International Journal of Pharmacy and Analytical Research (IJPAR)

IJPAR |Vol.15 | Issue 1 | Jan - Mar -2026

www.ijpar.com

DOI : https://doi.org/10.61096/ijpar.v15.iss1.2026.250-258

ISSN: 2320-2831

Review

Comprehensive Stability-Indicating RP-HPLC Assay of Candesartan: Method Development, Validation and Degradation Kinetics

Muskan Khanum*, Priyanka. K[1], G. Bhavani[2], M. Bhaskar[3], K. Srivani[4], N. Sandhya Rani[5]

Smt. Sarojini Ramulamma College of Pharmacy, Seshadrinagar, Mahabubnagar, Telangana – 509001, India

*Author for Correspondence: Muskan Khanum
Email: teelavath@gmail.com

Published on: 24.02.2026

Published by: Futuristic Publications

Abstract

A simple isocratic reverse-phase HPLC (RP-HPLC) method was developed and validated for quantitative estimation of candesartan with demonstrated stability-indicating capability under forced degradation. Chromatographic separation was achieved on a C18 column (250 × 4.6 mm, 5 µm) using acetonitrile:0.02 M KH_2PO_4 buffer (70:30, v/v; pH 3.5 ± 0.1) at 1.0 mL/min with UV detection at 254 nm. Candesartan eluted at approximately 4.2 min with good peak symmetry. The method was linear over 2–40 µg/mL (r^2 = 0.9994), accurate (mean recovery 99.10–100.33%) and precise (intra-/inter-day % RSD ≤ 0.85%). Limits of detection and quantitation were approximately 0.2 and 0.6 µg/mL, respectively. Robustness testing showed no significant impact on assay or system suitability upon small deliberate changes in flow rate, organic composition and wavelength. Forced degradation under acidic, alkaline and oxidative conditions produced appreciable degradation, while neutral hydrolysis, thermal and photolytic stress resulted in comparatively minor changes. Kinetic evaluation suggested apparent first-order behaviour under selected acidic and oxidative stress with estimated rate constants of 2.32 × 10^{-3} min^{-1} (acid, 60 °C) and 2.98 × 10^{-3} min^{-1} (oxidation, RT).

Keywords: Candesartan; RP-HPLC; stability-indicating method; method validation; forced degradation; degradation kinetics; ICH.

INTRODUCTION

Candesartan cilexetil is a prodrug angiotensin II receptor blocker widely used in the management of hypertension and heart failure. Given the susceptibility of many drug substances to hydrolytic and oxidative degradation, a validated stability-indicating method is necessary for routine quality control and for understanding degradation pathways during formulation development and stability studies. Regulatory expectations for stress testing and analytical method validation are defined in the International Council for Harmonisation (ICH) guidance, particularly ICH Q1A(R2) for stability testing and stress studies and ICH Q2(R1) for validation of analytical procedures.

Several spectrophotometric, HPLC and UPLC methods have been developed for candesartan and candesartan cilexetil in bulk drug, dosage forms and biological matrices [1–5]. A subset of these are explicitly stability-indicating, particularly those focused on impurity profiling or analysis in fixed-dose combinations [1–2, 4]. Nevertheless, many reported procedures involve gradient elution, specialised columns or relatively complex mobile phases, which may limit their direct adoption in resource-constrained or teaching laboratories.

There is therefore a practical need for a simple, isocratic RP-HPLC method for candesartan that uses readily available reagents, a conventional C18 column and moderate run times, while still meeting ICH expectations for stability-indicating capability and full method validation. Integrating forced degradation and basic degradation kinetic evaluation within this method would further enhance its utility, providing a coherent analytical framework for candesartan-containing products.

The present work aimed to develop a straightforward, isocratic Stability-Indicating RP-HPLC Assay of Candesartan using conventional equipment and readily available reagents, validate it for assay applications, and demonstrate its stability-indicating performance with forced degradation and kinetic evaluation under selected stress conditions.

MATERIALS AND METHODS

The study employed a conventional HPLC system with UV detection and standard laboratory instrumentation for solution preparation and stress studies. Key instrumentation is summarised in Table 1.

