**Ind. J. Pharm. Edu. Res., 2026; Krupapharmacon:207-219.**
https://www.ijper.org

Original Article

# Development and Validation of a New Stability Indicating Reversed Phase Ultra-Performance Liquid Chromatography Method for the Determination of Cinnarizine and Domperidone Fixed-Dose Combination

**Ravindra Ashritha*, Manandi Krishna Murthi Ranganath, Kedar Bharadwaj Nayak**

Department of Pharmaceutical Analysis, Krupanidhi College of Pharmacy, Carmelaram, Varthur Hobli, Sarjapur Road, Bengaluru, Karnataka, INDIA.

**ABSTRACT**

**Aim:** Vertigo, nausea, motion sickness and vomiting due to gastrointestinal and vestibular diseases are controlled by the Combination of Cinnarizine (CIN) and Domperidone (DOM). A rapid, stable and accurate RP-UPLC method was developed and validated for both medicines in the medicinal formulations. **Materials and Methods:** An ACQUITY UPLC HSS C18 column (100×2.1 mm, 1.8 µm) with eluate of 0.1% formic acid buffer and acetonitrile in 35:65 ratio, at injected flow of 0.3 mL/min for separation. The column was heated to 30ºC and the detection was made at 226 nm. **Results:** The two have been proven to retain for 1.170 and 1.574 min, respectively. The approach proved to have good accuracy, as %RSD of 0.8 for both medications. The recovery percentages of 99.82% and 99.50% for cinnarizine and domperidone, respectively, showed excellent accuracy. Limit of detection and Limit of quantification values for cinnarizine of 0.07 and 0.22, and domperidone of 0.02 and 0.05, respectively. The run time and retention time reductions indicated that the devised approach was easy to use, quick and cost-effective. **Conclusion:** For this reason, periodic quality control testing of these two medications in drug products can be readily accomplished with the adopted approach.

**Keywords:** Cinnarizine, Domperidone, Method validation, Pharmaceutical analysis, RP-UPLC.

**Correspondence:**
**Ms. Ravindra Ashritha**
Department of Pharmaceutical Analysis, Krupanidhi College of Pharmacy, Carmelaram, Varthur Hobli, Sarjapur Road, Bengaluru, Karnataka, INDIA.
Email: ashritharnaik2885@gmail.com

## INTRODUCTION

A derivative of piperazine, cinnarizine exhibits antihistaminic and antivertigo effects in addition to primarily inhibiting calcium channels.[1,2] Reducing vestibular stimulation and symptoms associated with balance issues can be achieved by improving inner ear blood circulation.[1] By inhibiting dopamine receptors in the chemoreceptor trigger zone, the selective dopamine $D_2$ receptor antagonist shows anti-vomiting properties.[2] It also improves gastrointestinal motility, which helps in the relief of nausea and vomiting.[2,3]

In pharmacological dose regimens, these two medications are frequently combined.[3] Reliable techniques are required to guarantee the quality, safety, and efficacy of these formulations due to medicinal significance.[4] Numerous testing methods for determining, either separately or in combination, have been documented.[4,5,9] Although, UV spectrophotometric techniques are affordable, they do not have sufficient specificity in the existence of contaminants.[5] For the concurrent assessment of these pharmaceutical preparations in dosage formulations and raw drug material, "(RP-HPLC) approaches are widely used.[6] But several of these techniques consume more solvent and have longer run durations.[6,7]

Ultra-Performance Liquid Chromatography (UPLC) has received a lot of interest due to recent developments in analytical procedures.[7] Faster isolation, better peak separation, and increased detectability are the outcomes of this technology, which uses columns filled with tiny particles (less than 2 µm) and runs at greater pressure.[7-10] Furthermore, when examined with the conventional HPLC method, UPLC techniques often use limited solvent and increase quantitative effectiveness.[4]

RP-HPLC and bioanalytical analysis for the concurrent quantification of two drugs in pharmaceutical formulations have been published in recent works.[3,6] Rapid and stability-indicating analytical techniques that can reduce analysis duration and improve effectiveness are still needed.[4]

**DOI:** 10.5530/ijper.krupapharmacon.38

**Copyright Information :**
Copyright Author (s) 2026 Distributed under Creative Commons CC-BY 4.0

**Publishing Partner :** Manuscript Technomedia. [www.mstechnomedia.com]

Therefore, the objective of this work was to develop and verify a quick, accurate, and stability-assessing RP-UPLC technique for the simultaneous analysis of two medicines in formulated goods.

## MATERIALS AND METHODS

### Research Design

The aim of the research was to establish the accurate and rapid rpHPLC method for simultaneous estimation of DOM and CIN in the marketed dosage form. Standard analytical evaluation criteria were used to validate the technique.

### Materials

The pharmaceutical grade Active Ingredients (APIs) for both medicines were used in the study. All analytical reagent grade materials such as acetonitrile, methanol and distilled water, as well as buffer components such as potassium dihydrogen orthophosphate and orthophosphoric acid obtained from Rankem.

### Instruments

Separation was performed on a Waters ACQUITY UPLC system consisting of a quaternary pump, autosampler and Tunable UV (TUV) detector, controlled by Empower 2 software. The auxiliary equipment consisted of a PG Instruments UV-visible Spectrophotometer (model T60) and software (UV Win 6), a pH meter (Labman), a digital balance (Sartorius) and an ultrasonic processor (Labman).

### Method

Diluent: Acetonitrile and water were mixed thoroughly and utilized as a diluent.

### Preparation of Standard Stock Solutions

To prepare primary stock of CNZ (200 ug/mL), 10 mg of the analyte was quantitatively transferred and diluted to the mark. A separate stock for DOM (150 ug/mL) was made with dissolving 7.5 mg of the medication in diluent, assisted by sonication, and then adjusting to a final volume of 50 mL.

### Standard working Solution

The working standard comprising 20 ug/mL of Cinnarizine and 15 ug/mL of Domperidone was produced through a secondary dilution. Specifically, 1 mL of CNZ stock and 0.6 mL of DOM stock was pipetted into a single 10 mL flask. Final volume was then adjusted using diluent.

### Sample Preparation

20 pills were ground into a fine powder after being weighed to find the average unit mass. A flask of 100 mL was quantitatively filled with an powder equal to the dosage of one tablet. The volume was reached by adding diluent of 75 mL and agitating mechanically. A membrane filter with a pore size of 0.45 µm was used to clarify this mixture.

### Method Validation

#### *System suitability parameters*

The system suitability parameters that were tested were injected with standard solutions of cinnarizine (20 ppm), domperidone (15 ppm) six times to measure the characteristics of system suitability, including peak tailing factor, resolution, and theoretical plate count. In the cases of repeat inoculations of the standard solution, the %RSD of the peak area was to be a maximum of 2%.

The **theoretical count** down of the plates (N) was calculated by the equation below:

$$N = 16\left(\frac{t_R}{W}\right)^2$$

where $t_R$ is the retention time of the analyte and W is the width of a peak at the bottom. The calculated plate count was found to be greater than 2000, indicating good column efficiency.

