

ECO-ANALYTICAL STABILITY-INDICATING LC METHOD FOR EPLERENONE AND DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE: EVALUATION USING ECO ANALYTICAL SCALE, AGREE PREP, BAGI, AND COMPLEX GAPI

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ABSTRACT

The integration of green analytical chemistry (GAC) principles into method development is essential for aligning pharmaceutical analysis with sustainability goals. Within this outline, high-performance liquid chromatography (HPLC) remains a widely used technique, yet it's based on organic solvents and energy-intensive processes highlights the need for greener method. In the present study, an HPLC method was developed, optimized, and validated for the simultaneous quantification of eplerenone and dapagliflozin propanediol monohydrate in bulk drug substances and laboratory-formulated tablets. Chromatographic separation was achieved on a Shimpack C18 column using a mobile phase consisting of phosphate buffer (pH 3.0, adjusted with 0.01% orthophosphoric acid), acetonitrile, and methanol in the ratio of 50:20:30 (v/v/v), with a flow rate of 1.0 mL/min. Detection was performed at 225 nm. The method demonstrated robust linearity ($r > 0.99$ for both analytes), with limits of detection and quantification of 2.95 and 8.96 $\mu\text{g/mL}$ for eplerenone, and 1.99 and 6.03 $\mu\text{g/mL}$ for dapagliflozin propanediol monohydrate, respectively. Validation parameters, including accuracy, precision, and robustness, met the acceptance criteria outlined in ICH Q2(R2). Specificity was confirmed by effective resolution of the drugs from its degradation products produced under stress conditions. The environmental performance of the method was systematically evaluated using Eco-Scale, AGREEprep, BAGI, and Complex GAPI tools, all of which indicated low ecological impact and minimal hazard potential. Collectively, these findings establish the method as not only analytically reliable and regulatory compliant but also environmentally responsible, thereby offering a sustainable approach for routine quality control in pharmaceutical laboratories.

KEYWORDS: Forced degradation studies, dapagliflozin propanediol monohydrate, spironolactone, Green Analytical Chemistry, Greenness Assessment Tools

INTRODUCTION

The incorporation of green chemistry principles into pharmaceutical analysis has become a critical step toward reducing the environmental and occupational hazards associated with laboratory practices. Several greenness assessment tools have been developed, and each tool have a distinct perspective on the ecological sustainability of analytical methodologies. One widely used tools is AGREEprep, which translates the twelve principles of green analytical chemistry into a single quantitative score ranging from 0 to 1, where values closer to 1 reflect superior environmental performance [1]. In contrast, the Eco-analytical Scale employs a penalty-point system that deducts points for deviations from ideal green practices—such as excessive reagent use, waste generation, or energy consumption. The resulting score, derived from 100 minus the penalties, classifies methods as excellent (>75), acceptable (>50), or inadequate (<50) [2]. The Complementary green analytical procedure index (Complex GAPI) refines the original GAPI by combining its visual pictogram with a quantitative scoring system, allowing both qualitative assessment and objective comparison of analytical methods. It evaluates key parameters—including sample preparation, reagent use, energy consumption, and waste management—with greener practices earning higher credits. This combine approach provides a more comprehensive and discriminative measure of methodological sustainability in analytical chemistry [3]. More recently, the Blue Applicability Grade Index (BAGI) has been introduced to extend beyond ecological considerations by evaluating practical aspects, including automation, sample throughput, reagent accessibility, and instrumentation demands [4, 5]. Together, these complementary metrics not only benchmark the environmental footprint of analytical procedures but also guide researchers toward designing methods that balance sustainability with practicality.

Chronic kidney disease (CKD) is a progressive condition of global concern, marked by persistent albuminuria, declining glomerular filtration rate, and a heightened risk of cardiovascular complications [6]. Although current standard therapies slow disease progression, a substantial residual risk of renal and cardiovascular events remains, underscoring the need for innovative treatment strategies. Among these emerging options, mineralocorticoid receptor antagonists (MRAs) and sodium–glucose cotransporter-2 (SGLT2) inhibitors have gained attention for their complementary renoprotective mechanisms. Eplerenone (EPL), a selective MRA, interrupts aldosterone-

mediated processes that promote fibrosis, inflammation, and sodium retention, thereby reducing albuminuria and attenuating functional decline. Its clinical utility, however, can be constrained by hyperkalaemia risk [7]. Dapagliflozin propanediol monohydrate (DPM), an SGLT2 inhibitor, reduces intraglomerular pressure by restoring tubuloglomerular feedback, while also improving glycaemic control, blood pressure, and body weight. Importantly, its nephroprotective effects extend beyond glycaemic regulation, benefiting patients irrespective of diabetes status [8]. The combination of these agents offers a rational approach by targeting distinct hemodynamic and molecular pathways. Preliminary evidence, including findings from randomized trials (EudraCT No. 2017-004641-25), indicates that dual therapy may enhance albuminuria reduction compared with monotherapy, without disproportionate safety concerns. This synergistic strategy represents a promising direction for addressing residual renal risk in CKD and warrants validation in large-scale outcome studies [9].