Table 1: Instrumentation Used in the Study

S. No.	Instrument	Model/Make	Purpose
1	HPLC system with UV	Shimadzu LC-20AD	Chromatographic analysis
2	RP-HPLC column, C18, 250 × 4.6 mm, 5 µm	Inertsil ODS-3 or equivalent	Separation of candesartan
3	Analytical balance (0.1 mg)	Shimadzu AY220 or equivalent	Accurate weighing of standards and samples
4	Ultrasonic bath	PCI / Microclean	Dissolution and degassing of solutions
5	pH meter with glass electrode	Eutech / Thermo	Measurement and adjustment of buffer pH
6	Stability chamber	Thermo / Equivalent	Controlled temperature–humidity storage and stress studies
7	Hot air oven	—	Dry-heat degradation experiments

Chromatographic conditions were optimised to provide a sharp, symmetric peak with adequate retention and reproducibility. The final method conditions are summarised in Table 2.

Table 2: Optimised Chromatographic Parameters for Candesartan

Parameter	**Condition**
Column	C18, 250 × 4.6 mm, 5 µm
Mobile phase	Acetonitrile : 0.02 M KH_2PO_4 buffer (70:30, v/v)
Buffer pH	3.5 ± 0.1 (orthophosphoric acid)
Flow rate	1.0 mL/min
Detection wavelength	254 nm
Column temperature	30 °C
Injection volume	20 µL
Run time	10 min

Standard and sample solutions were prepared using the mobile phase as diluent. Method validation was performed in line with ICH Q2(R1), including assessment of system suitability, specificity, linearity, accuracy, precision, sensitivity (LOD/LOQ) and robustness. Forced degradation studies were conducted under acidic, alkaline, oxidative, neutral, thermal and photolytic conditions in accordance with ICH Q1A(R2).

METHOD DEVELOPMENT AND OPTIMISATION

Representative method-development trials explored organic solvent choice, buffer inclusion and pH control to improve peak shape and retention-time reproducibility. The selected condition used acetonitrile with phosphate buffer at acidic pH, which provided high efficiency and near-ideal peak symmetry (Table 3).

Table 3: Representative Method-Development Trials for Candesartan

Trial	**Mobile phase (organic : aqueous)**	**Buffer pH**	**Rt (min)**	**Tailing factor**	**Remarks**
T1	MeOH : Water (60:40)	-	6.5	1.6	Broad, tailing peak; long run time
T2	ACN : Water (60:40)	-	5.8	1.4	Improved shape but variable retention
T3	ACN :	4.5	5.0	1.3	Better

	Phosphate buffer (60:40)				efficiency; peak slightly broad
T4	ACN : Phosphate buffer (70:30)	4.0	4.4	1.2	Good peak shape; minor variability
T5	ACN : Phosphate buffer (70:30)	3.5	4.2	1.1	Sharp, symmetric peak; selected

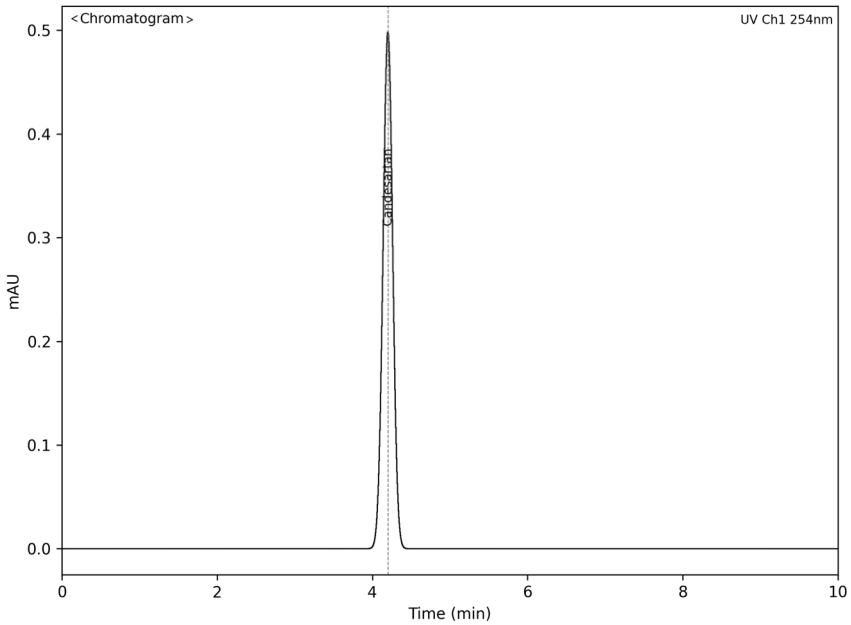
System suitability was verified with six replicate injections of a 20 µg/mL working standard to ensure adequate performance at the start of analytical sequences (Table 4).