### Tailing Factor (T)

Used to measure peak symmetry in chromatography.

$$T = \frac{W_{0.05}}{2f}$$

Where:

$W_{0.05}$= width of the peak at 5% height

$f$= distance from peak maximum to the front side of the peak at 5% height

### Resolution (Rs)

Used to measure separation between two chromatographic peaks.

$$R_s = \frac{2(t_{R2} - t_{R1})}{W_1 + W_2}$$

Where:

$t_{R1}$= retention time of first peak

$t_{R2}$= retention time of second peak

$W_1$and $W_2$= widths of the two peaks

Generally:

**Rs ≥ 2** indicates good separation.

### Specificity

We tested specificity of novel approach via assessing potential influence from blank and placebo samples. Because no peaks appeared at the expected retention times for cinnarizine and domperidone, the method was deemed specific for these medications.

## Linearity

A range of concentrations, from 25% to 150% of the nominal concentration, were used to evaluate linearity. Duplicate injections were performed for six calibration levels of Cinnarizine (5-30µg/mL) and Domperidone (3.75-22.5 µg/mL). The $R^2$ achieved was 0.999 for two drugs.

## Accuracy

The spike recovery method prepared three levels of concentration of the accuracy samples. Each level of accuracy was administered by injections three times and the average recovery value was obtained as 99.82% and 99.50% of Cinnarizine, Domperidone.

## Precision

Precision was performed in terms of interday and intraday. Average peak response, SD and %RSD was performed with two drugs. % RSD obtained as 0.8% and 0.7% for Cinnarizine and Domperidone.

## Robustness

Small deliberate changes in method, like Flow rate, mobile phase ratio, and temperature, were made, but there were no recognised changes in the result and are within range as per ICH Guidelines.[11]

## LOD and LOQ

LOD and LOQ were calculated using the standard deviation of the response and the slope of the calibration curve obtained from the linearity study.[11] The following equations were used:

$$LOD=3.3\times(\sigma/S)$$

$$LOQ=10\times(\sigma / S)$$

Where:

σ = standard deviation of the response

S = slope of the calibration curve

## STATISTICAL ANALYSIS

The statistical treatment of validation data was conducted in accordance with ICH Q2(R1) guidelines. The following mathematical models were used to verify the precision and reliability of the method.

## Residual Standard Deviation (Sy/x)

$$Sy/x = \sqrt{[\ \Sigma(yi - \hat{y}i)^2 / (n - 2)\ ]}$$

Measures the spread of data points around the regression line. Lower value indicates better fit.

yi = experimental peak area

ŷi = predicted peak area from regression equation

n = number of samples

## Standard Error of the Slope (Sb)

$$Sb = Sy/x / \sqrt{[\ \Sigma(xi - \bar{x})^2\ ]}$$

Measures uncertainty in the slope of calibration curve.

xi = concentration

$\bar{x}$ = mean concentration

## 95% Confidence Interval (CI) for Slope

$$CI = Slope \pm (tcrit \times Sb)$$

Gives the range within which the true slope lies with 95% confidence.

tcrit = critical t-value based on $(n - 2)$ degrees of freedom.

## Degradation Studies

### *Oxidative Degradation*

Individual 1 mL aliquots of the drug stocks were treated with 1 mL of 20% $H_20_2$. Following a 60-min incubation at 60°C, the samples diluted to working concentrations (20 ug/mL and 15 ug/mL) and subjected to UPLC analysis via 1 uL injections to evaluate oxidative stability.[12]

## Acid and Alkaline Hydrolysis

To study hydrolytic stability, 1 mL of stock solution was reacted with 1 mL of either 2N HCl (acidic) or 2N NaOH (basic). Both mixtures were refluxed for 1 hr at 60°C. Post-treatment, the solutions were neutralized, diluted to the target concentration, and analysed chromatographically.

## Thermal and Photolytic Stress

The standard drug solution was evaluated by the dry heat degradation testing in an oven with constant temperature (60°C) in 1 hr. To determine photostability, solutions were incubated in a UV chamber over 7 days (or 200Watt-hours/$m^2$). The samples were then processed and introduced to the UPLC system after exposure to observe degradation peaks.

## Neutral Degradation Studies

Aqueous stress testing was done by keeping drug solution at 60°C in reflux. Aliquots were diluted after degradation to the necessary concentrations of analysis. 1 uL of the solution was then put into UPLC system and the elution profiles were observed to determine the stability of the drugs in a neutral environment.

# RESULTS

## Methods Development and Optimisation of RP-UPLC Method

The current experiment was to design a simple, fast, and dependable RP-UPLC technique of the simultaneous quantification of Cinnarizine and Domperidone in pharmaceutical dosage forms. During method development, several chromatographic parameters such as the mobile phase composition, stationary phase, flow rate, column temperature, and detection wavelength were carefully optimised to obtain good peak shape, proper resolution, and acceptable system suitability results.[13]

The UV absorption spectra of both drugs were studied to select an appropriate detection wavelength. Both Cinnarizine and Domperidone showed good absorbance at 226 nm, and therefore, this wavelength was selected for the analysis to ensure adequate sensitivity and accurate quantification.

## Column Selection

Selection of a suitable stationary phase is an important step in chromatographic method development. The separation of the analytes was performed well in different columns. The HSS C18 column (2.1×50 mm, 1.8 µm) was found to be the best column due to a better peak symmetry, good resolution, and increase in theoretical plate count. Hence, this column was selected for further analysis.[14]

## Mobile Phase Optimisation

Various organic solvents–aqueous phases were tried and tested to get proper separation of analytes. A series of ratios were first tried to determine their influence on the changes in the peak shape and in the retention. 0.1% formic acid and the acetonitrile was used in the ratio of 65:35(v/v) for the appropriate separation. The addition of formic acid in the aqueous phase helped to improve the peak shape and minimize peak the tailing.[15,16] This mobile phase provided clear and well-resolved peaks for both Cinnarizine and Domperidone.

## Optimized Chromatographic Conditions

Optimisation was done for the flow rate, column temperature and inoculation volume to achieve efficient separation. The separation of Cinnarizine and Domperidone was done by chromatography on ACQUITY UPLC HSS C18 column (100 mm×2.1 mm, 1.8 µm). The acetonitrile and 0.1% formic acid in a 65:35 (v/v) solution constituted the mobile phase. The temperature of the column were set at less than 30°C and flow rate of 0.3 mL/min. A PDA detector operating at 226 nm was used for detection. 1 µL was injected. Under these optimum conditions, both analytes showed good peak shape and peak resolution, and were sufficiently retained for the method to be suitable for analysis. The corresponding chromatogram is presented in Figure 1.

## Optimization of RP-UPLC Method

**Observation:** Cinnarizine and Domperidone were eluted at 1.170 min and 1.574 min, respectively with a good resolution. Tailing factor and plate count were very satisfactory and hence this method was optimised and proved.

## Methods Validation

### *System suitability parameters*

**Discussion:** Testing for system appropriateness showed that the approach was appropriate for its intended use. In particular, the peak symmetry (tailing factor) was <2 and the observed resolution was >2, both of which are in compliance with ICH requirements.

