are assay of the active drug and degradation products generated during the stability study. The drug product in a stability test sample needs to be determined using a stability indicating method, as recommended by the International Conference on Harmonization (ICH) guidelines[3] and U.S. Pharmacopeia (USP) 26[4]. Although stability indicating methods have been reported for assay of various drugs in drug products, most of them describe assay procedures for drug products containing only one active drug substance. Only few stability indicating methods are reported for assay of combination drug products containing two or more active drug substances. The objective of this work was to develop a simple, precise, and rapid column liquid chromatography (LC) procedure that would serve as stability indicating assay method for combination drug product of VAL and AML.

VAL is official in USP[5], while AML is official in IP[6], BP[7], EP[8] and USP[9] in which HPLC method is describe for both drug in alone. The combination of VAL and AML is not official in any pharmacopoeia. Literature survey revealed HPLC[10-12], RP-HPLC[13, 14], HPTLC[15, 16], LCMS/MS[17], LC-MS[18] and simultaneous UV Spectrophotometric methods[19, 20] are reported for the estimation of AML alone or in combination with other anti-hypertensive agents. Methods such as HPLC[21-23], LC-MS[24-26], Protein precipitation[27], Capillary electrophoresis[28] and simultaneous UV spectrophotometer methods[29, 30] are reported for estimation of VAL alone or in combination with other agents. stability indicating RP-HPLC assay method for AML alone[31] and in combination with atorvastatin calcium[14] and benazepril hydrochloride[32], respectively are available in literatures but no method is reported for AML and VAL in combination, the aim of the present study was to develop accurate, precise and selective reverse phase HPLC assay procedure for the analysis of AML and VAL in bulk drug samples and in combined dosage formulation.

## MATERIALS AND METHOD

AMLB and VAL reference standards were gifted by Hetero drugs LTD, Hyderabad, India, with purity of 99.12% and 99.18% respectively and were used without further purification for the study. The commercial fixed combination product containing 10 mg AMLB and 160 mg VAL was procured from Pfizer. Milli-Q water: - (MILLIPORE SAS 67120, France), HPLC grade Acetonitrile (Spectrum, New Brunswick). ACS grades Orthophosphoric acid (Spectrum, New Brunswick). Sodium Hydroxide (Labchem, Zelienople), Triethylamine (Labchem, Zelienople), Orthophosphoric acid (Spectrum, New Brunswick). Water- Acetonitrile in the ratio 50:50, v/v, was used as a diluent.

**Instrument and conditions:**

Chromatography was performed with a Shimadzu's HPLC (LC-2010-HT, Shimadzu, Singapore) equipped with UV-Visible & Diode Array detectors. The LC separations were performed at 25°C on an XTerra® $RP_{18}$, 5 µm, 150 mm × 4.6 mm chromatographic column and Class-VP software was used for LC peak integration. The mobile phase was degassed by sonication with an Ultrasonic bath (Sweep zone). The standard substances were weighed on Analytical balance (AUW220D, Shimadzu, Columbia). Mobile phase consisted mixture of solution A (2.0 ml of triethylamine + 1000 ml of water) and solution B (ACN) with flow rate of 1.0 mL/ min and UV detection was carried out at 237 nm for AML and VAL, respectively with injection volume of 10 µL.

**Preparation of VAL and AML Standard Stock**

**Solutions:**

20 mg of accurately weighed Amlodipine besylate or 640 mg of Valsartan is taken into a 200 ml volumetric flask, sonicated and the volume is made with degassed mixture of buffer: methanol in the ratio of 50:50 v/v. 2 ml of above solution is diluted to 50 ml with degassed mixture of buffer: methanol in the ratio of 50:50 v/v.

**Analysis of the Marketed Formulation:**

Twenty tablets were accurately weighed, their mean weight was determined, and were ground to fine powder in a glass mortar. An amount of the powder equivalent to 2 tablets was dissolved in 150 mL of diluent, solution was sonicated for 30 minutes with intermittent shaking and diluted to 200 mL with diluent and mixed. The resulted mixture was filtered through 0.22µ nylon filter; first 5 mL of the filtrate was discarded. From the filtrate 5 mL of aliquot was transferred to 100 mL volumetric flask for VAL and 10 mL aliquot was transferred to 50 mL volumetric flask for AML. After dilution 10 µL of both solutions were injected for chromatographic analysis.

The above solutions were diluted to achieve the solutions having final concentration of 160 and 20 mg/mL for VAL and AML, respectively.

## RESULTS AND DISCUSSION

### Method Development and optimization

The proposed method was developed by several concurrent trails in order to establish the preferred chromatographic conditions which would be helpful to conduct a complete validation study. Details of the trails for method development and optimization were shown in table no 1 and table no 2 and the chromatograms were shown in figures 1-7. The mobile phase consisting of Methanol: Acetonitrile (1: 1, % V/V) at 1 $mL.min^{-1}$ flow rate and detection wavelength of 225 nm and 237 nm was optimized which gave sharp peak, minimum tailing factor with short run time for AML and VAL. The retention time for AMLB and VAL was found to be 5.089 minutes and 8.311 minutes respectively.

### Validation of method

The proposed method was validated as per the guidelines of ICH Q2 (R1). System suitability parameters and optimized chromatographic conditions are shown in Table 8. The specificity was studied for the examination of the presence of interfering components, while the comparison of chromatograms there was no interference from placebo (Figure 18) with sample peak. They do not disturb the elution or quantification of AML and VAL furthermore the well-shaped peaks also indicate the specificity of the method. Therefore, it was concluded the method is specific. The specificity results are summarized in Table 6. The chromatographic results for the calibration standards are presented in Table 6. The calibration curve for AML was found to be linear over the range of 20-160 µg/ml and VAL was found to be linear over the range of 50-200 µg/ml. The data of the calibration is shown in Table 10 and Table 11 and the chromatograms for calibration are present in Figure 11 to Figure 12. The regression equation for AML was found to be Y=25798X-3168 with correlation coefficient, $r^2$= 0.999 and for VAL was Y= 21543X+4312 with correlation coefficient, $r^2$= 0.999 which indicate this method has good linearity. The data for regression analysis of the calibration results is presented in Table 10 and 11. The linearity graphs are shown in Figure 11 and Figure 12 for AML and VAL respectively. Precision was studied to find out intraday and inter-day variation in the test methods of AML and VAL for 6 times on the same day and different day. The Intra-day and Inter-day precision obtained was %RSD (< 2.0) indicates that the proposed method is quite precise and reproducible and results are shown in Table 14 for inter-day and Table 15 for intra-day precision studies. The representative chromatograms are depicted in Figure 10 for precision studies. Recovery studies of the drug were carried out for the accuracy parameters at three different concentration levels that is multiple level recovery studies. A known amount standard was

added into pre analyzed sample and subjected them to proposed HPLC method. The % recovery was found to be within the limits as listed in Table 8 and Table 9. The representative chromatograms for recovery studies at various levels for recovery levels 80%, 100% and 120% respectively. Generally the main percentage recovery of AML and VAL at each level was not less than 98% and not more than 102%. Robustness was done by small changes in chromatographic conditions like mobile phase flow rate, detection wavelength, mobile phase composition etc. It was observed that there were no marked changes in the chromatograms. In fact the parameters are within the limits which indicates that the method has robustness and suitable for routine use. The robustness results are presented in Table 19.