Table 4: System-Suitability Parameters for Candesartan (n = 6)

Parameter	**Mean ± SD**	**%RSD**	**Acceptance criterion**
Retention time (min)	4.20 ± 0.03	0.71	—
Theoretical plates (N)	6500 ± 180	2.77	N ≥ 2000
Tailing factor (T)	1.10 ± 0.03	2.73	T ≤ 2.0
Peak area	420000 ± 2500	0.60	%RSD ≤ 2.0

Under the final chromatographic conditions, candesartan produced a single well-resolved peak at approximately 4.2 min, consistent with stable retention and minimal interference from the diluent or matrix. A representative standard chromatogram is shown in Figure 1.

Figure 1: Typical chromatogram of standard Candesartan



CHAPTER 5: METHOD VALIDATION RESULTS

Linearity was established across six concentration levels (2–40 µg/mL). Peak area exhibited a strong linear relationship with concentration, supporting quantitation across the specified range (Tables 5 and 6).

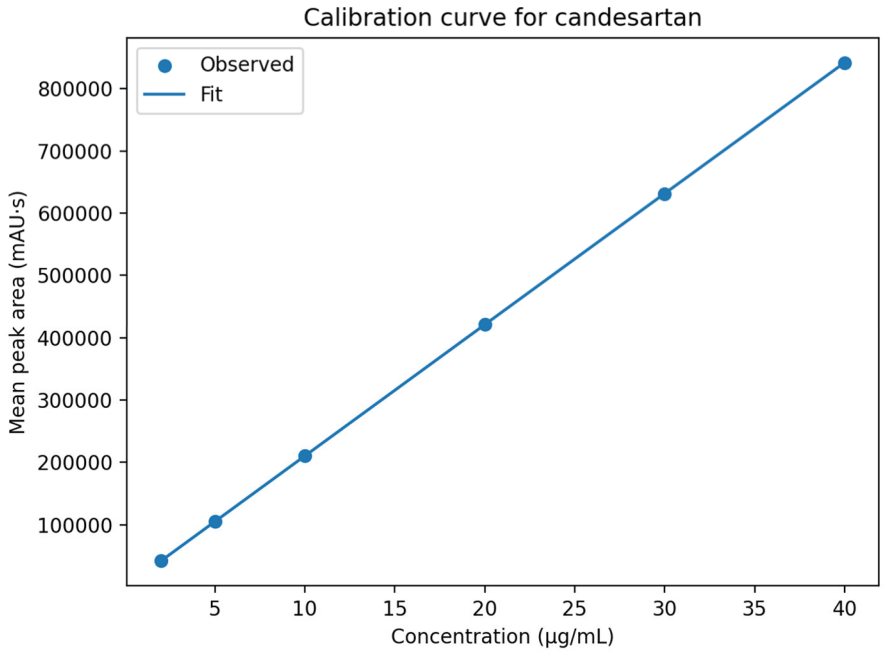
Table 5: Linearity Data for Candesartan

Concentration (µg/mL)	**Mean peak area (mAU·s)**
2	42000
5	105000
10	210500
20	421000
30	631500
40	842000

Table 6: Regression Parameters for Candesartan

Range (µg/mL)	**Slope (a)**	**Intercept (b)**	**Correlation coefficient (r^2)**
2–40	21054.28	-135	0.9994

Figure 2: Calibration curve for Candesartan (2–40 µg/mL)



Accuracy assessed by standard addition at 80–120% levels showed mean recovery within typical assay acceptance limits and low variability (Table 7).

Table 7: Accuracy Results for Candesartan (n = 3)

Level (%)	**Amount added (µg/mL)**	**Amount found (µg/mL)**	**% Recovery**	**SD**	**%RSD**
80	16.0	15.86	99.10	0.15	0.15
100	20.0	19.92	99.60	0.18	0.18
120	24.0	24.08	100.33	0.20	0.20

Precision (repeatability and intermediate precision) showed %RSD values well below 2.0% across 80–120% concentration levels (Table 8), supporting method repeatability in routine use.

Table 8: Precision Results for Candesartan

Level	**Intra-day mean assay (%)**	**Intra-day %RSD**	**Inter-day mean assay (%)**	**Inter-day %RSD**	**Acceptance criterion**
80%	99.2	0.60	98.9	0.85	≤ 2.0
100%	99.5	0.55	99.1	0.80	≤ 2.0
120%	99.8	0.50	99.4	0.78	≤ 2.0

Sensitivity was adequate for assay and stability applications, with estimated LOD and LOQ of approximately 0.2 and 0.6 µg/mL, respectively. Robustness testing indicated that small deliberate changes in flow rate, organic composition and detection wavelength did not materially affect assay or chromatographic performance (Table 9).