A comprehensive review of the literature revealed a few analytical methods reported for EPL and DPM, both as individual agents and in combination with other drugs. DPM have been measured by HPLC [10, 11], UV spectrophotometry [12–14] and HPTLC [15–17] and same EPL also estimated by HPLC [18–20], UV spectrophotometry [21, 22] and HPTLC [23, 24]. But no stability indicating HPLC method reported for the simultaneous estimation of EPL and DPM as well as no greenness assessment done.

This study reports, for the first time, the development and validation of a stability-indicating reversed-phase high-performance liquid chromatography (RP-HPLC) method for the simultaneous quantification of eplerenone and dapagliflozin propanediol monohydrate. Development of a validated, stability-indicating method is critical not only for accurate quantification in pharmaceutical formulations but also for applications in biological matrices, enabling studies of drug–drug interactions, pharmacokinetics, and formulation performance. HPLC method confirms accurate detection of the analytes in the presence of excipients and potential degradation products, thereby supporting comprehensive quality assessment. The method was thoroughly validated in accordance with ICH Q2(R2) guidelines, addressing parameters including precision, accuracy, specificity, robustness and stability testing. Beyond analytical robustness, the environmental sustainability of the method was systematically evaluated using multiple greenness assessment tools—AGREEprep, Eco-Analytical Scale, Complex GAPI, and BAGI—demonstrating minimal ecological impact and suitability for routine laboratory use. The proposed RP-HPLC method integrating the regulatory compliance with eco-efficient practice, highlights both the novelty and practical relevance of analytical method.

Experimental Section

Reagents and Chemicals

The API eplerenone (purity 99.85%) and dapagliflozin propanediol monohydrate (purity 99.63%) reference standards were obtained as gift sample from Cipla Ltd. and Zydus Pharmaceutical Ltd., Ahmedabad, Gujarat. All solvents (HPLC-grade acetonitrile, methanol, water) and chemicals (e.g. orthophosphoric acid, hydrochloric acid, sodium hydroxide) were of analytical grade.

Instrumentation and Chromatographic Conditions

Chromatographic separation was carried out using a Shimpack ODS C18 column (250 mm × 4.6 mm i.d., 5 µm particle size) as the stationary phase. The method was developed using a Shimadzu Prominence series HPLC system, comprising a quaternary gradient pump (LC-20AD), degasser (DGU-20AR), column oven (CTO-10ASVP), photodiode array detector (SPD-M40), and auto-sampler (SIL-20AC), all operated via LabSolutions software. The mobile phase was a mixture of phosphate buffer (pH adjusted to 3.0 with 0.01% orthophosphoric acid), acetonitrile, and methanol in a 50:20:30 (v/v/v) ratio, which was filtered and degassed before use. Separation was achieved at a flow rate of 1.0 mL/min, with the column maintained at 25 °C, and analyte detection performed at 225 nm. The mobile phase also served as the diluent.

Standard solution Preparation

Stock solutions of EPL and DPM were individually prepared by accurately weighing 10 mg of each compound and dissolving in 10 mL of methanol, resulting in concentrations of 1000 µg/mL. The working standard mixture was prepared by transferring 2.5 mL of the EPL stock solution and 1.0 mL of the DPM stock solution into a 10 mL volumetric flask, followed by dilution to the mark with diluent. This yielded final concentrations of 250 µg/mL for EPL and 100 µg/mL for DPM.

Validation of the Method

The method was validated as per ICH Q2(R2) guidelines [25].

System suitability test

To confirm the adequacy of the chromatographic system, six replicate injections were performed using a mixture containing 100 µg/mL of EPL and 40 µg/mL of DPM.

Linearity and Sensitivity

Calibration curves were constructed using at least six different concentration levels. Aliquots from the working standard solutions (250 µg/mL for EPL and 100 µg/mL for DPM) were appropriately diluted to yield final concentrations ranging from 25–150 µg/mL for EPL and 10–60 µg/mL for DPM. The peak areas obtained for each concentration were recorded and used to plot calibration curves via linear regression analysis. Method sensitivity

was evaluated in terms of the limit of detection (LOD) and limit of quantitation (LOQ), which were estimated based on signal-to-noise ratios of 3:1 and 10:1, respectively. The low LOD and LOQ values indicate high sensitivity of the method.

Precision

Precision evaluated as intra-day and inter-day precision by assaying three replicates of samples at 25, 75, 150 µg/ml for EPL and 10, 30, 60 µg/ml for DPM. The percent relative standard deviation of peak areas was calculated.

Accuracy

Accuracy was evaluated by spiking known quantities of EPL and DPM into pre-analyzed synthetic mixture samples at 50%, 100%, and 150% of their target concentrations (50 µg/mL for EPL and 20 µg/mL for DPM), with three replicates at each level (n = 3). Percent recoveries were subsequently calculated to assess the method's accuracy.

Robustness

Method robustness was assessed by introducing deliberate, small variations in instrumental parameters, including mobile phase composition, flow rate, and detection wavelength. Standard solutions of EPL (100 µg/mL) and DPM (40 µg/mL) were injected in triplicate under each modified condition. The effect of these variations was evaluated by monitoring changes in peak areas and calculating the percent relative standard deviation (%RSD).