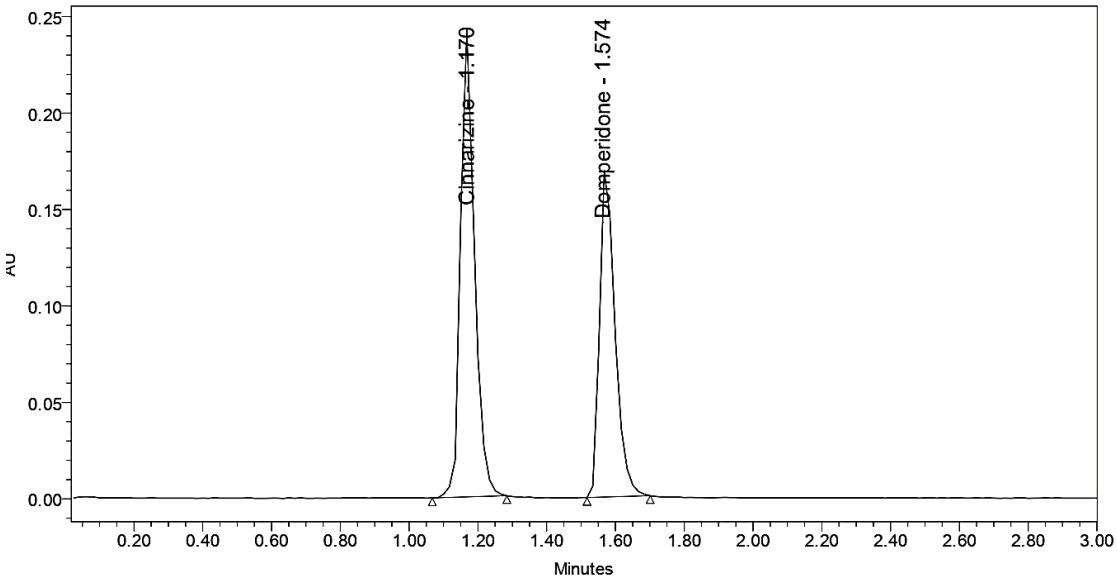


**Figure 1:** Optimized Chromatogram.

**Table 1: System suitability of cinnarizine and Domperidone.**

| Sl. No. | Cinnarizine | | | | Domperidone | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Inj | RT(min) | Plate Count | Tailing | Area | RT(min) | Plate Count | Tailing | Resolution | area |
| 1. | 1.161 | 3260 | 1.22 | 2870132 | 1.541 | 5055 | 1.37 | 4.3 | 1466274 |
| 2. | 1.164 | 2985 | 1.22 | 2810821 | 1.545 | 4824 | 1.20 | 4.3 | 1464786 |
| 3. | 1.165 | 3093 | 1.21 | 2847514 | 1.550 | 4903 | 1.24 | 4.5 | 1449829 |
| 4. | 1.165 | 3089 | 1.21 | 2831157 | 1.551 | 4538 | 1.27 | 4.4 | 1469813 |
| 5. | 1.165 | 3019 | 1.21 | 2841851 | 1.553 | 4489 | 1.28 | 4.4 | 1486351 |
| 6. | 1.170 | 3222 | 1.38 | 2813415 | 1.571 | 4870 | 1.34 | 4.6 | 1458277 |
| Avg | | | | 2835815 | | | | | 1465888 |
| Stdev | | | | 22356.7 | | | | | 12258.2 |
| RSD | | | | 0.8 | | | | | 0.8 |

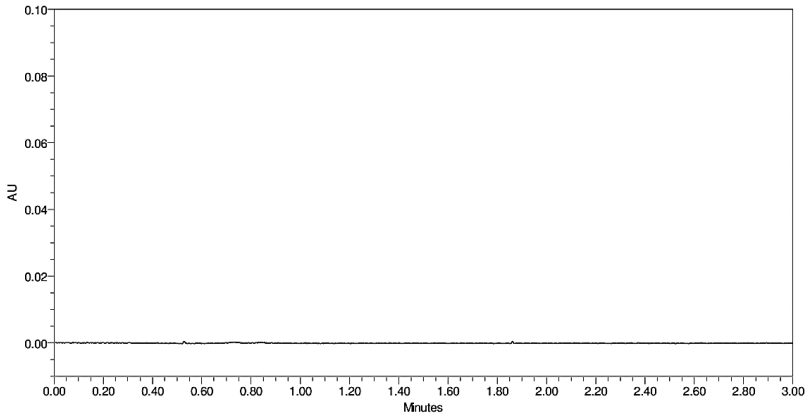


**Figure 2a:** Chromatogram of blank.

Additionally, the column efficiency was well within the defined validation limits, as evidenced by a plate count of more than 2000, as summarized in Table 1.[11]

## Specificity

## Discussion

DOM and CIN have retention times of 1.574 and 1.170 min respectively. With this approach, we could not find any interfering peaks in the blank and placebo at the medication retention periods, as shown in Figures 2a-2c. This way was therefore regarded as a special way.

## Linearity

## Discussion

The linearity of the analytical method for Cinnarizine and Domperidone was evaluated by analyzing six concentration levels in triplicate. As detailed in Table 2, the concentration ranges were 5-30 µg/mL for Cinnarizine and 3.75-22.5µg/mL for Domperidone. The resulting calibration curves, illustrated in Figures 3a, 3b, demonstrate a high degree of linearity.

This is further supported by the final regression statistics presented in Table 3, where the correlation coefficients ($R^2$) were found to be >0.999 for both analytes. To ensure mathematical reliability as per ICH Q2($R^1$) guidelines, the standard error of the slope and intercept was calculated. As shown in Table 3, the narrow 95% confidence intervals for the slopes confirm that the method is highly precise for quantification. Furthermore, the residual standard deviation was found to be minimal, indicating that the experimental data points are closely aligned with the regression line.

## Precision

### *Repeatability*

## Discussion

A total of six injections using the same volumetric flask of working standard solution resulted in the areas obtained as shown. The standard deviation, average area and the percentage RSD were calculated in the case of two medications. The RS was established to be 0.8% and 0.7% in cinnarizine and domperidone respectively, as shown in Table 4. This way, the system accuracy was transferred because the accuracy threshold was below "2."

## Intermediate precision

## Discussion

System precision was assessed by analyzing six replicate working solutions prepared from a single stock solution after 24 hr of storage. The calculated %RSD for the peak areas of domperidone and cinnarizine was 0.3% in both cases, as shown in Table 5 (Figures 4a, 4b). These results demonstrate excellent method repeatability, satisfying the ICH acceptance criterion of %RSD ≤ 2.0%.

## Accuracy

## Discussion

Three levels of accuracy of samples were obtained through the conventional addition procedure. All the levels of accuracy were carried out in three replicates and the avg of the percentage of cinnarizine and domperidone was obtained to be 99.82 and 99.50 respectively, as summarized in Tables 6-8.

## Sensitivity

## Robustness

## Discussion: Robustness Impact Analysis

The robustness was evaluated by making small, deliberate changes to the method parameters, as shown in Table 9. The impact of these variations is summarized:

- **Flow Rate Impact (± 0.1 mL/min):** As seen in the system suitability data, changing the flow rate caused a shift in retention times (tR). However, the Resolution (Rs>4.0) remained well above the ICH limit of 2.0. This indicates that minor pump fluctuations will not cause peak overlap, ensuring the method's reliability.
- **Temperature Impact (± 5°C):** Variations in column temperature showed no significant impact on the Tailing Factor (approximately 1.2) or peak areas. This proves the method is thermally rugged and suitable for different laboratory climates.