**Table 1:Chromatographic conditions used for method development and optimization**

| Chromatographic condition | Trail 1 | Trail 2 | Trail 3 | Trail 4 | Optimized |
|---|---|---|---|---|---|
| Column | Symmetry C-18, (150 × 3.4 mm, 5 µ) | Symmetry C-18, (150 × 3.4 mm, 5 µ) | Symmetry C-18, (150 × 3.4 mm, 5 µ) | Symmetry C-18, (150 × 3.4 mm, 5 µ) | Symmetry C-18, (150 × 3.4 mm, 5 µ) |
| Detector wavelength (nm) | 225 and 237 | 225 and 237 | 237 | 237 | 237 |
| Column temperature (◦C) | 40 | 40 | 35 | 35 | 35 |
| Injection volume (µl) | 10 | 10 | 10 | 10 | 10 |
| Flow rate (ml/min) | 1.2 | 1.2 | 1.0 | 1.0 | 1.0 |
| Run time (min) | 25 | 25 | 20 | 20 | 20 |

**Table 2: Gradient programme for method development and optimization**

| Trail No. | Time(min) | %A | %B | Mobile phase A | Mobile phase B |
|---|---|---|---|---|---|
| Trail 1 | 0.00 | 90 | 10 | Buffer 3.0 | Acetonitrile : Methanol (1 : 1) |
| | 18.00 | 20 | 80 | | |
| | 19.00 | 90 | 10 | | |
| | 25.00 | 90 | 10 | | |
| Trail 2 | 0.00 | 95 | 5 | Buffer 3.0 | Acetonitrile : Methanol (1 : 1) |
| | 18.00 | 20 | 80 | | |
| | 19.00 | 95 | 5 | | |
| | 25.00 | 95 | 5 | | |
| Trail 3 | 0.01 | 75 | 25 | Buffer 3.0 | Acetonitrile |
| | 12.00 | 10 | 90 | | |
| | 15.00 | 75 | 25 | | |
| | 20.00 | 75 | 25 | | |
| Trail 4 | 0.01 | 75 | 25 | Buffer 3.0 | Acetonitrile |
| | 12.00 | 10 | 90 | | |
| | 15.00 | 75 | 25 | | |
| | 20.00 | 75 | 25 | | |
| Optimized method | 0.00 | 75 | 25 | Buffer 3.0 | Acetonitrile |
| | 12.00 | 10 | 90 | | |
| | 15.00 | 75 | 25 | | |
| | 20.00 | 75 | 25 | | |