Table 9: Robustness Results for Candesartan

Condition	**Flow / Composition / λ**	**Rt (min)**	**Tailing factor**	**%Assay**	**%RSD**
Flow 0.9 mL/min	-0.1 mL/min	4.50	1.12	99.4	0.70
Flow 1.1 mL/min	+0.1 mL/min	3.95	1.09	99.1	0.75

ACN 68%	-2% ACN	4.35	1.11	99.6	0.68
ACN 72%	+2% ACN	4.05	1.10	99.2	0.72
λ = 252 nm	-2 nm	4.20	1.10	99.3	0.65
λ = 256 nm	+2 nm	4.19	1.10	99.5	0.67

FORCED DEGRADATION AND DEGRADATION KINETICS

Forced degradation studies demonstrated that the developed method can resolve candesartan from degradation-related peaks under multiple stress conditions, supporting its stability-indicating capability. A summary of assay loss and observations is provided in Table 10.

Table 10: Forced Degradation Results for Candesartan

Stress condition	**% Assay remaining**	**% Degradation**	**Major degradant Rt (min)**	**Mass balance (%)**
Acidic (1 N HCl, 60 °C, 2 h)	80.5	19.5	2.1	99.4
Alkaline (0.1 N NaOH, 60 °C, 1 h)	83.0	17.0	5.8	99.0
Oxidative (3% H_2O_2, RT, 2 h)	76.0	24.0	3.0	98.8
Neutral (water, 80 °C, 4 h)	93.5	6.5	—	100.0
Thermal (80 °C, solid, 24 h)	95.8	4.2	—	100.0
Photolytic (1.2 M lux h, solid)	94.0	6.0	—	99.6

For kinetic evaluation, degradation data under acidic (1 N HCl, 60 °C) and oxidative (3% H_2O_2, room temperature) stress were analysed using ln(% remaining) versus time. The data were approximately linear, suggesting apparent first-order behaviour within the evaluated time frames (Tables 11 and 12).

Table 11: Acidic Degradation Kinetic Data for Candesartan (1 N HCl, 60 °C)

Time (min)	**% Remaining**	**ln(% Remaining)**
0	100.0	4.605

30	92.0	4.523
60	85.0	4.443
90	79.0	4.369
120	74.0	4.304
180	66.0	4.189

Figure 3: Acidic degradation kinetics (ln% remaining vs time)