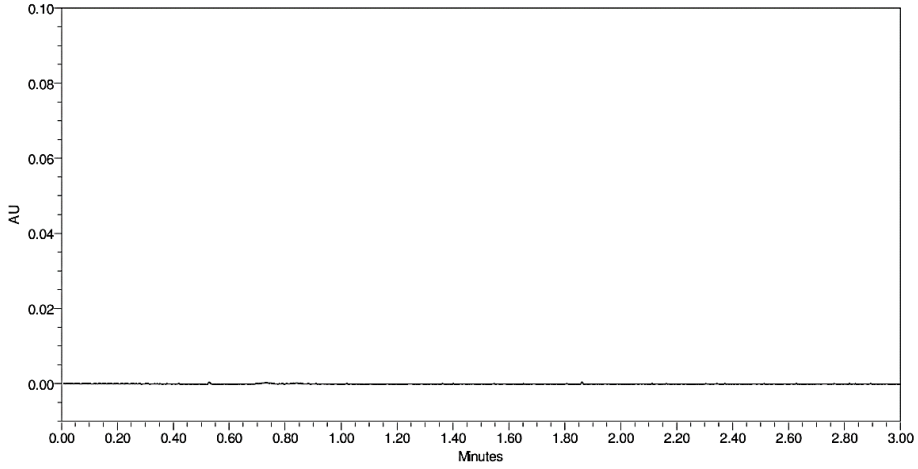


**Figure 2b:** Chromatogram of placebo.

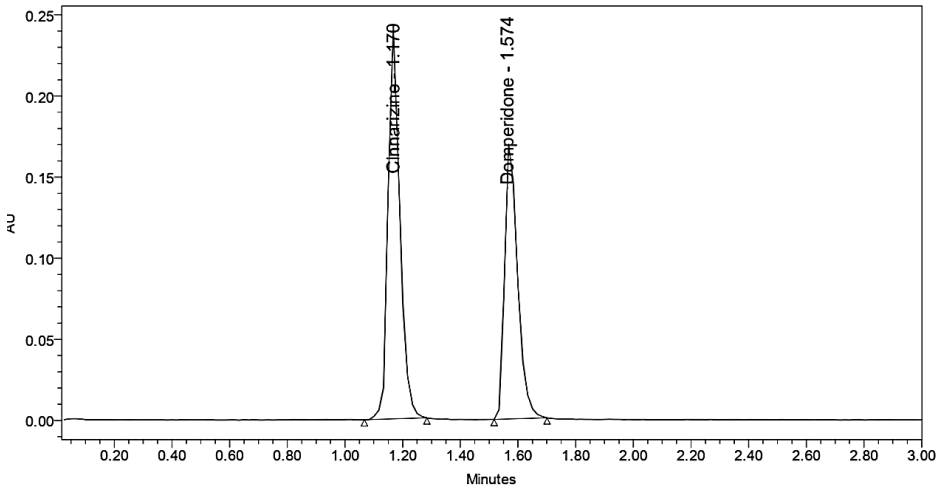


**Figure 2c:** Typical Chromatogram.

**Table 2: Linearity Table for Cinnarizine and Domperidone.**

| Cinnarizine | | Domperidone | |
|---|---|---|---|
| Conc (µg/mL) | Peak area | Conc (µg/mL) | Peak area |
| 0 | 0 | 0 | 0 |
| 5 | 710255 | 3.75 | 367159 |
| 10 | 1430801 | 7.5 | 744101 |
| 15 | 2115415 | 11.25 | 1069679 |
| 20 | 2801018 | 15 | 1467979 |
| 25 | 3546050 | 18.75 | 1825717 |
| 30 | 4138731 | 22.5 | 2130522 |

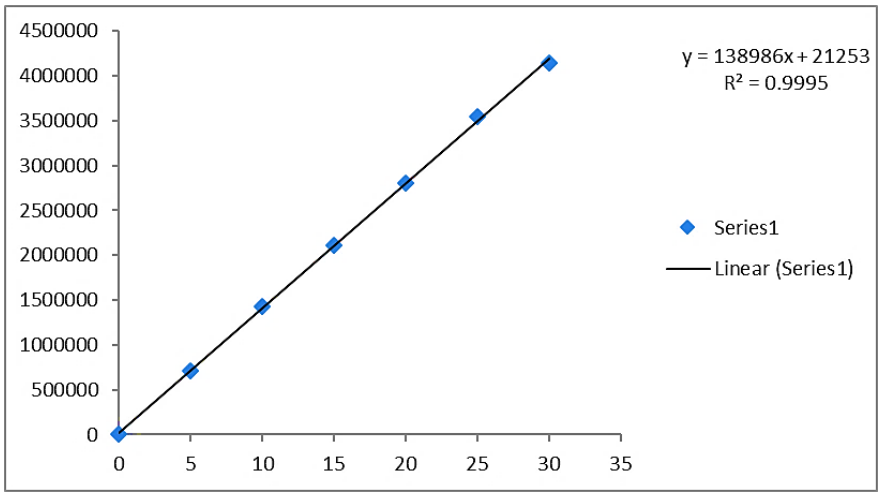


**Figure 3a:** Calibration curve of Cinnarizine.

**Table 3: Final Regression Statistics for Cinnarizine and Domperidone.**

| Statistical Parameter | Cinnarizine | Domperidone |
|---|---|---|
| Linearity Range (µg/ml) | 5 - 30 | 3.75 – 22.5 |
| Regression Equation | y = 138986x + 21253 | y = 95548x + 11534 |
| Slope (m) | 138985.7 | 95548.2 |
| Intercept (c) | 21252.9 | 11533.9 |
| Std. Error of Slope | 1330.05 | 1166.75 |
| Std. Error of Intercept | 23977.84 | 15775.47 |
| 95% Confidence Interval (Slope) | 135567, 142405 | 92549, 98547 |
| Correlation Coefficient ($R^2$) | 0.9995 | 0.9993 |

- **Mobile Phase Impact (± 2% Organic):** Minor errors in mobile phase preparation did not lead to co-elution with degradation products. The stability-indicating nature of the method remained intact, with %RSD values <2.0%, confirming high reproducibility.

## Assay

Label claim containing Cinnarizine 20 mg and Domperidone 15 mg. The assay was calculated and found to be 99.16% and 99.84%, as shown in Table 10 and Figures 5.1 and 5.2.

# DEGRADATION

## Degradation Studies

Degradation research was done with the formulation and the degraded samples were inoculated. The limits of degradation were met in all the injected samples after the assay was established.

## Degradation Pathway

**1. Hydrolytic Degradation Pathways (Acid and Base)**

Both drugs showed vulnerability to pH-induced stress.

**Acidic Hydrolysis:** Cinnarizine degraded by 6.24% and Domperidone by 4.06% in 2N HCl. The higher degradation in acid suggests that the piperazine and benzimidazole linkages are more sensitive to protonation and subsequent cleavage.