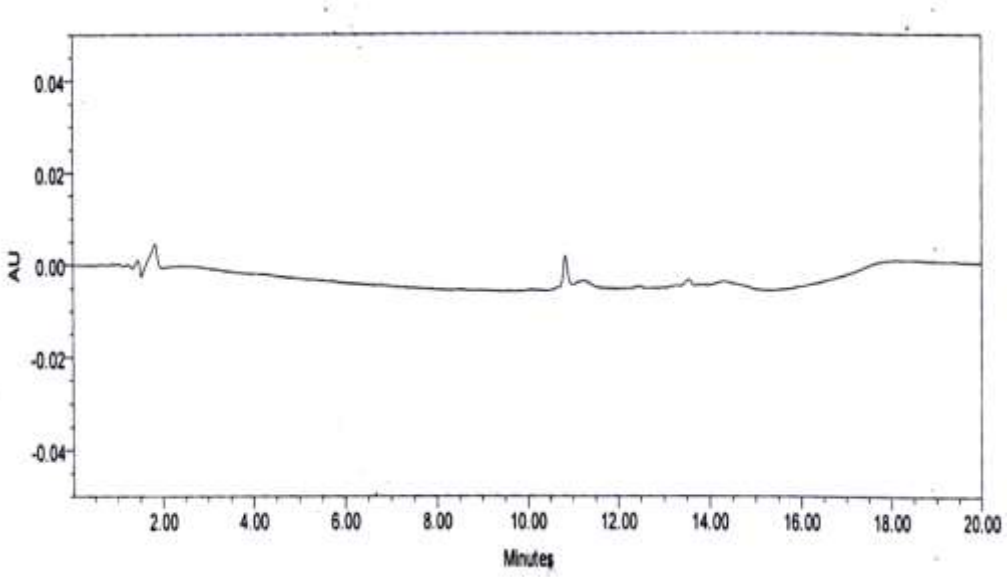


**Figure 1: Blank chromatogram**

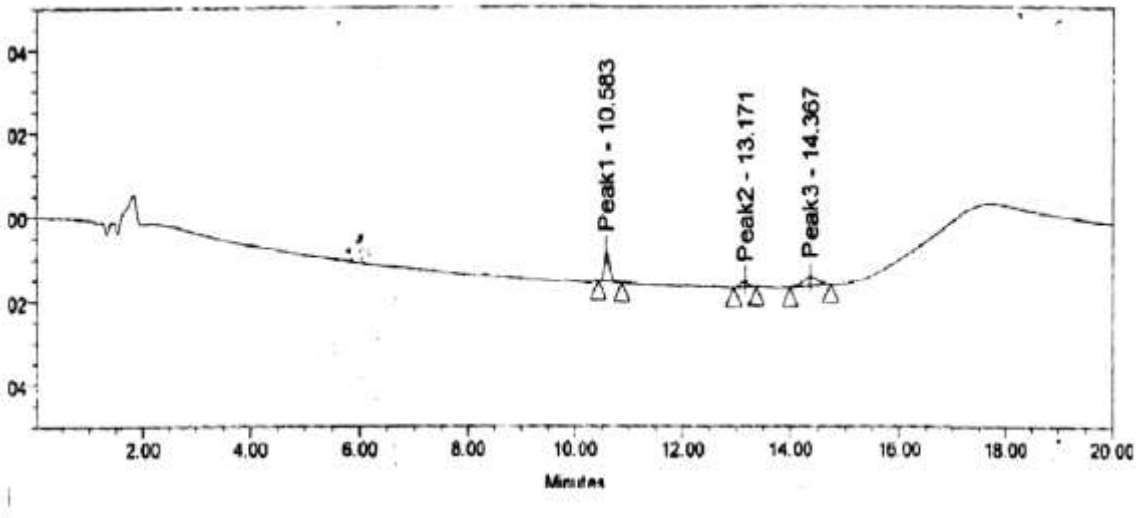


**Figure 2: Blank chromatogram**

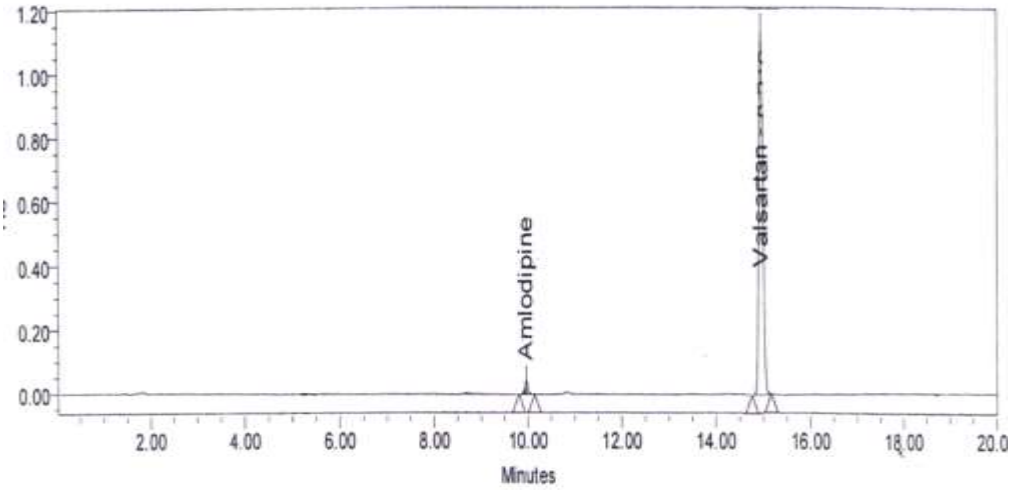


**Figure 3: Standard chromatogram for trial 1**

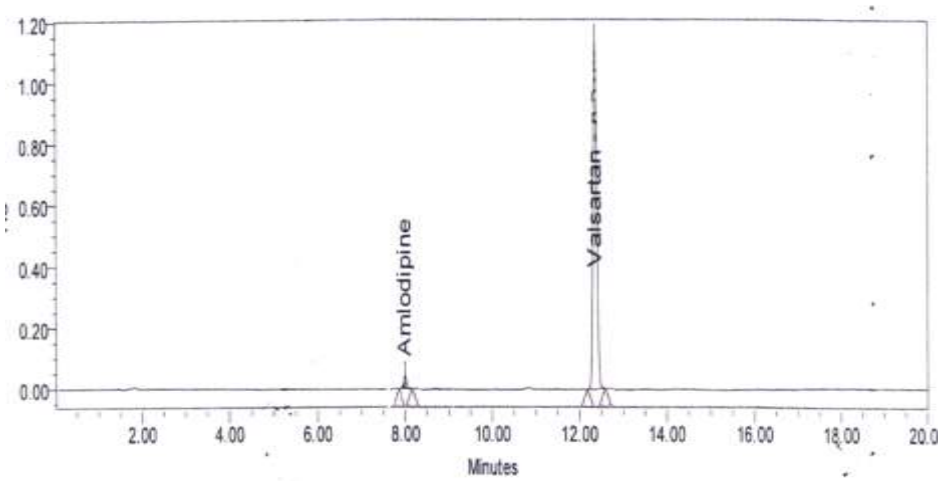


**Figure 4: Standard chromatogram for trial 2**

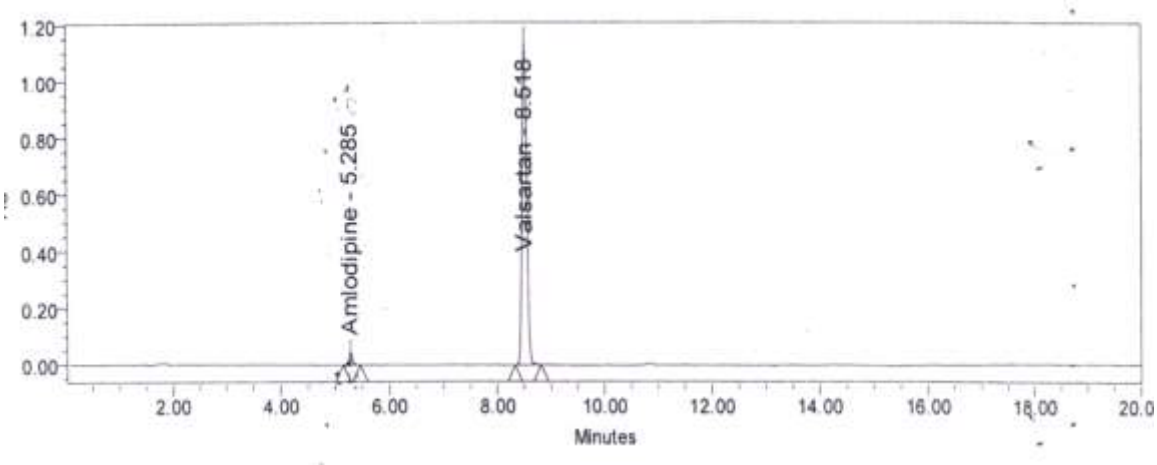


**Figure 5: Standard chromatogram for trial 3**

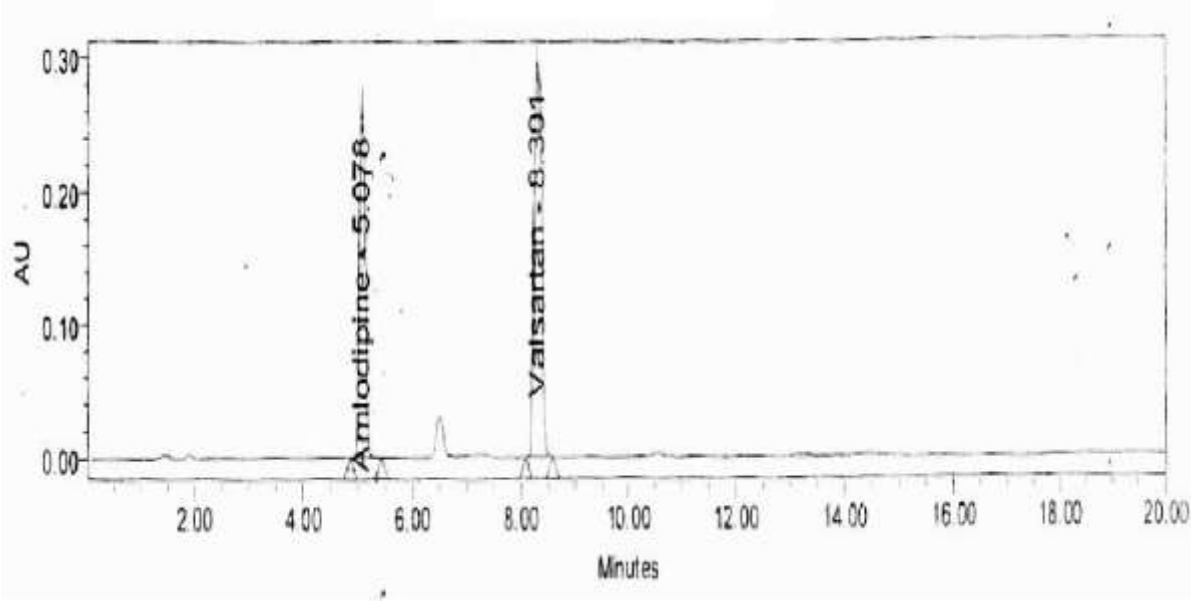


**Figure 6: Standard chromatogram for trial 4**

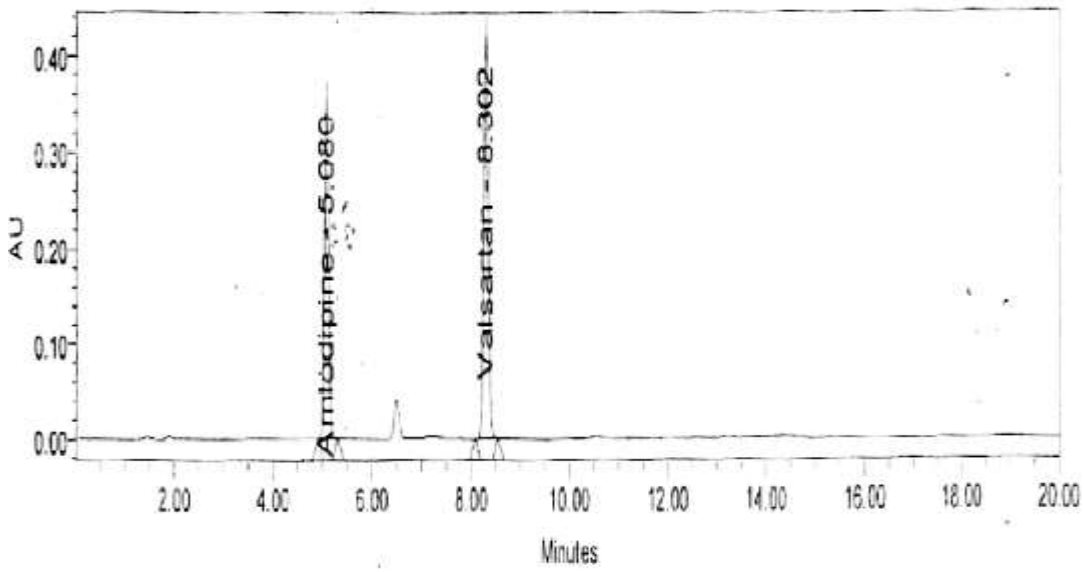


**Figure 7: Standard chromatogram for optimized method**

**Table 3: Data for assay in tablet formulations**

| S. no. | Sample name | AMBL | | VAL | |
|---|---|---|---|---|---|
| | | RT | Peak area | RT | Peak area |
| 1 | Assay stock spl-1 | 5.068 | 2585376 | 8.288 | 2660937 |
| 2 | Assay stock spl-2 | 5.068 | 2584325 | 8.283 | 2656499 |
| 3 | Assay stock spl-3 | 5.063 | 2578138 | 8.273 | 2678468 |
| 4 | Assay stock spl-4 | 5.080 | 2586304 | 8.269 | 2681350 |
| Mean | | 5.070 | 2583535.89 | 8.278 | 2669313.61 |
| %RSD | | 0.1 | 0.1 | 0.1 | 0.5 |
| SD | | 0.007 | | 0.009 | |

**Table 4: Assay method**

| S. No. | Content | Label claim (mg) | Peak area | RT | Percentage Content |
