# Development and Validation of a Green UV Spectrophotometric Method for Estimation of Ramipril Using a Propylene Glycol–Water Solvent System

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**Abstract:**

A simple, precise, and environmentally friendly UV spectrophotometric method was developed and validated for the estimation of Ramipril in bulk and pharmaceutical dosage forms. The method employs a green solvent system comprising propylene glycol and water in a 1:9 v/v ratio, enhancing the solubility and stability of Ramipril. The absorbance of Ramipril was measured at its maximum wavelength (λmax) of 207 nm. The calibration curve exhibited linearity over the concentration range of 4–16 µg/mL, adhering to Beer-Lambert's law with a correlation coefficient ($R^2$) of 0.999. Validation parameters, conducted in accordance with ICH Q2(R1) guidelines, demonstrated the method's precision, accuracy, and robustness. The method exhibited a recovery rate ranging from 98.5% to 101.2%, with relative standard deviation (RSD) values below 2%, indicating high reproducibility. This straightforward and rapid approach is suitable for routine quality control analysis of Ramipril in pharmaceutical environments.

**Keywords**: Ramipril, UV spectrophotometry, Method development, Validation, Precision, Accuracy, Specificity, Robustness, Stability studies.

## 1. Introduction

Angiotensin-converting enzyme (ACE) inhibitors like Ramipril are frequently recommended to treat heart failure, hypertension, and lower the risk of cardiovascular events. As a prodrug, ramipril is broken down into its active form, ramiprilat, which lowers blood pressure and causes vasodilation by preventing angiotensin I from becoming angiotensin II [1–3].

For pharmaceutical formulations to be effective and safe for patients, Ramipril must be precisely and consistently quantified. Even if they are precise, traditional analytical techniques like high-performance liquid chromatography (HPLC) are frequently time-consuming and need sophisticated equipment [4–6]. On the other hand, UV spectrophotometric techniques are easy to use, economical, and quick to analyze, which makes them appropriate for regular quality control in pharmaceutical environments [7].

This work attempts to create a straightforward and environmentally friendly UV spectrophotometric method for the estimation of Ramipril in accordance with the principles of green analytical chemistry, which support the use of environmentally friendly solvents and reagents [8,9]. The technique improves Ramipril's solubility and stability while reducing its negative effects on the environment by using a green solvent solution made up of propylene glycol and water in a 1:9 v/v ratio [10–12].

In compliance with International Conference on Harmonization (ICH) Q2(R1) requirements, the main goal of this work is to create and validate a new, straightforward, and environmentally friendly UV spectrophotometric method for estimating Ramipril in pharmaceutical dosage forms and bulk.

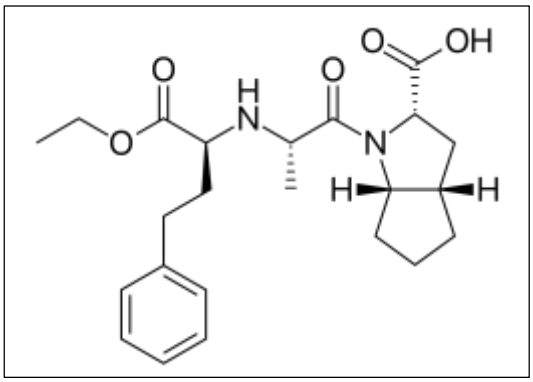

**Figure 1: Molecular structure of Ramipril**

## 2. Materials and Methods

Pure drug samples of Ramipril were generously provided as gift samples by a certified pharmaceutical manufacturer. All chemicals and reagents used in this study were of analytical grade. A green solvent system consisting of Propylene Glycol and distilled water in a 1:9 (v/v) ratio was employed for the preparation of all solutions. This eco-friendly solvent system was selected to enhance the solubility and stability of Ramipril, aligning with the principles of green analytical chemistry by minimizing environmental impact.

### 2.2 Instrumentation

Spectral analyses were performed using a double-beam UV-Visible spectrophotometer (JASCO V-730) equipped with 1 cm path length matched quartz cuvettes and UV-Probe software.