**Alkaline Hydrolysis:** Degradation was slightly lower in 2N NaOH (5.03% and 4.48%).

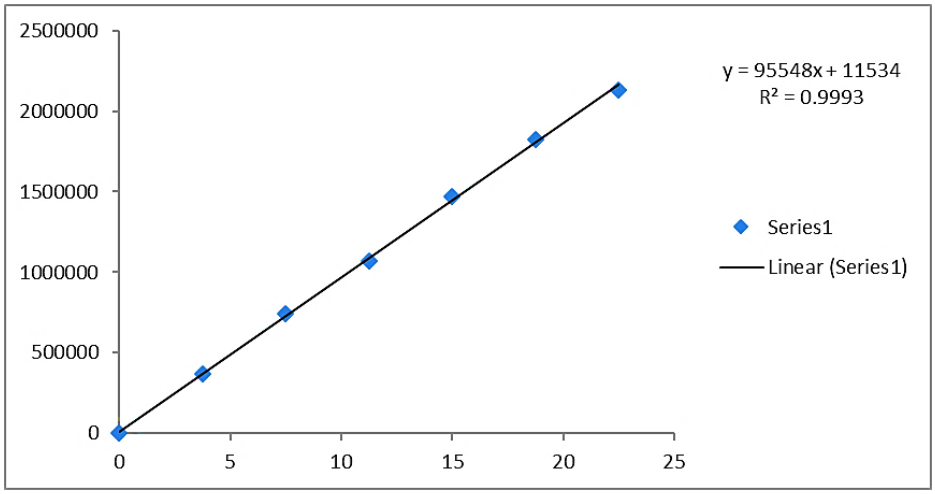


**Figure 3b:** Calibration curve of Domperidone.

**Table 4: Repeatability Table of Cinnarizine and Domperidone.**

| Sl. No. | Area of Cinnarizine | Area of Domperidone |
|---|---|---|
| 1. | 2816985 | 1449947 |
| 2. | 2779038 | 1478222 |
| 3. | 2829838 | 1457112 |
| 4. | 2815374 | 1474179 |
| 5. | 2782355 | 1467164 |
| 6. | 2824144 | 1462987 |
| Mean | 2807956 | 1464935 |
| S.D | 21767.3 | 10550.8 |
| %RSD | 0.8 | 0.7 |

**Table 5: Intermediate precision Table of Cinnarizine and Domperidone.**

| Sl. No. | Area of Cinnarizine | Area of Domperidone |
|---|---|---|
| 1. | 2731304 | 2731304 |
| 2. | 2723576 | 2723576 |
| 3. | 2708549 | 2708549 |
| 4. | 2716273 | 2716273 |
| 5. | 2719885 | 2719885 |
| 6. | 2725275 | 2725275 |
| Mean | 2720810 | 2720810 |
| S.D | 7867.4 | 7867.4 |
| %RSD | 0.3 | 0.3 |

The degradation likely involves the hydrolytic cleavage of amide or amine-alkyl bonds. The Acid chromatogram and Base chromatogram provide chromatographic evidence that while the parent drug concentration decreased, no interfering peaks elute at the same retention times (1.170 min and 1.574 min).

**2. Oxidative Degradation Pathway**

This was the most significant pathway for both drugs. Cinnarizine showed the highest degradation at 6.64%, and Domperidone at 4.87%. A distinct degradation product peak (impurity) is observed at approximately 1.395 min. The presence of a clear impurity peak (DP1) that is baseline-resolved from the APIs confirms the stability-indicating nature of the method.

**3. Thermal Degradation Pathway**

Thermal stress (60°C for 1 hr) resulted in 4.81% degradation for Cinnarizine and 4.05% for Domperidone.

**4. UV and Water Stability**

**UV:** The drugs showed minimal degradation under UV light (2.63% and 1.23%). This indicates the molecules have a stable chromophore that does not easily undergo photo-excitation or cleavage under the tested conditions.

**Neutral (Water):** The drugs were most stable in water, with degradation below 1% (0.33% and 0.43%). This confirms that the drugs are stable in neutral aqueous environments at 60°C.

**Discussion:** The stability-indicating nature of the developed method is confirmed through the chromatographic evidence presented in Table 11 and Figures 6.1-6.6. Under all forced degradation conditions, the peaks for cinnarizine and Domperidone remained baseline-resolved from degradation products". For instance, in the peroxide stress trail (Fig. 6.3), a degradation peak eluting at 1.395 min was clearly separated from the API peaks. Furthermore, the peak symmetry and retention times remained constant across the study, ensuring that the qualification of the formulation is not compromised by the presence of stress-induced impurities.