|---|---|---|---|---|---|
| **1.** | AMBL | 10 mg | 2583535.89 | 5.07 | 99.28 % |
| **2.** | VAL | 320 mg | 2669313.61 | 8.2 | 99.39 % |

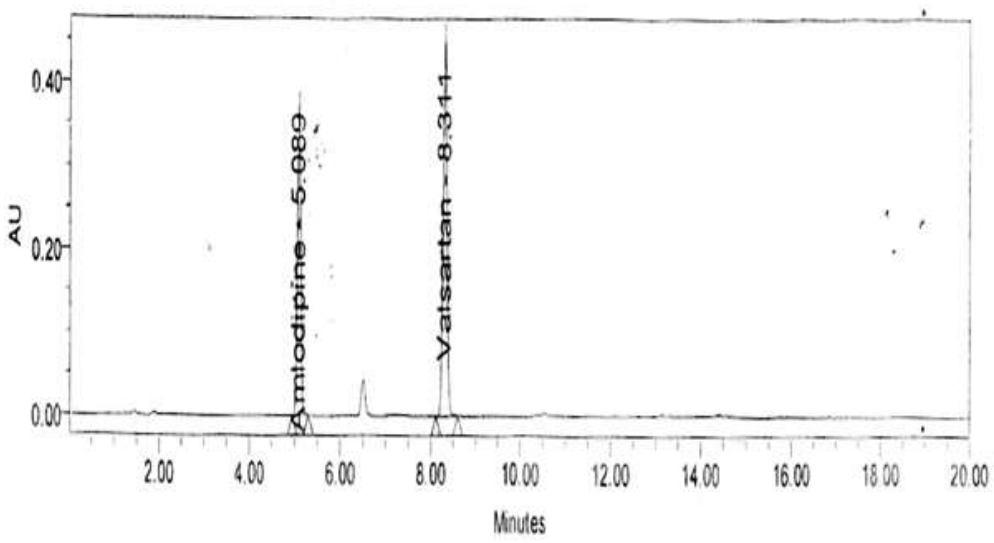


**Figure 8: Standard chromatogram for system suitability**

**Table 5: Data for system suitability parameters for AML and VAL**

| Parameters& Acceptance value | AMBL Mean | SD | %RSD | VAL Mean | SD | %RSD |
|---|---|---|---|---|---|---|
| RT(%RSD NMT 2) | 5.0735 | 0.006737 | 0.132791 | 8.3024 | 0.009107 | 0.109688 |
| Peak area (%RSD NMT 2) | 2585903 | 495.6531 | 0.019168 | 2767763 | 887.4316 | 0.032063 |
| USP plate count (NLT 3000) | 7172.233 | 11.4703 | 0.159924 | 11750.61 | 20.08686 | 0.170943 |
| Tailing factor (%RSD NMT 2) | 1.0891 | 0.011005 | 1.01 | 1.11 | 0.01959 | 1.764867 |

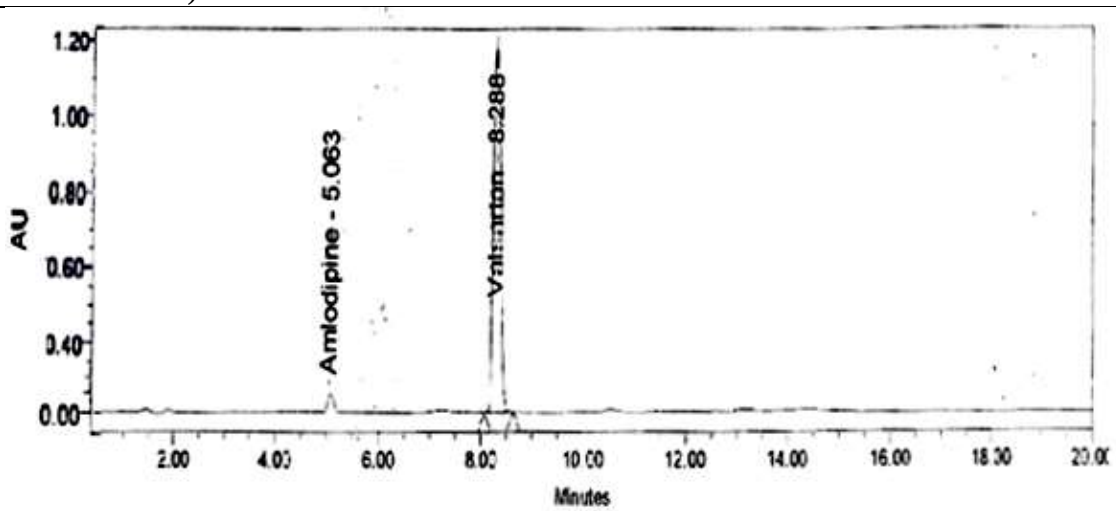


**Figure 6: Amlodipine and valsartan sample chromatogram for interference study**

**Table 6: Data for specificity**

| Injections | Interference | RT |
|---|---|---|
| Blank | Nil | No interference at RT of Analyte Peak |
| Placebo | Nil | No interference at RT of Analyte Peak |
| Sample | Nil | AMBL - 5.0 min<br>VAL - 8.2 min |