### 2.3 Method Development

#### 2.3.1 Determination of wavelength of maximum absorption

Pure Ramipril (1 mg) was accurately weighed and dissolved in 1 mL of Propylene Glycol and distilled water in a 1:9 (v/v). further dilutions are made to 20ug/ml solution.

The resulting solution was scanned in the UV-visible region from 190 to 800 nm using a JASCO V-730 UV-Visible Spectrophotometer. The scan was conducted with solvent mixture aqueous serving as the reagent blank. The wavelength corresponding to the maximum absorbance (λmax) was identified to be 207 nm, which was subsequently utilized for the quantification of Ramipril in bulk and pharmaceutical dosage forms.

#### 2.3.2 Calibration Curves

A calibration curve for Ramipril was constructed within the concentration range of 4–16 µg/mL**.** Linearity was assessed by calculating the regression coefficient ($r^2$).

**Table 1: Calibration Curves**

| Concentration (µg/mL) | Absorbance at 207 nm (Ramipril) |
|---|---|
| 4 | 0.1994 |
| 6 | 0.2718 |
| 8 | 0.3466 |
| 10 | 0.4534 |
| 12 | 0.5509 |
| 14 | 0.6714 |
| 16 | 0.7885 |

#### 2.3.3 Sample Preparation from Dosage Form

Commercially available Ramipril Tablets IP 10 mg were used for the study. Twenty tablets were accurately weighed and finely powdered. An amount of the powder equivalent to 10 mg of Ramipril was transferred to a 100 mL volumetric flask. About 25 mL of the Propylene Glycol: Water solvent was added, and the solution was sonicated for 15 minutes, The volume was then made up

to 100 mL with distilled water to obtain a stock solution of 100 µg/mL. The solution was filtered through Whatman filter paper No. 41 to remove excipients. From this filtrate, appropriate aliquots were diluted with distilled water to prepare concentrations in the range of 4–16 µg/mL. The absorbance of each solution was recorded at 207 nm against a distilled water blank.

**3. Method Validation**

The developed method was validated in accordance with the ICH guidelines to assess its performance in terms of linearity, accuracy, precision, specificity, and robustness.

**3.1 Linearity**

Linearity ranges of 4-16 µg/mL for Ramipril were tested in triplicate using the stock solution and measuring absorbance at 207 nm. Using absorbance versus concentration, the calibration curve was plotted and a linear regression equation was generated.

**3.2 Accuracy**

Accuracy was determined by recovery studies. Known amounts of drug was added to the tablet formulation, and the recovery was calculated. The average recovery for both drugs was 98–102%, indicating high accuracy.

**3.3 Precision**

**System Precision**

From the above-mentioned stock solution, three replicates of concentrations of 4,10 and16 µg/mL of Ramipril, were prepared, analyzed and the percentage RSD was computed.

**Intraday precision**

On the same day, the concentrations of 4,10 and16 µg/mL Ramipril in triplicate were made from the above-mentioned stock solutions, analyzed and the percentage RSD was computed at various intervals.

**Interday precision**

On three consecutive days, the concentrations of 4,10 and16 µg/mL Ramipril in triplicate were made from the above-mentioned stock solutions, analyzed and the percentage RSD was computed.

**3.4 Specificity**

The UV spectra of the ramipril solution and the blank solvent (Propylene Glycol: Water, 1:9 v/v) were scanned from 800 nm to 200 nm in wavelength. This was done to check for solvent-induced interference at the wavelength at which each analyte has its greatest absorbance.