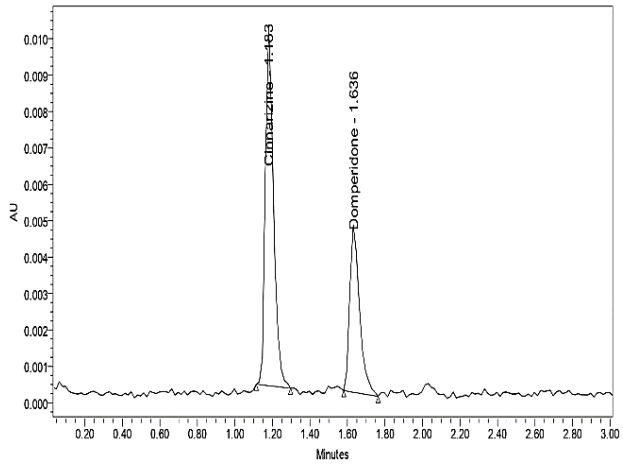


**Figure 4a:** LOD Chromatogram of Standard.

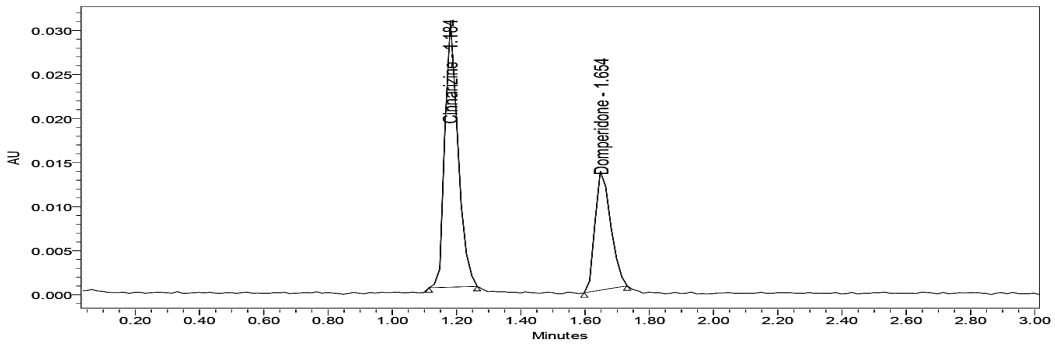


**Figure 4b:** LOQ Chromatogram of Standard.

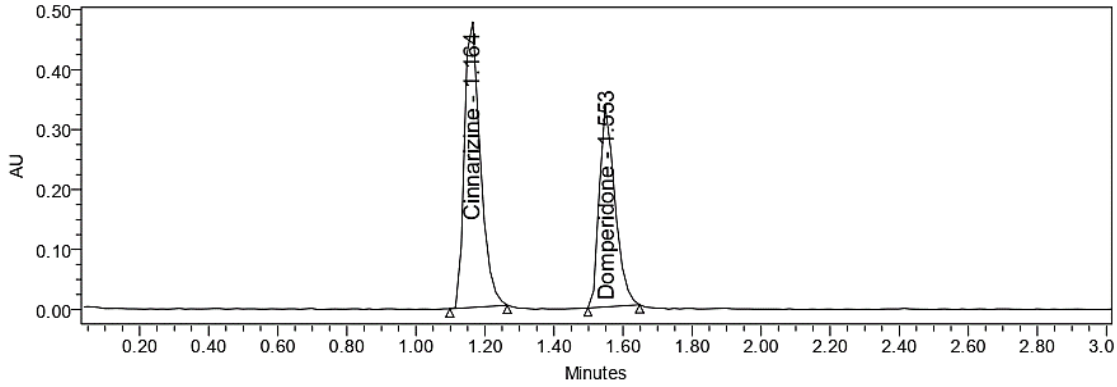


**Figure 5.1:** Chromatogram of working standard.

**Table 6: Accuracy Table of Cinnarizine.**

| % Level | Amount Spiked (µg/mL) | Amount recovered (µg/mL) | % Recovery | Mean %Recovery |
|---|---|---|---|---|
| 50% | 10 | 9.846 | 98.46 | 99.82% |
| | 10 | 9.958 | 99.58 | |
| | 10 | 9.956 | 99.56 | |
| 100% | 20 | 20.049 | 100.24 | |
| | 20 | 19.734 | 98.67 | |
| | 20 | 20.016 | 100.08 | |
| 150% | 30 | 30.239 | 100.80 | |
| | 30 | 30.173 | 100.58 | |
| | 30 | 30.122 | 100.41 | |

**Table 7:** **Accuracy Table of Domperidone.**

| % Level | Amount Spiked (µg/mL) | Amount recovered (µg/mL) | % Recovery | Mean %Recovery |
|---|---|---|---|---|
| 50% | 7.5 | 7.416 | 98.88 | 99.50% |
| | 7.5 | 7.545 | 100.61 | |
| | 7.5 | 7.529 | 100.38 | |
| 100% | 15 | 14.749 | 98.33 | |
| | 15 | 14.862 | 99.08 | |
| | 15 | 14.873 | 99.15 | |
| 150% | 22.5 | 22.418 | 99.64 | |
| | 22.5 | 22.459 | 99.82 | |
| | 22.5 | 22.418 | 99.63 | |

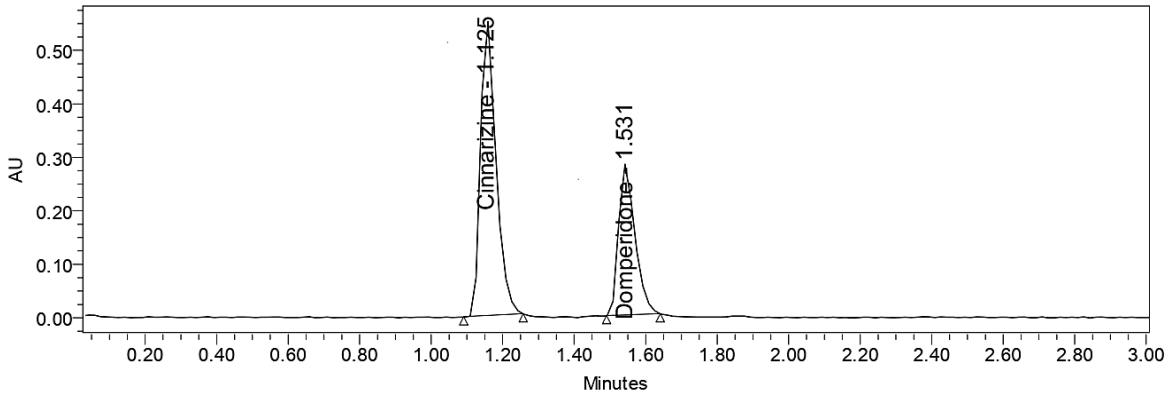


**Figure 5.2:** Chromatogram of working sample solution.

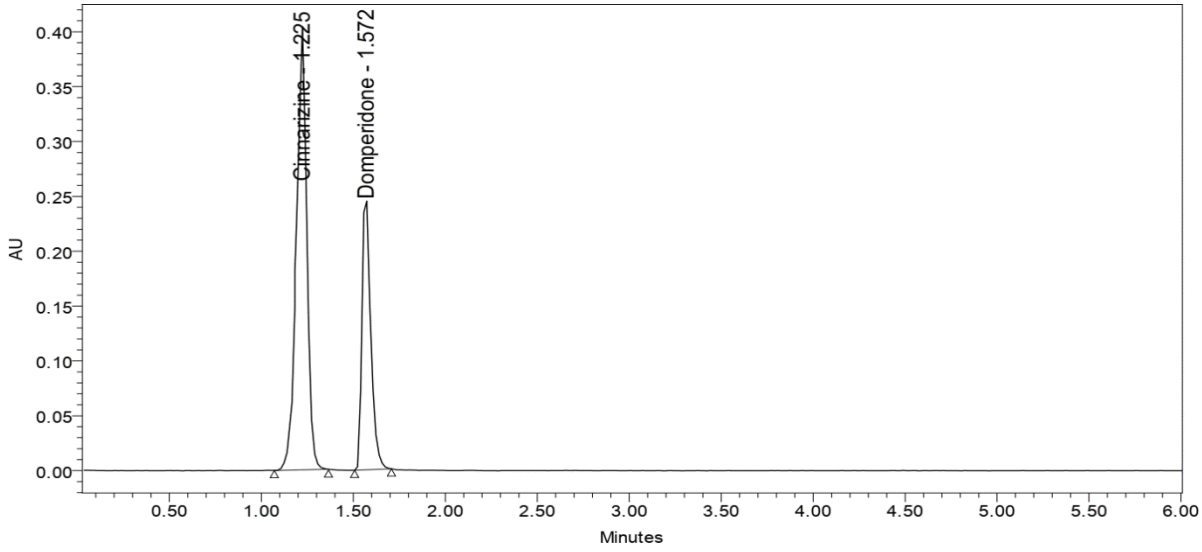


**Figure 6.1:** Acid chromatogram of Cinnarizine and Domperidone.

**Table 8:** **Sensitivity Table of Cinnarizine and Domperidone.**

| Molecule | LOD | LOQ |
|---|---|---|
| Cinnarizine | 0.07 | 0.22 |
| Domperidone | 0.02 | 0.05 |