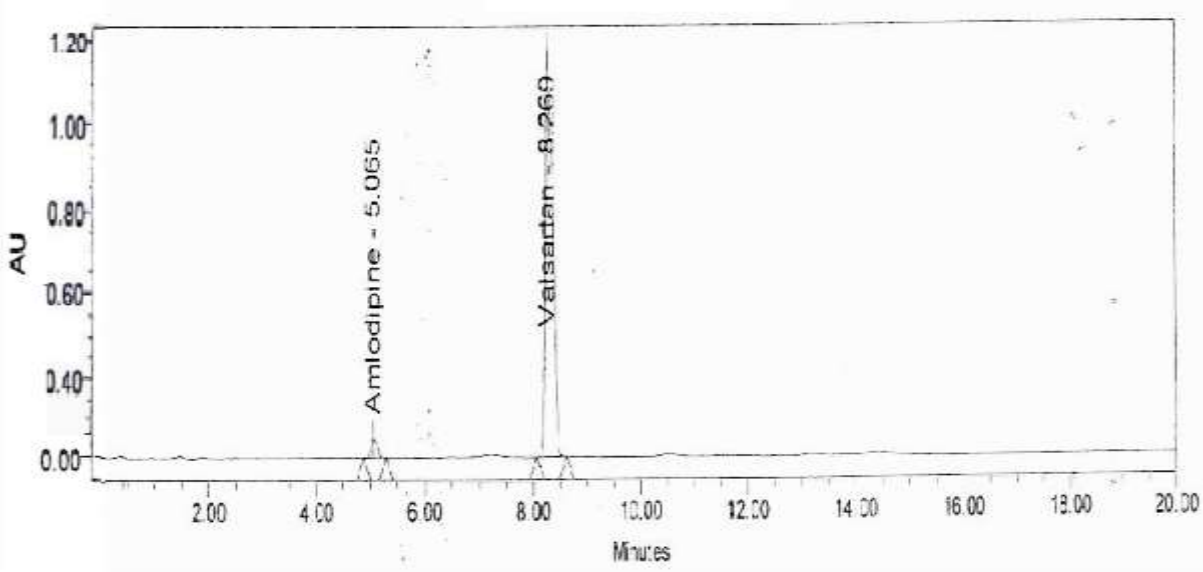


**Figure 10: Amlodipine and valsartan sample chromatogram**

**Table 7: Data for method precision**

| S.no | AMBL | | VAL | |
|---|---|---|---|---|
| | RT | Peak area | RT | Peak area |
| 1 | 5.089 | 1932075 | 8.311 | 2768666 |
| 2 | 5.077 | 1937803 | 8.294 | 2774111 |
| 3 | 5.078 | 1941938 | 8.298 | 2780808 |
| 4 | 5.08 | 1945530 | 8.302 | 2777299 |
| 5 | 5.082 | 1945255 | 8.304 | 2782394 |
| Mean | 5.081 | 1940519.91 | 8.302 | 2776655.4 |
| SD | 5661.8 | 5661.84 | 0.006 | 5497.59 |
| %RSD | 0.3 | 0.3 | 0.1 | 0.2 |

**Table 8: Accuracy data for amlodipine besylate**

| Concentration of spiked level | Amount added(ppm) | Amount found(ppm) | % Recovery | Statistical analysis of % recovery | |
|---|---|---|---|---|---|
| | 50.08 | 49.63 | 99.1 | Mean | 99.78 |
| 50% sample | 50.56 | 50.4 | 99.68 | SD | 0.534 |
| | 50.03 | 49.53 | 100.1 | %RSD | 0.535 |
| | 100.01 | 98.46 | 98.36 | Mean | 99.28 |
| 100% sample | 100.13 | 99.391 | 99.26 | SD | 0.462 |
| | 100.23 | 100.07 | 100.15 | %RSD | 0.468 |
| | 150.12 | 150.05 | 99.95 | Mean | 99.28 |
| 150% sample | 150.23 | 150.15 | 99.96 | SD | 0.447 |
| | 150.3 | 149.94 | 99.76 | %RSD | 0.4471 |

**Table 9: Accuracy data for valsartan**

| Concentration of spiked level | Amount added(ppm) | Amount found(ppm) | % Recovery | Statistical analysis of % Recovery | |
|---|---|---|---|---|---|
| | 64.58 | 64.32 | 99.59 | Mean | 9.67 |
| 50% sample | 64.98 | 64.17 | 98.75 | SD | 0.505 |
| | 64.63 | 64.01 | 99.04 | %RSD | 0.595 |
| | 128.86 | 127.23 | 99.07 | Mean | 99.39 |
| 100% sample | 129.03 | 128.76 | 99.79 | SD | 0.701 |
| | 129.45 | 128.69 | 99.41 | %RSD | 0.698 |
| | 192.56 | 192.36 | 99.89 | Mean | 100.22 |
| 150% sample | 193.98 | 191.64 | 98.79 | SD | 0.35 |
| | 192.66 | 192.24 | 100.23 | %RSD | 0.249 |

**Table 10: Linearity data for amlodipine**

| Linearity Level | Concentration(ppm) | Average area | %RSD | Statistical Analysis | |
|---|---|---|---|---|---|
| L1-50% | 50.56 | 1292693.3 | 0.58 | Slope | 16028 |
| L2-60% | 60.08 | 1551226.8 | 0.47 | Y-intercept | 25670 |
| L3-80% | 80.45 | 2068302.4 | 0.36 | % of Y-intercept | 0.132 |
| L4-100% | 100.23 | 2585378.2 | 0.57 | Correlation Coefficient $R^2$ | |
| L5-120% | 120.26 | 3102453.6 | 0.49 | | 0.999 |
| L6-150% | 150.5 | 3878068.2 | 0.52 | | |