Forced degradation studies

Assessment of drug stability under stress conditions is a critical aspect of pharmaceutical research. The specificity and stability-indicating capability of the method were evaluated by subjecting a standard mixture of EPL and DPM to various stress conditions. A stock solution containing 2500 µg/mL of EPL and 1000 µg/mL of DPM was prepared for these degradation studies. The samples were exposed to stress conditions including acid hydrolysis, base hydrolysis, heat, light, and oxidative stress to accelerate degradation. Such studies facilitate identification of potential degradation products, evaluation of drug stability, establishment of suitable storage conditions, and support for regulatory submissions. Following stress treatment, 1 mL aliquots of each degraded sample were diluted to 10 mL with the mobile phase, yielding final concentrations of 75 µg/mL for EPL and 30 µg/mL for DPM, and subsequently analyzed using the HPLC system.

Assay of Laboratory prepared tablets

For the formulation of a tablet containing eplerenone (25 mg) and dapagliflozin propanediol monohydrate (10 mg), the selected excipients included Microcrystalline cellulose (50 mg), Anhydrous lactose (10 mg), Polyvinylpyrrolidone (5 mg), Croscopovidone (3 mg), and Magnesium stearate (1 mg). To prepare the standard stock solution, a quantity of powder equivalent to one tablet (25 mg EPL and 10 mg DPM) was accurately weighed and transferred to a 10 mL volumetric flask. A small volume of methanol was added, and the mixture was sonicated for 5–10 minutes to ensure complete dissolution. The solution was then diluted to volume with methanol and filtered. Subsequent appropriate dilutions of this stock solution were prepared to obtain final working concentrations of 50 µg/mL for EPL and 20 µg/mL for DPM, which were used for HPLC analysis.

RESULTS AND DISCUSSION

Optimization of Chromatographic Conditions

The optimization of chromatographic conditions is critical to developing a precise and reproducible HPLC method for the simultaneous estimation of eplerenone (EPL) and dapagliflozin propanediol monohydrate (DPM). Initial experiments with binary solvent systems, including combinations of water, methanol, and acetonitrile, yielded either incomplete separation, peak splitting, or asymmetrical peaks. These observations highlighted the influence of mobile phase polarity and solvent composition on analyte retention and peak shape, particularly for compounds with differing hydrophobic characteristics. Incorporation of phosphate buffer at varying pH values improved retention but did not fully resolve asymmetry or tailing issues. The results suggested that neither low pH nor solvent proportion adjustments alone were sufficient to achieve symmetrical, well-resolved peaks. It was only through careful adjustment of a ternary mobile phase—comprising phosphate buffer (pH 3.0), methanol, and acetonitrile in an optimized ratio—that reproducible and symmetrical peaks were obtained for both EPL and DPM. This combination effectively balanced polarity, elution strength, and buffer capacity, ensuring consistent analyte separation. Maintaining a flow rate of 1.0 mL/min and column temperature at 25 °C provided stable retention times, while detection at 225 nm ensured sensitive monitoring of both compounds. The overlay of UV spectrum shown in figure 1. The final optimized method, employing a phosphate buffer (pH 3.0) with methanol and acetonitrile (50:20:30, v/v/v), produced well-resolved, symmetrical peaks suitable for quantitative analysis. The retention time for EPL and DPM was found to be 5.47 min and 9.06 min, respectively shown in figure 2.

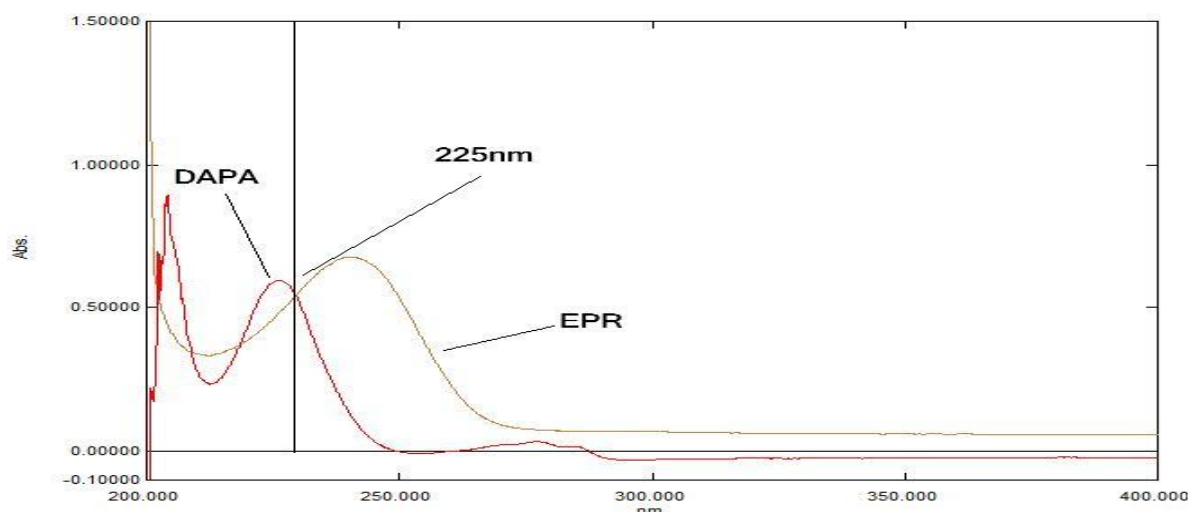


Figure 1. Overlay UV absorption spectra of eplerenone (EPL) and dapagliflozin propanediol monohydrate (DPM) in methanol.