**3.5 LOD and LOQ**

The linear curve was used to calculate the Limit of Detection (LOD) and Limit of Quantification (LOQ) by statistical methods utilizing the following formulas.

$$LOD = \frac{3.3 \times standard\ deviation\ of\ y - intercept}{slope\ of\ calibration\ curve}$$

$$LOQ = \frac{10 \times standard\ deviation\ of\ y - intercept}{slope\ of\ the\ calibration\ curve}$$

**3.6 Ruggedness**

Ruggedness was achieved by altering both the instrument and the analyst. The concentrations of 10, 20 and 30 µg/mL of Ramipril in triplicate of each were prepared from the above stock solutions and measured absorption at 207 nm, and measured by different analysts and with a different instrument, the same concentration as previously mentioned was measured, examined and the percentage RSD was computed

### 3.7 Robustness

Robustness parameter was achieved by a change in the wavelength. The concentrations of 10, 20 and 30 µg/mL of Ramipril in triplicate of each were prepared from the above stock solutions and measured absorption at 205 nm, 207 nm and 209 nm of Ramipril analysed and %RSD was computed.

### 3.8 Solvent and standard stock solution stability

The stability of the solvent and standard stock solution was demonstrated by making a fresh stock solution. Analyses were carried out on dilutions of 2, 6 and 10 µg/mL containing both analytes after a fresh stock solution was prepared. The absorbance was computed as a percentage of RSD and compared to that of the old stock dilutions.

## 4. Results

The developed green UV spectrophotometric simple method demonstrated reliable performance for the estimation of Ramipril. The method showed clear resolution at selected wavelength 207 nm for Ramipril using a green solvent system (Propylene Glycol: Water, 1:9 v/v).

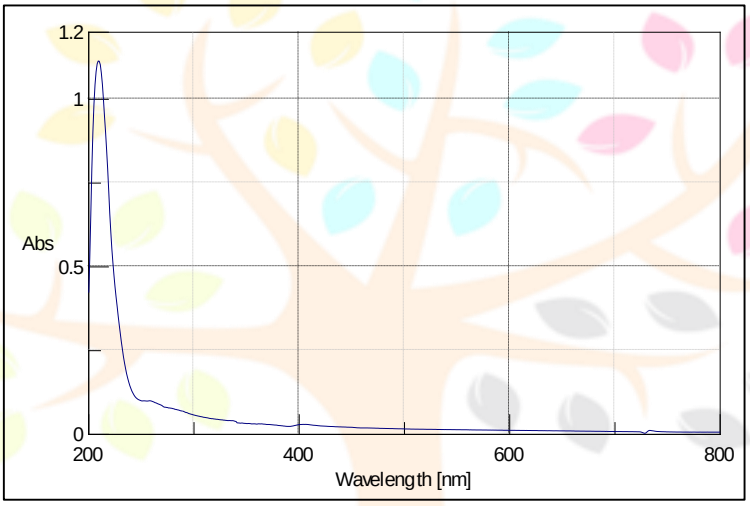


**Figure 2: UV- Spectrum of Ramipril**

### 4.1 Method Development

**Table 2: Method development parameters**

| Sr. No. | Parameters | Specifications |
|---|---|---|
| 1. | Analytes | Ramipril |
| 2. | Solvent | Propylene Glycol: Water, 1:9 v/v |
| 3. | Maximum absorbance of Ramipril | 207 nm |

### 4.2. Method Validation

#### 4.2.1. Linearity

The method was found to be linear for the Ramipril in the concentration range of 4–16 µg/mL. The correlation coefficients for Ramipril were 0.99 indicating excellent linearity.

**Table 3: Linearity data for Ramipril**

| Sr. No. | Concentration (µg/mL) Ramipril | Absorbance (nm) |
|---|---|---|
| 1. | 4 | |
| 2. | 6 | |
| 3. | 8 | |

| | | |
|---|---|---|
| 4. | 10 | |
| 5. | 12 | |
| 6. | 14 | |
| 7. | 16 | |
| $R^2$ | **$R^2$ = 0.9915** | |
| Slope | **y = 0.0495x – 0.0259** | |