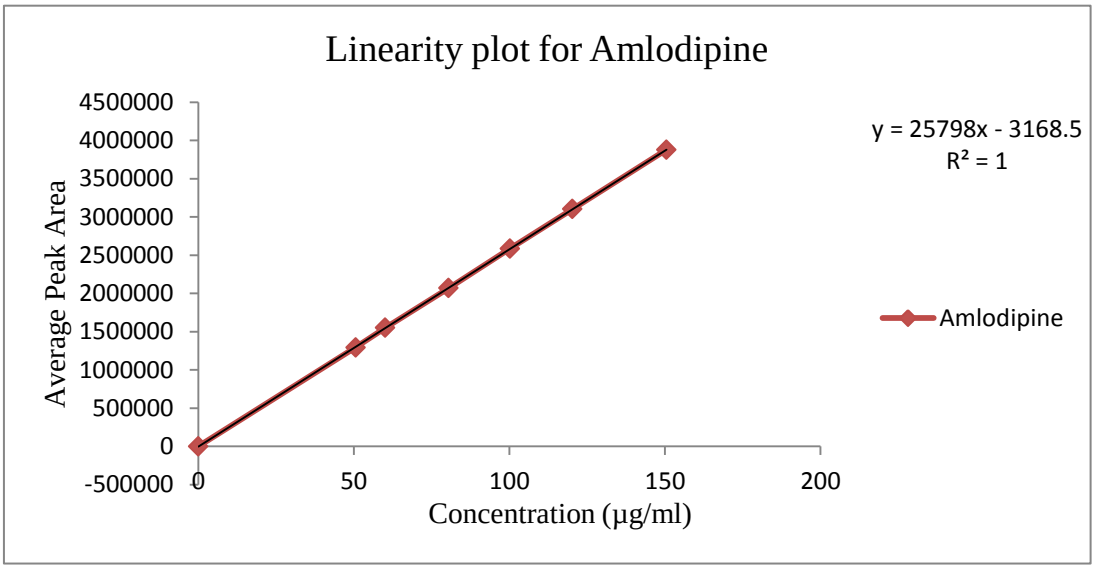


**Figure 11: Linearity graph for Amlodipine**

**Table 11: Linearity data for valsartan**

| Linearity Level | Concentration (ppm) | Average area | %RSD | Statistical Analysis | |
|---|---|---|---|---|---|
| L1-50% | 64.3 | 1384334.6 | 0.45 | Slope | 16379 |
| L2-60% | 76.8 | 1661201.52 | 0.35 | Y-intercept | 27595 |
| L3-80% | 102.4 | 2214935.36 | 0.56 | % of Y-intercept | 0.149 |
| L4-100% | 128 | 2768669.2 | 0.58 | Correlation Coefficient R2 | |
| L5-120% | 153.6 | 3322403.04 | 0.39 | | 1.00 |
| L6-150% | 193.2 | 4153003.8 | 0.48 | | |

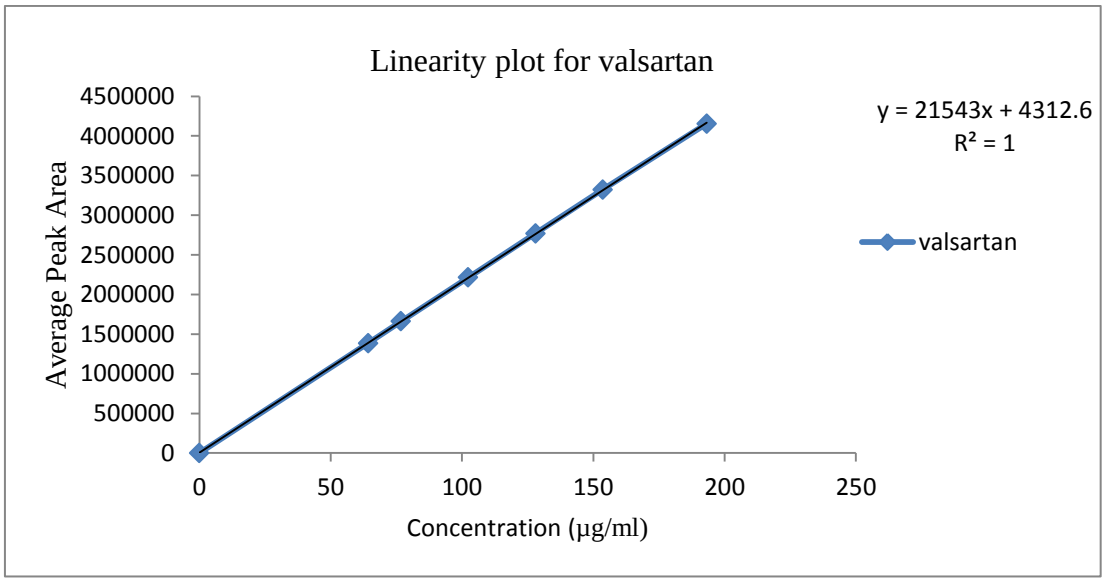


**Figure 12: Linearity graph Valsartan**

**Table 12: Data for the ruggedness study in system-1**

| Tablet ID | % Assay | | Statistical Analysis | | |
|---|---|---|---|---|---|
| | AMBL | VAL | | AMBL | VAL |
| 1 | 99.24 | 98.28 | Mean | 98.878 | 99.29 |
| 2 | 98.19 | 99.36 | | | |
| 3 | 98.34 | 99.78 | SD | 1.01 | 0.68 |
| 4 | 98.12 | 99.04 | | | |
| 5 | 100.5 | 100.03 | %RSD | 1.02 | 0.68 |

**Table 13: Data for the ruggedness study in system-2**

| Tablet ID | % Assay | | Statistical Analysis | | |
|---|---|---|---|---|---|
| | AMBL | VAL | | AMBL | VAL |
| 1 | 99.19 | 99.28 | Mean | 98.834 | 98.838 |
| 2 | 98.14 | 99.06 | | | |
| 3 | 99.32 | 98.78 | SD | 0.698 | 0.48 |
| 4 | 98.02 | 98.04 | | | |
| 5 | 99.5 | 99.03 | %RSD | 0.7 | 0.48 |

**Table 14: Data for interday variation**

| Tablet ID | % Assay | | Statistical Analysis | | |
|---|---|---|---|---|---|
| | AMBL | VAL | | AMBL | VAL |
| 1 | 99.54 | 99.34 | Mean | 99.39 | 99.4 |
| 2 | 98.02 | 99.13 | | | |
| 3 | 99.87 | 101 | SD | 1.05 | 0.592 |
| 4 | 101.02 | 99.76 | | | |
| 5 | 98.5 | 98.76 | %RSD | 1.06 | 0.598 |
| 6 | 99.43 | 101.16 | | | |

**Table 15: Data for intraday variation**

| Tablet ID | % Assay | | Statistical Analysis | | |
|---|---|---|---|---|---|
| | AMBL | VAL | | AMBL | VAL |
| 1 | 99.14 | 99.38 | Mean | 98.954 | 99.185 |
| 2 | 98.24 | 98.46 | | | |
| 3 | 98.77 | 99.78 | SD | 0.732107 | 0.684 |
| 4 | 100.12 | 100.04 | | | |
| 5 | 98.5 | 99.9 | %RSD | 0.739845 | 0.69 |