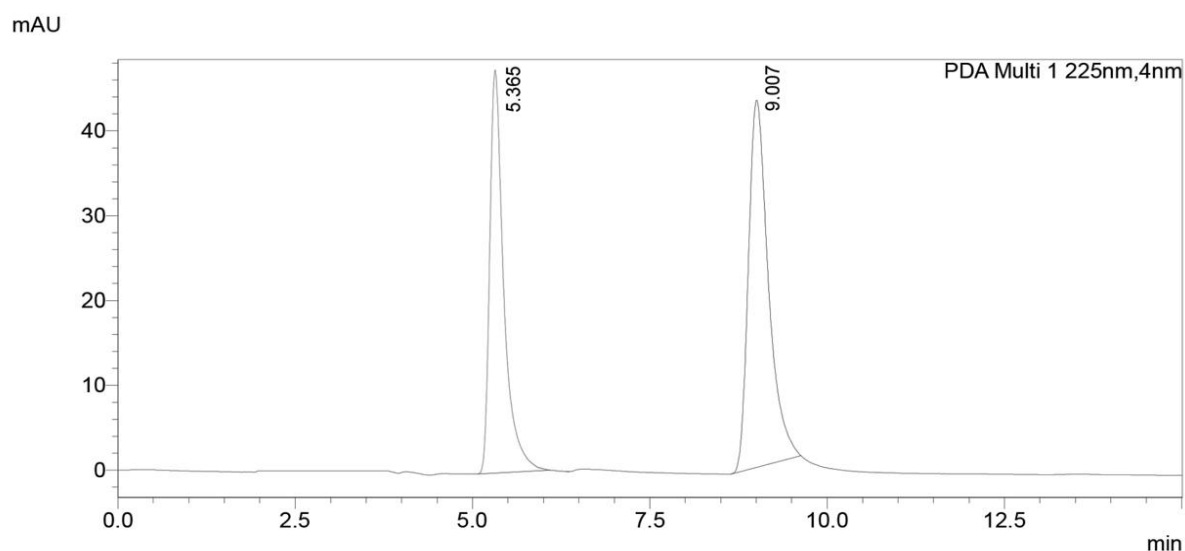


Figure 2. Representative HPLC chromatogram of EPL and DPM under optimized chromatographic conditions

Validation of the method

The optimized chromatographic conditions yielded well-defined peaks with acceptable system suitability parameters confirming method efficiency and reliability, data shown in Table I.

Linearity was evaluated over the concentration range of 25–150 µg/mL for EPL and 10–60 µg/mL for DPM and overlay shown in figure 3. The regression analysis data shown in Table I. Sensitivity was determined by calculating the limit of detection (LOD) and limit of quantification (LOQ). The LODs and LOQs were shown in Table I.

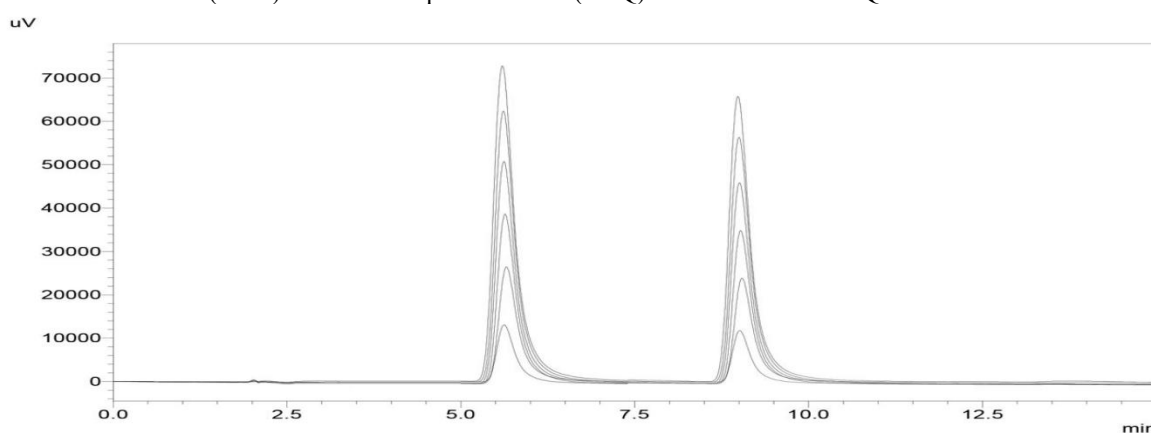


Figure 3. Overlay of HPLC chromatograms of EPL and DPM at different concentration levels within the established linearity ranges.