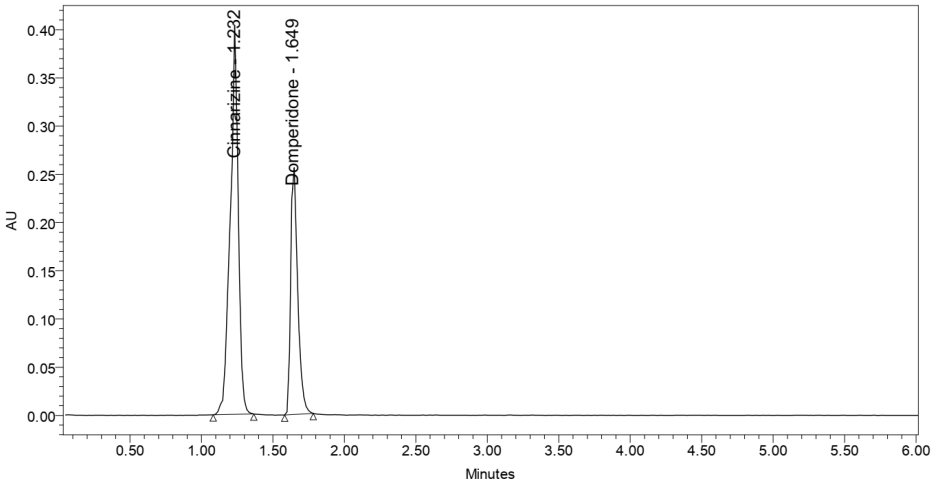


**Figure 6.2:** Base chromatogram of Cinnarizine and Domperidone.

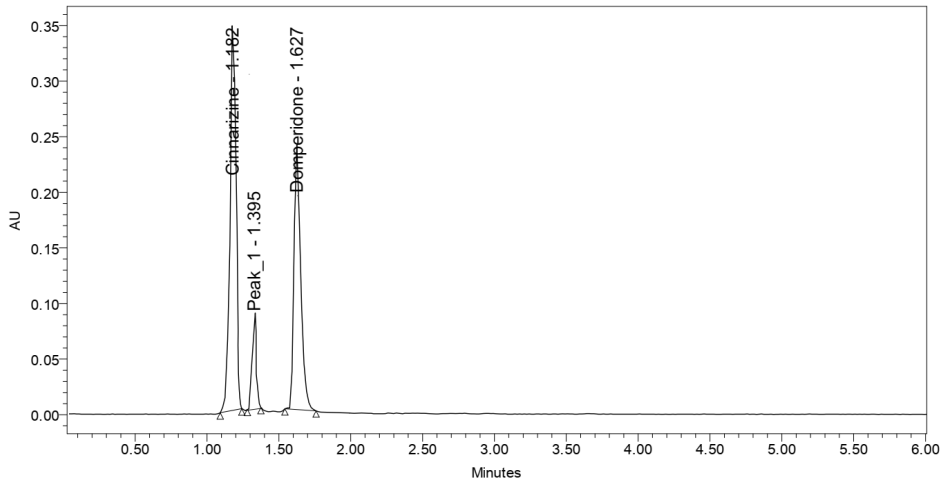


**Figure 6.3:** Peroxide chromatogram of Cinnarizine and Domperidone.

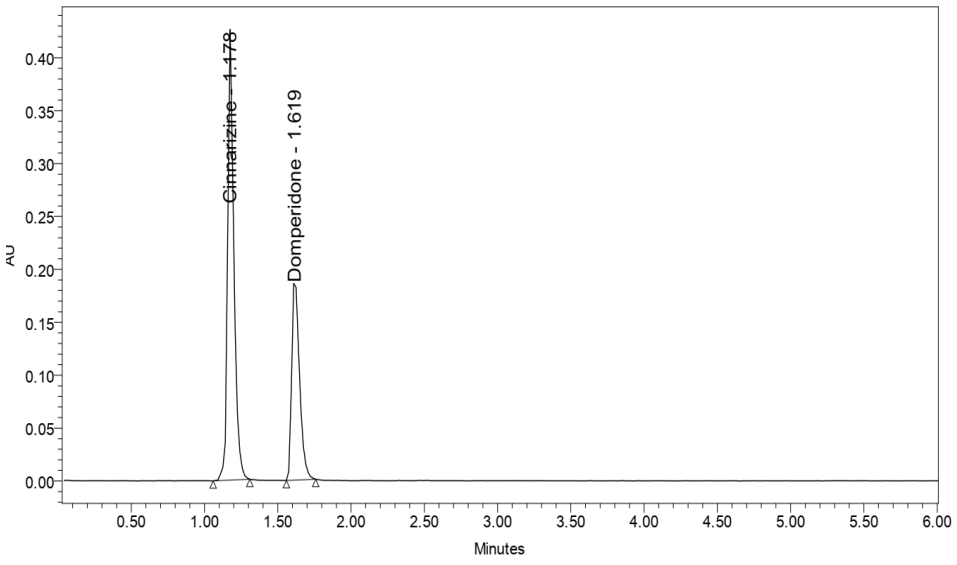


**Figure 6.4:** Thermal chromatogram of Cinnarizine and Domperidone.

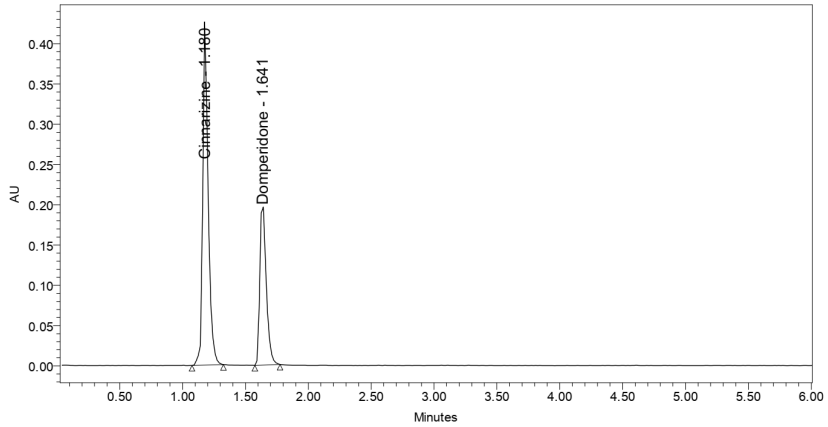


**Figure 6.5:** UV chromatogram of Cinnarizine and Domperidone.

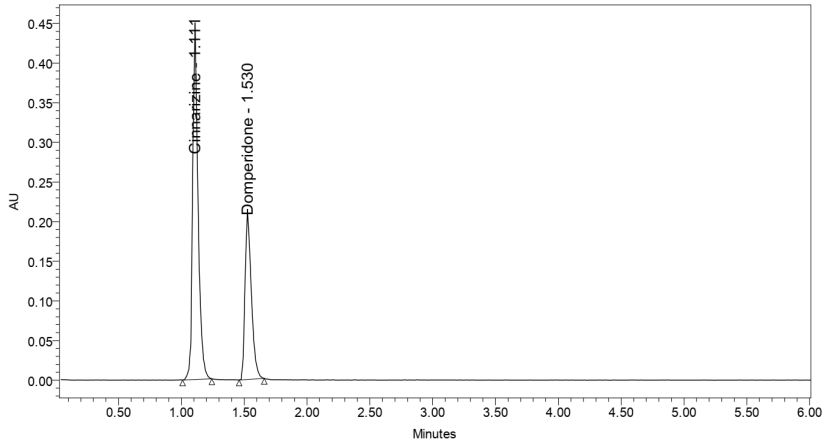


**Figure 6.6:** Water chromatogram of Cinnarizine and Domperidone.

**Table 9: Robustness data for Cinnarizine and Domperidone.**

| Sl. No. | Condition | %RSD of Cinnarizine | %RSD of Domperidone |
|---|---|---|---|
| 1. | Flow rate (-) 0.2 mL/min | 1.0 | 0.6 |
| 2. | Flow rate (+) 0.4 mL/min | 0.8 | 0.5 |
| 3. | Mobile phase (-) 60B:40A | 1.1 | 1.6 |
| 4. | Mobile phase (+) 70B:30A | 0.9 | 0.6 |
| 5. | Temperature (-) 25°C | 0.4 | 1.0 |
| 6. | Temperature (+) 35°C | 1.2 | 0.3 |