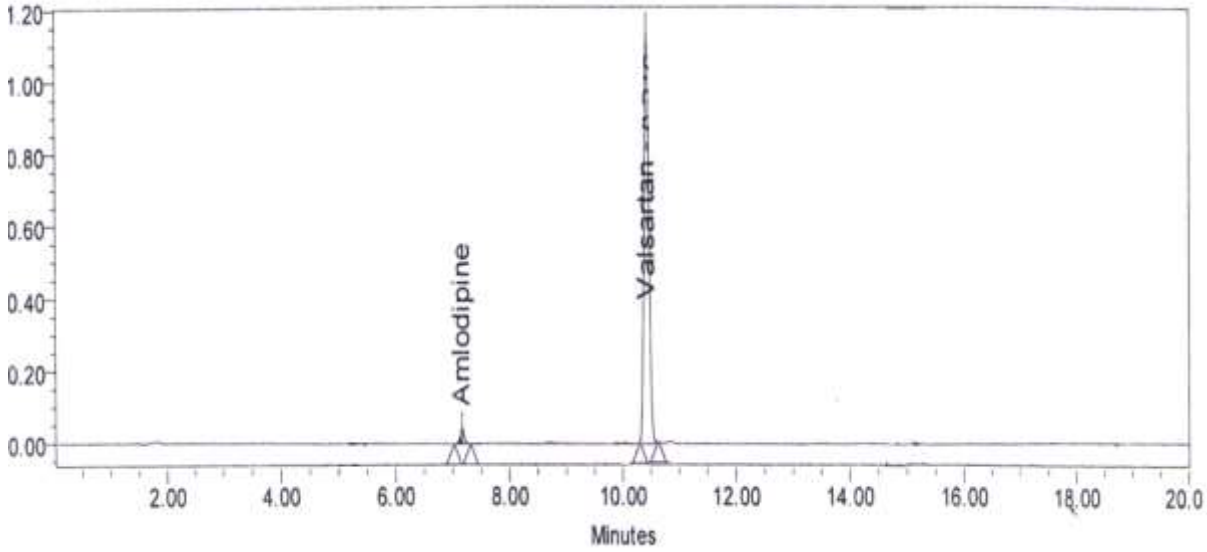


**Figure 13: Amlodipine and valsartan chromatogram at the flow rate of 0.9 ml/min**

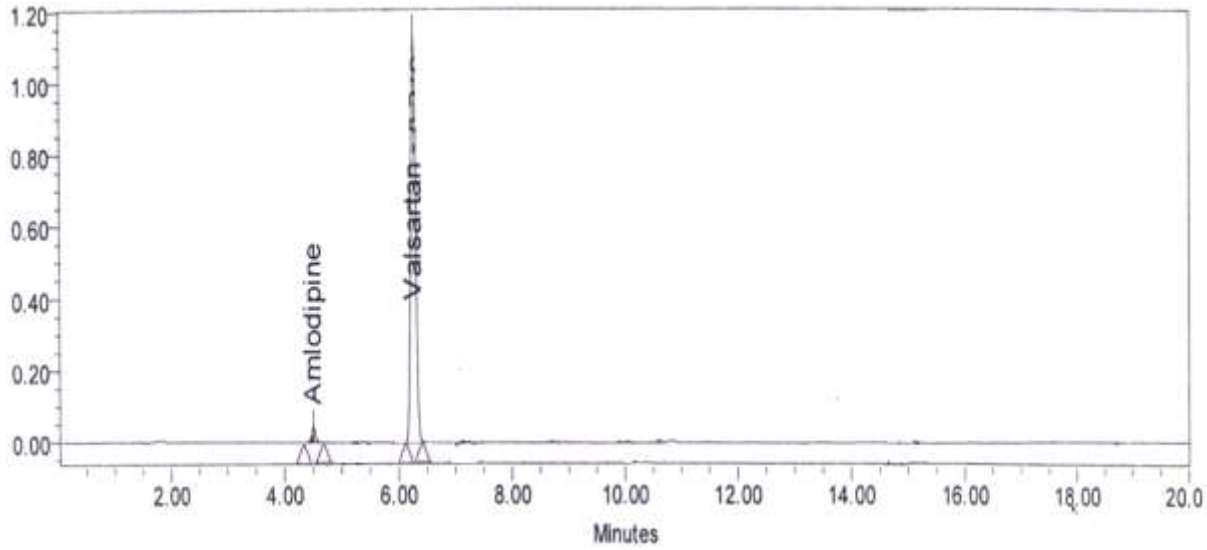


**Figure 14: Amlodipine and valsartan chromatogram at the flow rate of 1.1 ml/min**

**Table 16: Data for variation in flow rate**

| Parameters | AMBL | | VAL | |
|---|---|---|---|---|
| | RT | Peak | RT | Peak |
| Normal (1.0 ml/min, | 5.1 | 2583537 | 8.2 | 2669313 |
| Flow rate 0.9 ml/min | 7.3 | 262361 | 10.7 | 285436 |
| Flow rate 1.1 ml/min | 4.5 | 218313 | 6.3 | 229632 |
| %RSD | | 0.205 | | 0.27 |

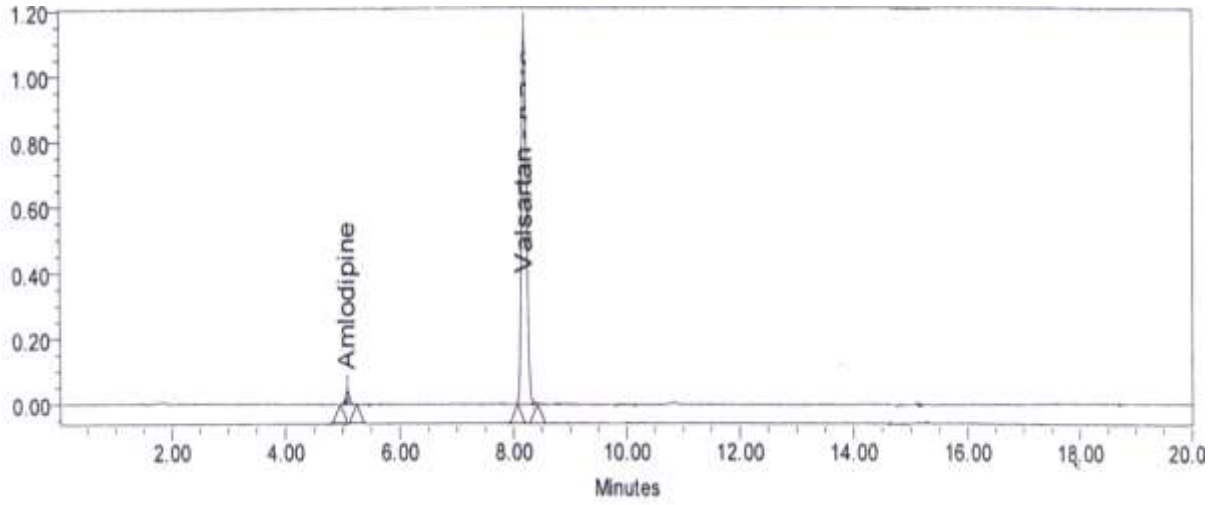


**Figure 15: Amlodipine and valsartan chromatogram at the temperature of 30°C**

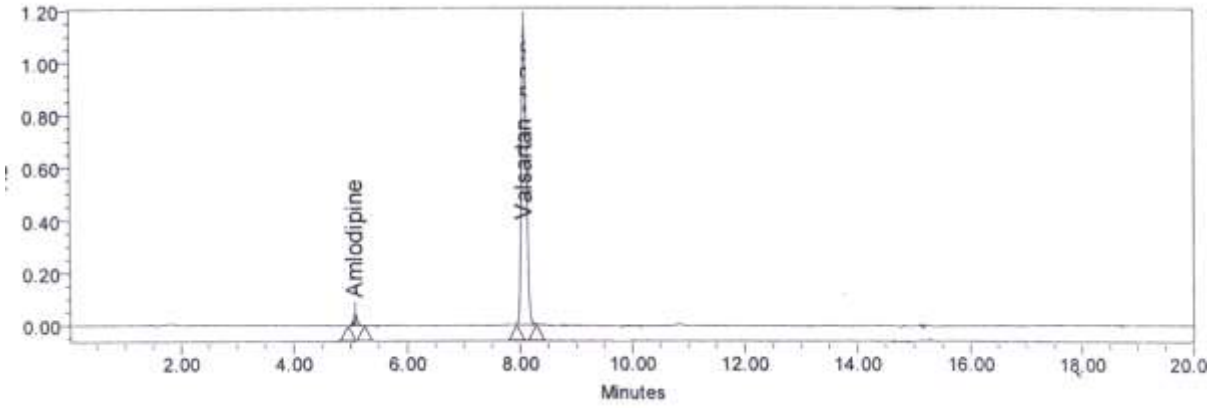


**Figure 16: Amlodipine and valsartan chromatogram at the temperature of 40°C**

**Table 17: Data for variation in column temperature**

| Parameters | AMBL | | VAL | |
|---|---|---|---|---|
| | RT | Peak | RT | Peak |
| Normal (35 °C, %RSD-0.04, 0.5) | 5.1 | 2583537 | 8.2 | 2669313 |
| Column temperature 30°C | 5.2 | 2482427 | 8.3 | 2774128 |
| Column temperature 40°C | 5.1 | 2468953 | 8.1 | 2796459 |
| %RSD | | 0.095 | | 0.055 |