Table I: System suitability and regression analysis data of EPL and DPM

Parameter	EPL	DPM
Retention time (Rt)	5.470 ± 0.073	9.069 ± 0.089
Tailing factor	1.21 ± 0.06	1.274 ± 0.014
Number of theoretical plates	31474 ± 361.66	35032 ± 412.79
Resolution	-	8.875 ± 0.099
Linearity and range	25-150 µg/mL	10-60 µg/mL
Regression equation	y = 10167x - 6518.7	y = 22999x + 5874.3
Correlation coefficients	0.997	0.998
Limit of detection (LOD)	2.95 µg/mL	1.99 µg/mL
limit of quantification (LOQ)	8.96 µg/mL	6.03 µg/mL

Accuracy, determined through recovery studies at 50%, 100%, and 150% levels (n=3), showed mean percentage recoveries ranging from and 98.20% to 101.28% for EPL and 98.72% to 100.15% for DAP, confirming the accuracy of the method (Table II).

Table II: Accuracy data of EPL and DPM

% Standard addition	Conc. of drug taken (µg/mL)	Conc. of drug added (µg/mL)	Total Conc. of drug (µg/mL)	Conc. of drug found (µg/mL) ± SD	Recovery (%) ± SD
EPL					
0	50	0	50	50.64 ± 0.32	101.28 ± 0.64
50	50	25	75	73.94 ± 0.68	98.59 ± 0.90
100	50	50	100	94.42 ± 1.17	94.42 ± 1.16
150	50	75	125	122.75 ± 0.68	98.20 ± 0.54
DPM					
0	20	0	20	20.03 ± 0.05	100.15 ± 0.2
50	20	10	30	29.71 ± 0.53	99.03 ± 1.76
100	20	20	40	39.95 ± 0.02	99.88 ± 0.05
150	20	30	50	49.36 ± 0.37	98.72 ± 0.74

Precision was assessed in terms of intra-day, and inter-day variability. Intra-day precision showed RSD values between 0.24%–1.26% for EPL and 0.93%–1.24% for DPM, while inter-day precision ranged from 1.36%-1.75% for EPL and 1.05%–1.81% for DPM, respectively. All values were within acceptable limits (<2%), demonstrating the method's reproducibility.

Robustness testing, involving deliberate small variations in flow rate, mobile phase composition, and detection wavelength, revealed no significant impact on peak area of both drugs shown in table III, affirming the method's robustness.

Table III: Robustness of proposed HPLC method of EPL and DPM

Parameter	Variations in parameters condition	Mean Peak Area ± S.D.	% R.S.D.	Mean Peak Area ± S.D.	% R.S.D.
		EPL		DPM	
Mobile Phase: Buffer (pH 3): MeOH: ACN (50:20:30 v/v)	45:20:35	731010.76±2407.05	0.33	731010.76±2407.05	0.33
	50:25:25	730456.35±13214.8	1.81	730456.35±13214.8	1.81

Flow rate (1 ml/min)	0.8 ml	728889.08±4723.95	0.65	728889.08±4723.95	0.65
	1.2 ml	720145.01±6277.66	0.87	720145.01±6277.66	0.87
Detection wavelength (225 nm)	222nm	739422.17±8048.52	1.09	739422.17±8048.52	1.09
	228nm	714804.41±5962.55	0.83	714804.41±5962.55	0.83

Forced degradation studies and Specificity

Forced degradation studies are essential for development of stability-indicating methods and understanding potential degradation pathways. In this research work, EPL and DPM were assessed under acid, base, oxidative, photolytic, and thermal stress to compare their intrinsic stability.

Both compounds demonstrated susceptibility to hydrolytic degradation, with EPL showing higher instability than DPM. EPL degraded 12.83% in acid and 16.78% in base, while DPM showed 11.88% and 14.34% degradation, respectively. The greater alkaline lability of EPL suggests a higher vulnerability of functional groups to base-catalyzed hydrolysis (figure 4(a) and (b)).