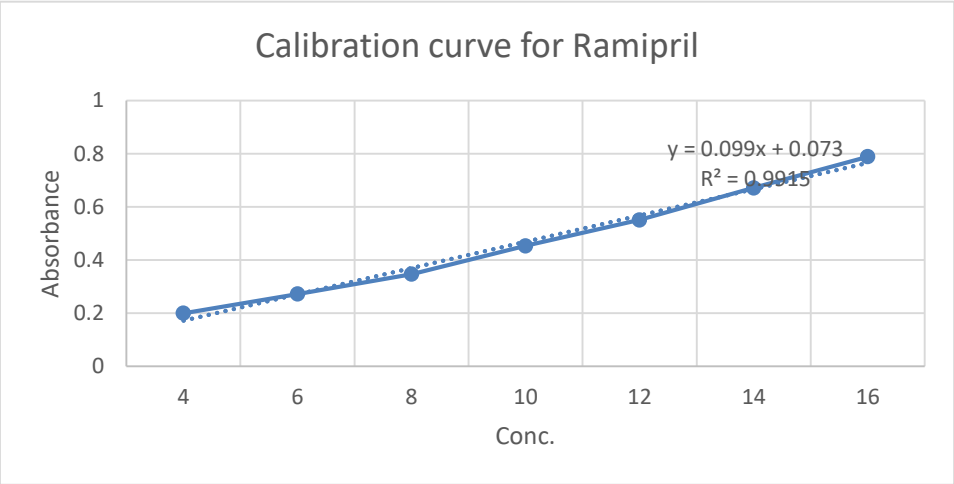


**Figure 3: Calibration curve of Ramipril at 207 nm**

**The calibration curve was constructed over the concentration range of 4–16 µg/mL. A strong linear relationship was obtained between absorbance and concentration with the regression equation: y = 0.0495x – 0.0259 ($R^2$ = 0.9915).**

### 4.2.2. Accuracy

**Table 4: Accuracy (Recovery Study)**

| Drug | Level (%) | Amount Added (µg/mL) | Amount Found (µg/mL) | % Recovery | % RSD |
|---|---|---|---|---|---|
| Ramipril | 80 | 8 | 7.95 | 99.0 | 1.01 |
| Ramipril | 100 | 10 | 10.1 | 100.5 | 0.89 |
| Ramipril | 120 | 12 | 12.05 | 99.6 | 0.92 |

### 4.2.3. Precision

Intraday precision and Interday precision and % RSD were calculated from the absorbance and found to be less than 2%. The precision data are illustrated in Tables 5, 6 and 7.

**Table 5: System precision (*n=3).**

| Sr. No. | Conc. (µg/mL) Ramipril | Absorbance at 207 nm | |
|---|---|---|---|
| | | SD | %RSD |
| 1. | 4 | 0.1994 | 1.20 |
| 2. | 10 | 0.4534 | 1.60 |
| 3. | 16 | 0.7885 | 1.16 |

**Table 6: Intraday precision (Initial Hour, 1st hr and 5th hr) (*n=3).**

| Concentration (µg/mL) | Ramipril | | | Ramipril | | | Ramipril | | |
|---|---|---|---|---|---|---|---|---|---|
| | Initial hr | | | 1st hr | | | 5th hr | | |
| Ramipril | Ab. | | | Ab. | | | Ab. | | |
| 4 | 0.197 | 0.199 | 0.202 | 0.200 | 0.198 | 0.201 | 0.198 | 0.200 | 0.201 |
| ± SD | 0.003 | | | 0.002 | | | 0.002 | | |
| %RSD | 1.50 | | | 1.00 | | | 1.10 | | |
| 10 | 0.451 | 0.455 | 0.454 | 0.452 | 0.456 | 0.454 | 0.453 | 0.454 | 0.456 |
| SD | 0.002 | | | 0.002 | | | 0.002 | | |
| %RSD | 0.44 | | | 0.48 | | | 0.44 | | |
| 16 | 0.785 | 0.790 | 0.791 | 0.787 | 0.788 | 0.790 | 0.786 | 0.7789 | 0.790 |
| SD | 0.003 | | | 0.002 | | | 0.002 | | |
| %RSD | 0.38 | | | 0.25 | | | 0.25 | | |