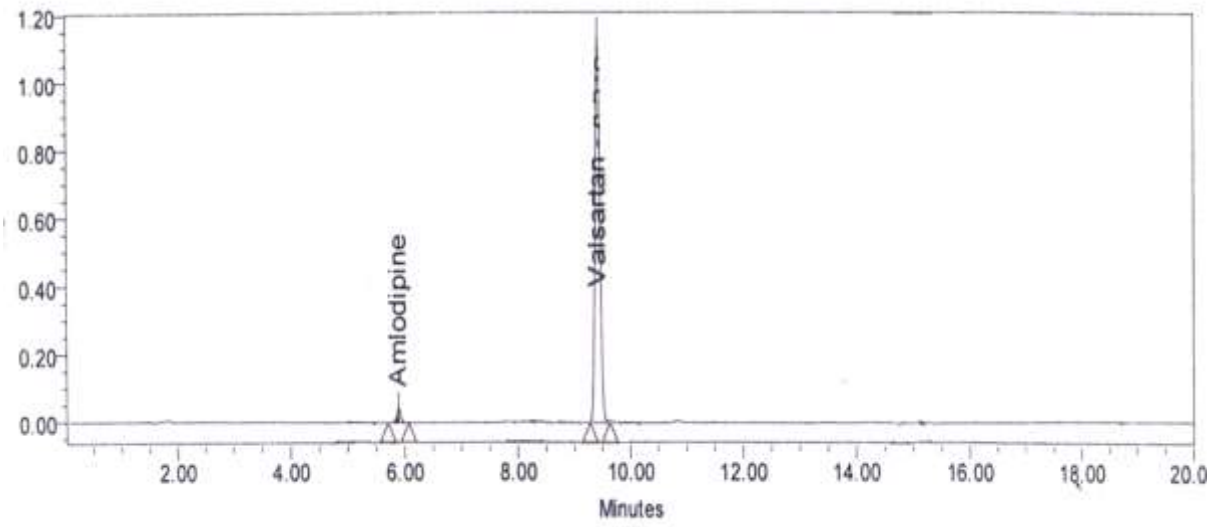


**Figure 17: Amlodipine and valsartan chromatogram at buffer pH: 2.8**

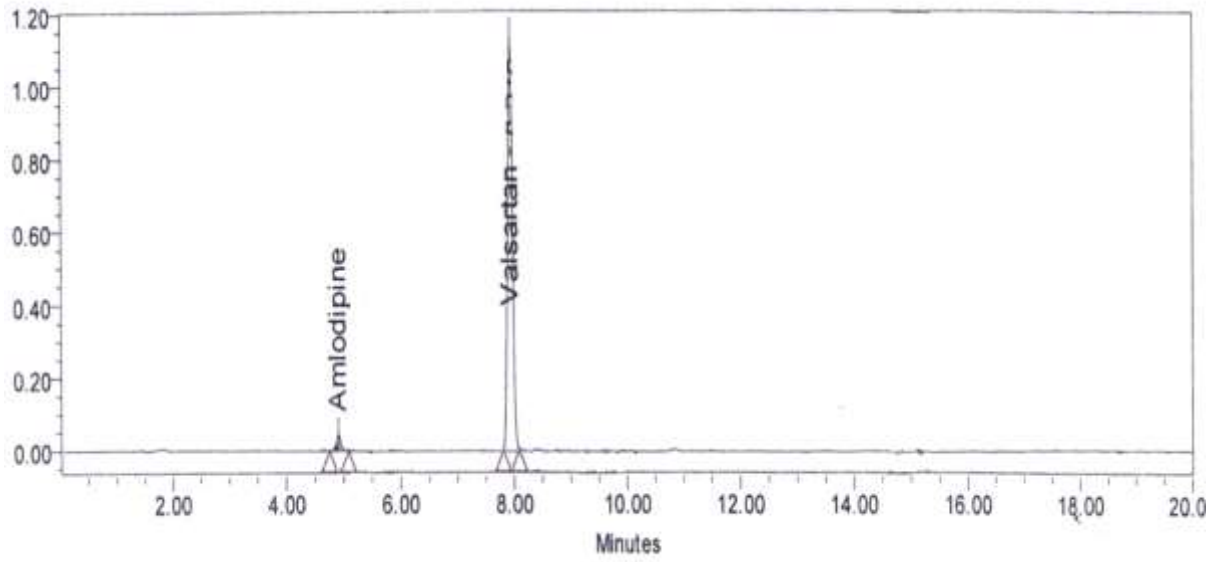


**Figure 18: Amlodipine and valsartan chromatogram at buffer pH: 3.2**

**Table 18: Data for variation in pH**

| **Parameters** | | **AMBL** | | **VAL** | |
|---|---|---|---|---|---|
| | | **RT** | **Peak area** | **RT** | **Peak area** |
| Normal (pH 3.0, %RSD-0.04, 0.5) | | 5.1 | 2583537 | 8.2 | 2669313 |
| Buffer pH | 2.8 | 5.9 | 2543198 | 9.6 | 2687432 |
| Buffer pH | 3.2 | 4.9 | 2574944 | 8.0 | 2753421 |
| %RSD | | | 0.245 | | 0.255 |

**Table 19: Remarks in robustness parameters**

| Parameters | Optimum range | Conditions in procedure | Remarks |
|---|---|---|---|
| Flow rate ml/min | 0.9-1.1 | 1 | Increase in flow rate resulted in early elution of all two active ingredients. Decrease in flow rate in late elution of all three actives but still within the proposed run time. |
| Temperature | 30-40$^{o}$C | 35 $^{o}$C | Increase in temperature resulted in early elution of all two active ingredients. Decrease in temperature resulted in late elution of all two actives but still within the proposed run time. |
| pH | 2.8-3.2 | 3.0 | Increase in pH resulted in early elution of all two active ingredients. Decrease in pH resulted in late elution of all two actives but still within the proposed run time |

**Applicability of the Developed Method to Marketed Formulations:**

The assay results of VAL and AML in tablet dosage forms were comparable with the value claimed on the label. The obtained results, presented in Table 5, indicated the suitability of the method for routine analysis of VAL and AML from their combination drug products.

## CONCLUSION

A new method was developed for the quantification of AMBL and VAL in combined tablet formulation. This method seems to obey the validation parameters and cost effective. This method can be routinely employed for the analysis of this combination. The reason behind selection of two different categories of antihypertensive drugs was also justified properly because of synergistic effect on lowering of blood pressure and reduction of side effects of one drug by another. Through there are several methods with acceptable level of confidence for determination of both the drugs, This method proven the aspects of less utilization of organic solvent, good accuracy and excellent correlation between the analyte and its response.

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