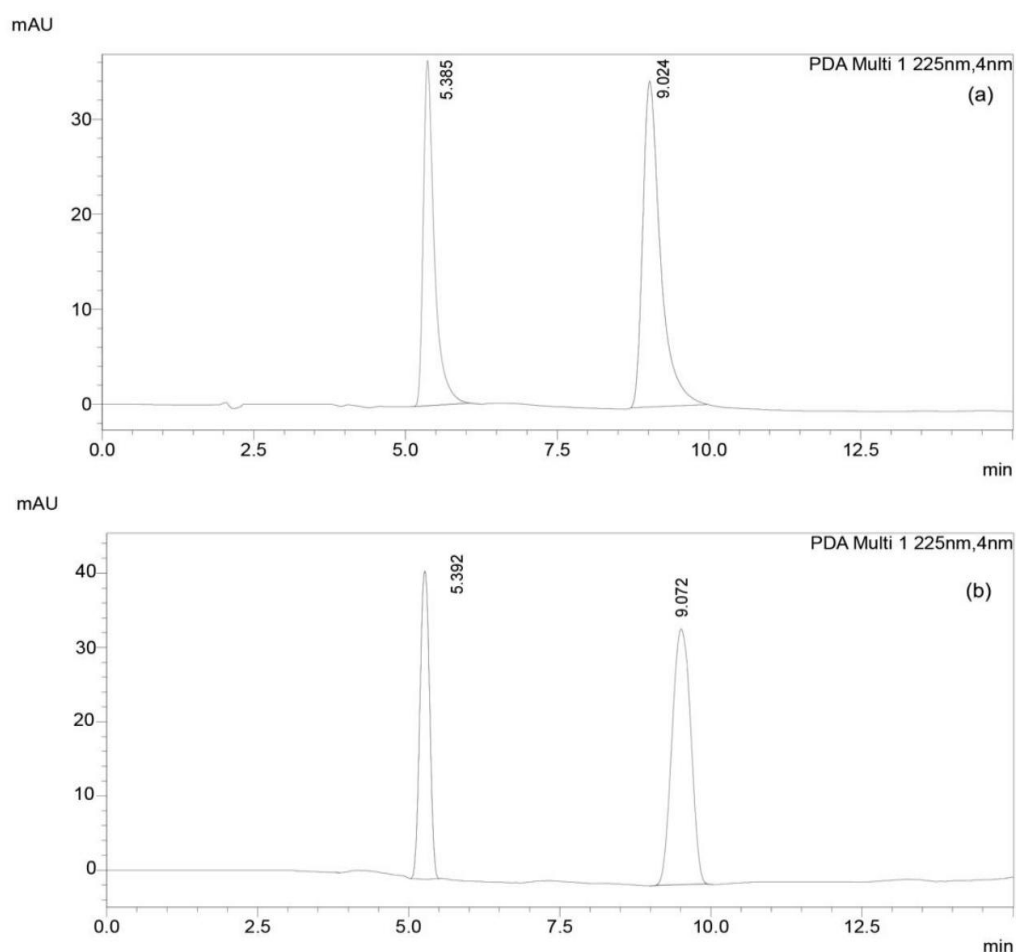


Figure 4. Representative HPLC chromatograms of EPL and DPM under hydrolytic and oxidative stress conditions: (a) acid hydrolysis, (b) alkaline hydrolysis, and (c) oxidative degradation.

Under oxidative stress, EPL retained 91.41% assay (8.59% degradation), performing better than DPM, which showed 12.58% degradation. This indicates EPL's relatively stable to oxidative cleavage (figure 5(c)). Photolytic stress caused mild degradation in both drugs, with EPL at 7.33% and DPM at 6.40%. While neither is highly photosensitive, protective packaging remains advisable (figure 5(a)). Thermal stress studies showed high stability, with DPM (5.20% degradation) and EPL (8.50% degradation) (figure 5(b)).

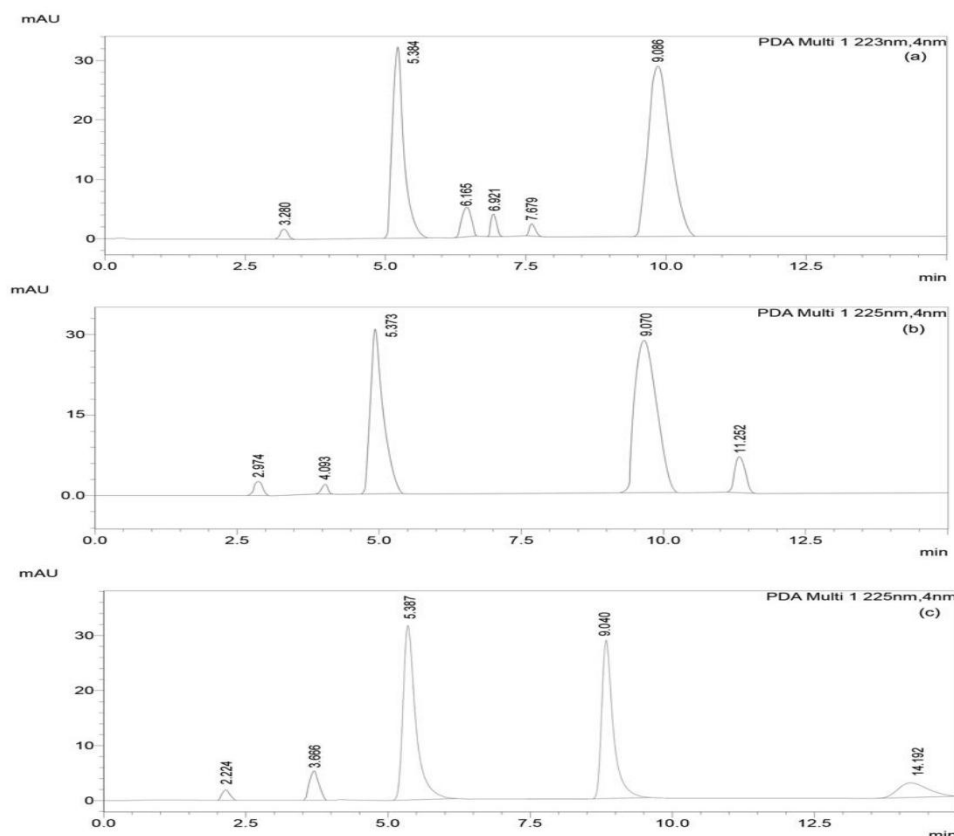


Figure 5. Representative HPLC chromatograms of EPL and DPM under thermal and photolytic stress conditions: (a) photolytic degradation and (b) thermal degradation.