**Table 7: Interday precision(*n=3).**

| Concentration (µg/mL) | Ramipril | | | Ramipril | | | Ramipril | | |
|---|---|---|---|---|---|---|---|---|---|
| | Initial hr | | | 1st hr | | | 5th hr | | |
| Ramipril | Ab. | | | Ab. | | | Ab. | | |
| 4 | 0.196 | 0.202 | 0.202 | 0.197 | 0.198 | 0.201 | 0.198 | 0.200 | 0.201 |
| ± SD | 0.003 | | | 0.002 | | | 0.002 | | |
| %RSD | 1.51 | | | 1.01 | | | 1.05 | | |
| 10 | 0.451 | 0.455 | 0.454 | 0.452 | 0.453 | 0.456 | 0.453 | 0.454 | 0.457 |
| SD | 0.002 | | | 0.002 | | | 0.002 | | |
| %RSD | 0.44 | | | 0.48 | | | 0.44 | | |
| 16 | 0.784 | 0.789 | 0.792 | 0.786 | 0.788 | 0.791 | 0.785 | 0.789 | 0.791 |
| SD | 0.004 | | | 0.002 | | | 0.003 | | |
| %RSD | 0.51 | | | 0.25 | | | 0.38 | | |

### 4.2.4 Specificity

The solvent (Propylene Glycol: Water, 1:9 v/v) was scanned and the UV spectra showed the absence of any solvent interference, as **shown in Figure 4**

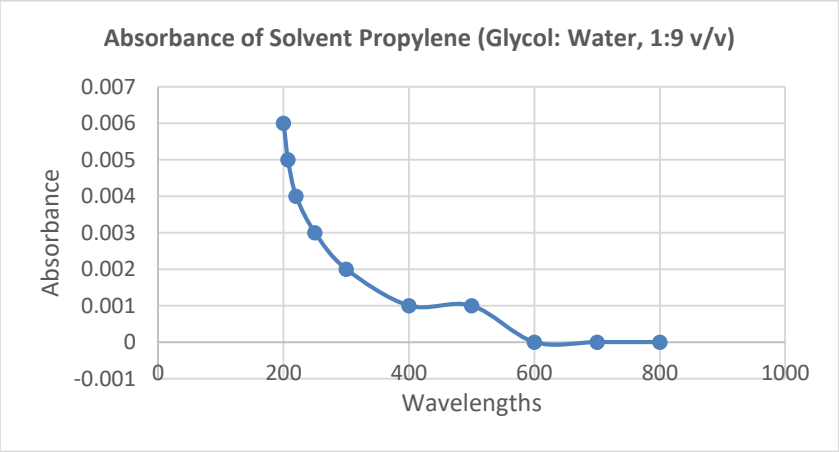


**Figure 4: UV- 4.2.5 LOD & LOQ Absorbance Values of Blank Solvent Across 200–800 nm**

### 4.2.5 LOD and LOQ

Ramipril has a Limit of Detection (LOD) of 0.59 µg/mL and a Limit of Quantification (LOQ) of 1.81 µg/mL.

### 4.2.6 Ruggedness

The ruggedness parameter was carried on both the analytes by changing the analyst and the instrument and %RSD was found to be less than 2%. Table 8 illustrates the ruggedness statistics.

**Table 8: Ruggedness (Change in Analyst and Change in Instrument) (*n=3).**

| **Concentration (µg/mL)** | **Ramipril (207 nm)** | | | **Ramipril (207 nm)** | | |
|---|---|---|---|---|---|---|
| | **Change in instrument** | | | **Change in Analyst** | | |
| **Ramipril** | **Ab.** | | | **Ab.** | | |
| **4** | 0.199 | 0.201 | 0.198 | 0.200 | 0.202 | 0.199 |
| **SD** | **0.0015** | | | **0.0015** | | |
| **%RSD** | **0.75** | | | **0.75** | | |
| **10** | 0.452 | 0.455 | 0.453 | 0.453 | 0.456 | 0.454 |
| **SD** | **0.0015** | | | **0.0015** | | |
| **%RSD** | **0.33** | | | **0.33** | | |
| **16** | 0.787 | 0.789 | 0.790 | 0.788 | 0.790 | 0.791 |
| **SD** | **0.0015** | | | **0.0015** | | |
| **%RSD** | **0.19** | | | **0.19** | | |