**Table 10: Assay Data of Domperidone and Cinnarizine.**

| Sl. No. | % Assay of Cinnarizine | % Assay Domperidone |
|---|---|---|
| 1. | 99.48 | 98.81 |
| 2. | 98.14 | 100.74 |
| 3. | 99.93 | 99.30 |
| 4. | 99.42 | 100.47 |
| 5. | 98.25 | 99.99 |
| 6. | 99.73 | 99.70 |
| Avg | 99.16 | 99.84 |
| Stdev | 0.769 | 0.72 |
| %RSD | 0.8 | 0.7 |

**Table 11: Degradation Data of Cinnarizine and Domperidone.**

| Type of degradation | Cinnarizine | | | Domperidone | | |
|---|---|---|---|---|---|---|
| | Area | %Recovered | % Degraded | Area | %Recovered | % Degraded |
| Acid | 2661564 | 93.76 | 6.24 | 1407832 | 95.94 | 4.06 |
| Base | 2695892 | 94.97 | 5.03 | 1401664 | 95.52 | 4.48 |
| Peroxide | 2650213 | 93.36 | 6.64 | 1395950 | 95.13 | 4.87 |
| Thermal | 2702072 | 95.19 | 4.81 | 1407953 | 95.95 | 4.05 |
| UV | 2763949 | 97.37 | 2.63 | 1449259 | 98.77 | 1.23 |
| Water | 2829218 | 99.67 | 0.33 | 1461011 | 99.57 | 0.43 |

## CONCLUSION

As it turned out, domperidone retention time was 1.574 and cinnarizine was 1.170 min respectively. It was found that domperidone and cinnarizine had standard percentage RSD of 0.8 and 0.8. In the case of domperidone and cinnarizine, recovery rates had been 99.50 and 99.82, respectively. Regression equations of cinnarizine and domperidone yield LOD values and LOQ values of 0.07, 0.22, and 0.02, and 0.05, respectively. y = 138986x + 21253 and y = 95548x + 11534 are the regression equations. This new method was simple and economical and can be applied in the daily quality control testing in industries because the retention times and run time were shorter.

## ACKNOWLEDGEMENT

The Department of Pharmaceutical Analysis and the Principal of Krupanidhi College of Pharmacy are acknowledged by the authors for their assistance in carrying out this study. For this study, no outside money was obtained.

## ABBREVIATIONS

**API:** Active Pharmaceutical Ingredients; **CIN:** Cinnarizine; **CNZ:** Cinnarizine; **DOM:** Domperidone; **HSS:** High Strength Silica; **ICH:** International Council for Harmonisation; **LOD:** Limit of Detection; **LOQ:** Limit of Quantification; **PDA:** Photodiode Array; **ppm:** parts per million; **RP-HPLC:** Reversed-Phase High-Performance Liquid Chromatography; **RP-UPLC:** Reversed-Phase Ultra-Performance Liquid Chromatography; **RSD:** Relative Standard Deviation; **SD:** Standard Deviation; **TUV:** Tunable UV; **UPLC:** Ultra-Performance Liquid Chromatography.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## SUMMARY

The method was proven brilliantly accurate, precise, linear and resilient after its validation in obedience with ICH standards. The fact that the proposed method can detect the presence of degradation products explained the appropriateness of the method in stability analysis. As such, the approach may be effectively applied in the daily quality check research of these drugs in pharmaceutical preparations.

## REFERENCES

1. Vij M, Dand N, Kumar L, Ankalgi A, Wadhwa P, Alshehri S, *et al.* RP-HPLC-based bioanalytical approach for simultaneous quantitation of cinnarizine and domperidone in rat plasma. Separations. 2023;10(3):159.
2. Vedashri JN, Veerapur VP, Rajeev S, Puttaraju R, Nagashree S, Prashanthi D, *et al.* A validated RP-HPLC method for the estimation of cinnarizine in tablet formulation: evaluation of intrinsic stability and greenness matrices. Future J Pharm Sci. 2025;11:131.
3. Dey P, Kalpana K, Katiyar P, Gupta N, Kurella KK, Ranjan R, *et al.* Analytical method development and validation for simultaneous estimation of domperidone and cinnarizine by RP-HPLC. J Cardiovasc Dis Res. 2023;14(11).
4. Goswami A, Rahman SNR, Pawde DM, Shunmugaperumal T. Analytical quality-by-design-driven RP-HPLC method conditions for concomitant determination of cinnarizine and morin hydrate. J AOAC Int. 2023;106(5):1154-64.
5. Jayaseelan S, Kannappan N, Ganesan V. Chemometric-assisted RP-HPLC method development for simultaneous determination of cinnarizine in pharmaceutical dosage forms. Int J Life Sci Pharma Res. 2022;12(1):L67-L78.
6. Edrees FH, Saad AS, Alsaadi MT, Amin NH, Abdelwahab NS. Experimentally designed chromatographic method for simultaneous analysis of dimenhydrinate, cinnarizine and their toxic impurities. RSC Adv. 2021;11:1450-60.
7. Shailaja G, Sai Kiran G, Ramana DV. Analytical method development and validation for simultaneous estimation of rabeprazole and domperidone by RP-HPLC. Int J Pharm Anal Res. 2024;13(4):454-62.
8. Cheke SN, Jadhav PS. Ultra Performance Liquid Chromatography (UPLC): A review. *world J Pharm Sci*. 2021;9(7):25-30.
9. Barakat NT, El-Brashy AM, Fathy ME. Green analytical quality-by-design RP-HPLC technique with fluorimetric detection for simultaneous assay of cinnarizine and domperidone. *R Soc Open Sci*. 2024;11(7):240829.
10. Gupta MK, Singh R, Sharma P. Comparative review of High-Performance Liquid Chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC) and High-Performance Thin-Layer Chromatography (HPTLC) with current updates. *Curr Issues Pharm Med Sci*. 2022;35(4):224-28.
11. International Council for Harmonisation (ICH). ICH Q2(R1): Validation of analytical procedures: Text and methodology. Geneva: ICH; 2005.
12. International Council for Harmonisation (ICH). ICH Q1A(R2): Stability testing of new drug substances and products. Geneva: ICH; 2003.
13. Snyder LR, Kirkland JJ, Dolan JW. Practical HPLC method development and optimization strategies for chromatographic separation. J Chromatogr A. 2020; 1612:460658.
14. Swartz ME. UPLC: an introduction and review of current technology. LC GC North Am. 2021;39(6):234-41.
15. Kazakevich Y, LoBrutto R. Influence of mobile phase composition on chromatographic peak shape and retention in reversed-phase liquid chromatography. J Chromatogr A. 2020; 1617:460824.
16. Abdelrahman MM, Abdelaleem EA, Abdelwahab NS. Stability-indicating chromatographic determination of domperidone in pharmaceutical formulations. J Chromatogr Sci. 2021;59(9):830-37.

**Cite this article:** Ashritha R, Ranganath MKM, Nayak KB. Development and Validation of a New Stability Indicating Reversed Phase Ultra-Performance Liquid Chromatography Method for the Determination of Cinnarizine and Domperidone Fixed-Dose Combination. Indian J of Pharmaceutical Education and Research. Krupapharmacon 2026:207-19.