Overall, EPL is more susceptible to hydrolysis, while DPM is less stable under oxidative stress but more thermally stable.

The blank chromatogram depicted together with the peak purity index and supporting spectral data presented in figure 6, clearly demonstrate the specificity of the developed analytical method. The results confirm that the method is capable of distinguishing the parent drugs from their degradation products across all applied stress conditions. The presence of well-resolved degradation peaks further substantiates the ability of the method to separate intact analytes from their degradants, thereby fulfilling the requirements of a stability-indicating assay. Notably, no co-elution of degradation peaks with the EPL and DPM analyte peaks was observed. Moreover, peak purity values obtained through diode-array spectral analysis exceeded 0.999, proved specificity of proposed method. A consolidated overview of the forced degradation studies for EPL and DPM is presented in Table IV.

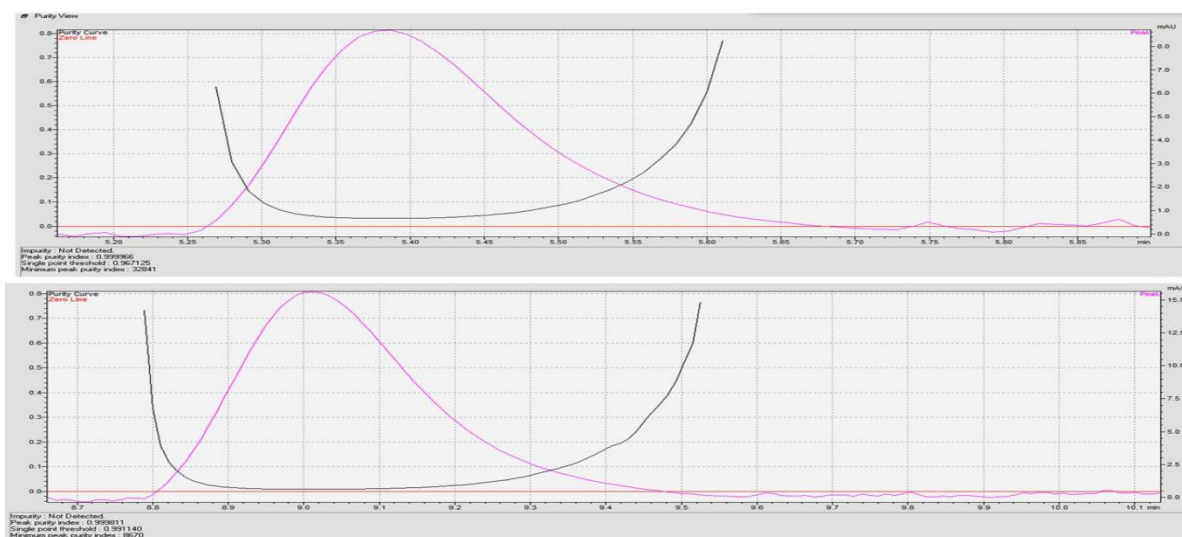


Figure 6. Specificity assessment of the proposed stability-indicating HPLC method showing blank chromatogram, analyte peak purity, and corresponding PDA spectral analysis of EPL and DPM.

Table IV: Stress degradation data of EPL and DPM

Stress condition	% EPL recovered	% EPL degraded	% DPM recovered	% DPM degraded
Acid Hydrolysis 0.1 N HCl, 60°C, 180 min	87.17	12.83	88.12	11.88
Alkali Hydrolysis 0.1 N NaOH, 60°C, 120 min	83.22	16.78	85.66	14.34
Oxidative degradation 3% H ₂ O ₂ , RT, 30 min	91.41	8.59	87.42	12.58
Dry heat, 70°C, 180 min (Thermal)	91.50	8.50	94.80	5.20
Photolytic, sunlight, 12 hrs	92.67	7.33	93.60	6.40

*Average of three determinations (each condition)

Assay of laboratory prepared tablet

The validated method was applied to estimation of EPL and DPM in laboratory prepared tablets. Assay of tablets yielded drug contents of 101.56 ± 0.04 % for EPL and 100.29 ± 0.52 % for DPM (n=3), confirming the method's applicability for formulation analysis. The results demonstrated that excipients and tablet processing did not interfere, and the method accurately quantifies both drugs in a solid dosage matrix.

Greenness Evaluation

The environmental sustainability of the developed HPLC method and published method was evaluated using four complementary green chemistry assessment tools: Eco analytical Scale, AGREE prep, BAGI, and mo-GAPI shown in Table V.