### 4.2.7 Robustness

The robustness parameter was carried out by a change in the wavelength for both analytes and %RSD was calculated and found to be less than 2%, hence the method was found to be robust. The robustness data is illustrated in Table 9**.**

**Table 9: Robustness (Change in Wavelength) (*n=3)**

| **Concentration (µg/ mL) Ramipril** | **Ramipril (205 nm)** | **Ramipril (207 nm)** | **Ramipril (209 nm)** |
|---|---|---|---|
| **4** | 0.198 | 0.199 | 0.197 |
| **SD** | 0.003 | 0.002 | 0.004 |
| **%RSD** | 0.152 | 1.00 | 2.03 |
| **10** | 0.452 | 0.453 | 0.451 |
| **SD** | 0.005 | 0.004 | 0.006 |
| **%RSD** | 1.11 | 0.88 | 1.33 |
| **16** | 0.787 | 0.788 | 0.785 |
| **SD** | 0.010 | 0.009 | 0.011 |
| **%RSD** | 1.27 | 1.14 | 1.40 |

### 4.2.7 Solvent and standard stock solution stability

After analyses of the fresh stock solution and the old standard stock solution for ten days, the %RSD for both analytes were determined to be less than 2%, indicating that the solvent and the standard stock solution were stable. The solution stability data are illustrated in Tables 10.

**Table 10: Solution stability (*n=3).**

| Concentration (µg/ mL) Ramipril | Ramipril (207 nm) | |
|---|---|---|
| | Fresh (Day 10) | Old (Day 1) |
| | Ab. | Ab. |
| **4** | 0.198 | 0.011 |
| **SD** | 0.002 | 0.002 |
| **%RSD** | 1.52 | 1 |
| **10** | 0.452 | 0.453 |
| **SD** | 0.004 | 0.004 |
| **%RSD** | 1.11 | 0.88 |
| **16** | 0.787 | 0.788 |
| **SD** | 0.009 | 0.009 |
| **%RSD** | 0.27 | 1.14 |

## 5. Discussion

The present study successfully developed and validated a straightforward, eco-friendly UV spectrophotometric method for the quantitative estimation of Ramipril in bulk and pharmaceutical formulations. Utilizing a solvent system of propylene glycol and distilled water in a 1:9 (v/v) ratio aligns with the principles of green analytical chemistry, minimizing the use of hazardous organic solvents and reducing environmental impact.

The method demonstrated a clear absorption maximum (λmax) at 207 nm, consistent with previously reported values for Ramipril, indicating the method's reliability in identifying the drug's characteristic absorbance peak. The calibration curve constructed over a concentration range of 4–16 µg/mL exhibited excellent linearity, with a correlation coefficient ($R^2$) approaching unity, confirming adherence to Beer-Lambert's law within this range.

Validation parameters, including accuracy, precision, specificity, and robustness, were assessed in accordance with ICH Q2(R1) guidelines. The method displayed high accuracy, with recovery studies yielding results within the acceptable range, and precision studies showed low relative standard deviation (RSD) values, indicating reproducibility. The specificity of the method was confirmed by the absence of interference from common excipients present in pharmaceutical formulations. Robustness tests, involving deliberate variations in analytical conditions, demonstrated the method's reliability under varied experimental parameters.

Compared to more complex analytical techniques, such as high-performance liquid chromatography (HPLC), this UV spectrophotometric method offers simplicity, cost-effectiveness, and rapid analysis, making it suitable for routine quality control in pharmaceutical settings. The adoption of a green solvent system further enhances the method's applicability by promoting safer laboratory practices and environmental sustainability.

## 6. Conclusion

In conclusion, the developed method provides a reliable, efficient, and environmentally conscious approach for the estimation of Ramipril, supporting its implementation in routine analytical and quality control laboratories.

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