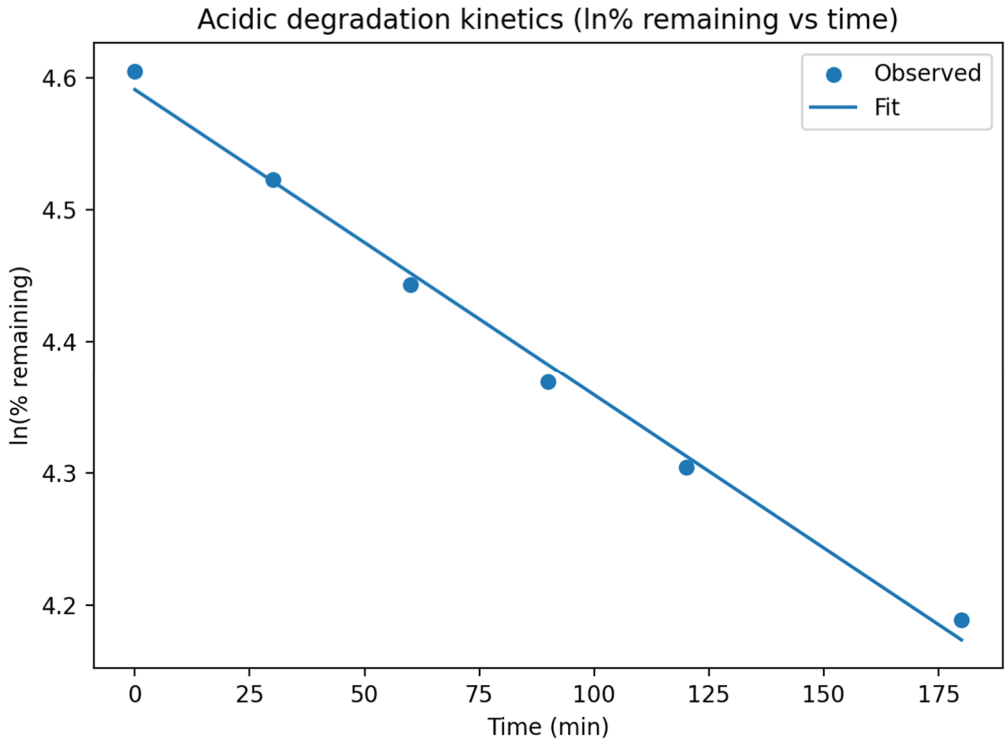
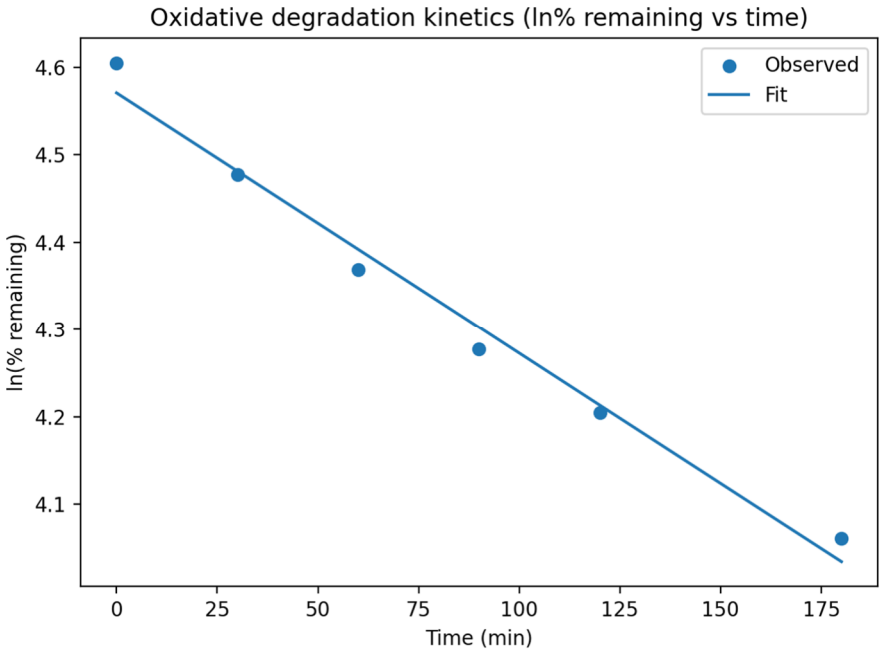


Table 12: Oxidative Degradation Kinetic Data for Candesartan (3% H_2O_2, RT)

Time (min)	**% Remaining**	**ln(% Remaining)**
0	100.0	4.605
30	88.0	4.477
60	79.0	4.369
90	72.0	4.277
120	67.0	4.205
180	58.0	4.061

Figure 4: Oxidative degradation kinetics (ln% remaining vs time)



Kinetic regression gave slopes of -0.002317 (acid) and -0.002979 (oxidation), corresponding to apparent first-order rate constants of 0.0023 min^{-1} and 0.0030 min^{-1}, respectively. Estimated half-lives were ~299 min (acid) and ~233 min (oxidation), indicating faster degradation under oxidative stress in the studied conditions.

CONCLUSION

A simple, rapid and isocratic RP-HPLC method for candesartan was developed and validated with acceptable linearity, accuracy, precision, sensitivity and robustness. The method demonstrated stability-indicating capability under forced degradation and supported basic kinetic evaluation under selected acidic and oxidative stress conditions, making it suitable for routine assay and stability studies in quality control and academic laboratories.

REFERENCES

1. Blessy M, Patel RD, Prajapati PN, Agrawal YK. Development of forced degradation and stability indicating studies of drugs—A review. J Pharm Anal. 2014;4(3):159–175.

2. Baertschi SW, Alsante KM, Reed RA, editors. Pharmaceutical Stress Testing: Predicting Drug Degradation. 2nd ed. New York: Informa Healthcare; 2011.

3. Srinivas G, Kumar KK, Kanumula GV, Priya MV, Mukkanti K. A stability indicating RP-HPLC method for determination of candesartan in bulk drug samples. Am J Anal Chem. 2012;3(10):704–709.

4. Kotthireddy K, Rama Devi B. Stability indicating RP-HPLC method development and validation for candesartan in bulk and tablet dosage form. Der Pharm Lett. 2015;7(12):114–121.

5. Carstensen JT, Rhodes CT. Drug Stability: Principles and Practices. 3rd ed. New York: Marcel Dekker; 2000.