The eco analytical scale score was calculated to be 76, which categorizes the method as "excellent green analysis" according to the established threshold (score >75) [26, 27]. The deduction in points primarily resulted from the use of organic solvents (acetonitrile and methanol) and electricity consumption associated with HPLC operation. However, the method avoids excessive reagent use, minimizes waste, and uses a simple isocratic elution, contributing to its strong eco-profile [2, 28, 29].

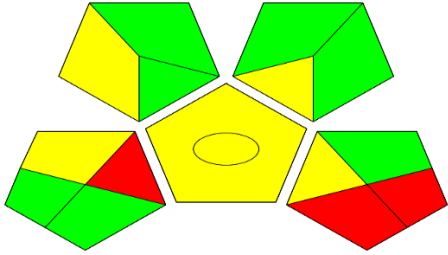
The AGREE prep metric, which quantifies a scale from 0 to 1, yielded a score of 0.53 (Table V). This represents a moderate greenness level, indicating that while the method incorporates several green principles—such as minimal sample preparation, low reagent volume, and direct analysis—there is still scope for improvement, particularly in solvent selection and energy efficiency [30–34].

In the BAGI assessment, the method received a score of 80, reflecting its high practical applicability and balanced greenness (Table V). The score accounts for features like sample throughput, automation potential, ease of execution, and method versatility. The simultaneous estimation of two analytes, short analysis time, and the use of standard HPLC instrumentation enhanced the method's BAGI performance [35, 36].

The complex GAPI assessment of the developed analytical method demonstrates a moderate level of environmental sustainability. The pictogram shows seven green zones, indicating that several aspects of the method, such as sample preparation, reagents, and certain instrumental conditions, align well with green chemistry principles (Table V). However, the presence of five yellow zones suggests intermediate concerns, reflecting areas where partial improvements are possible (e.g., solvent volume, energy use, or safety considerations). Importantly, three red zones highlight critical non-green features of the procedure, likely linked to the use of hazardous solvents, higher waste generation, or limited eco-friendly alternatives. Overall, while the method exhibits several favourable attributes, further optimization—particularly in areas highlighted in red—is required to enhance sustainability and minimize environmental impact [28, 31, 32, 37, 38].

Table V: Greenness score of proposed method by AGREEprep, BAGI, complexGAPI and eco analytical scale

Assessment Tools	Score
AGREE prep Score	

BAGI score																			
ComplexGAPI																			
Eco Analytical Scale	<table border="1"> <thead> <tr> <th>Reagents</th><th>Penalty points</th></tr> </thead> <tbody> <tr> <td>Acetonitrile-m</td><td>6</td></tr> <tr> <td>Methanol-m,s</td><td>12</td></tr> <tr> <td>Ortho phosphoric acid</td><td>0</td></tr> <tr> <td>Energy used for LC</td><td>1</td></tr> <tr> <td>Waste</td><td>5</td></tr> <tr> <td>Occupational hazard</td><td>0</td></tr> <tr> <td>Total penalty points</td><td>24</td></tr> <tr> <td>Analytical eco-scale</td><td>76</td></tr> </tbody> </table>	Reagents	Penalty points	Acetonitrile-m	6	Methanol-m,s	12	Ortho phosphoric acid	0	Energy used for LC	1	Waste	5	Occupational hazard	0	Total penalty points	24	Analytical eco-scale	76
Reagents	Penalty points																		
Acetonitrile-m	6																		
Methanol-m,s	12																		
Ortho phosphoric acid	0																		
Energy used for LC	1																		
Waste	5																		
Occupational hazard	0																		
Total penalty points	24																		
Analytical eco-scale	76																		

CONCLUSION

The successful stability-indicating HPLC method developed and validated for the simultaneous estimation of eplerenone and dapagliflozin propanediol monohydrate in bulk and laboratory prepared tablets. The validation of method shown by accuracy, precision, sensitivity, and specificity, and was able to resolve the parent compounds from their degradation products across ICH-recommended stress conditions. The validation parameters result further emphasizes the consistency of this method for both regulatory submissions and routine quality control. The proposed method environmental assessment was done using various greenness assessment tools. Multiple greenness metrics—including Eco-Scale score of 78, AGREEprep value of 0.53, BAGI index of 80, and a favourable complex GAPI profile—collectively indicate that the method is not only analytically robust but also aligned with the principles of sustainable laboratory practice. The proposed method integrates analytical consistency with ecological responsibility, present a practical and sustainable solution for the pharmaceutical industry. Its robustness, operational simplicity, and demonstrated compliance with quality standards make it a valuable tool for the simultaneous quantification of eplerenone and dapagliflozin propanediol monohydrate in quality control, pharmacokinetics studies as well as whenever marketed dosage form come in to market.

Author Contributions

Author 1 Rutvi D Patel: Conducting a research and investigation process, Project administration, Formal analysis, software, and writing the original draft,

Author 2 Dr. Priyanka Patil: Project supervision, methodology, Validation and Software,

Author 3 Dr. Umesh Upadhyay: Reviewing and editing

Data Availability

Data will be made available on request.

DECLARATION

Conflict of interest

The authors declare no conflict of interest.

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Informed consent: Not applicable.

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