WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 3, 2028-2045. Review Article ISSN 2277–7105

STABILITY INDICATING RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE AND EPLERENONE IN ITS SYNTHETIC MIXTURE

Dr. Avani N. Doshi[1]*, Ms. Honey Patel[2]

[1*]HOD & Professor of Pharmaceutical QA/ Chemistry, K. B. Raval College of Pharmacy, Gandhinagar, Gujarat, India.

[2]Research Scholar, K. B. Raval College of Pharmacy, Gandhinagar, Gujarat, India.

Article Received on 05 Jan. 2026,
Article Revised on 25 Jan. 2026,
Article Published on 04 Feb. 2026,

https://doi.org/10.5281/zenodo.18530638

***Corresponding Author**

Dr. Avani N. Doshi
HOD & Professor of Pharmaceutical QA/ Chemistry, K. B. Raval College of Pharmacy, Gandhinagar, Gujarat, India.

How to cite this Article: Dr. Avani N. Doshi[1]*, Ms. Honey Patel[2] (2026). Stability Indicating Rp-Hplc Method Development and Validation For Simultaneous Estimation of Dapagliflozin Propanediol Monohydrate and Eplerenone in Its Synthetic Mixture. World Journal of Pharmaceutical Research, 15(3), 2028–2045.

ABSTRACT

Metabolic disorders are increasingly recognized as systemic conditions with significant effects on both cardiac and renal health. Type 2 diabetes mellitus substantially contributes to the development and progression of cardiovascular disease and chronic kidney impairment through complex metabolic and hormonal disturbances. [1] Pharmacological agents that influence renal sodium handling have shown potential to modify disease outcomes beyond glycemic control. Dapagliflozin, an inhibitor of sodium–glucose cotransporter-2, facilitates glucose and sodium excretion via the kidneys, leading to beneficial metabolic and hemodynamic effects.[2] Eplerenone, a selective mineralocorticoid receptor antagonist, counteracts aldosterone-driven fluid retention and tissue fibrosis with improved tolerability.[2,3] The concurrent use of dapagliflozin and eplerenone targets distinct yet interrelated pathways within the cardio-renal system and may provide enhanced protective effects in patients with kidney and heart dysfunction.[2,3] Ongoing monitoring of renal function and electrolyte balance remains essential during combined therapy.

KEYWORDS: Dapagliflozin Propanediol Monohydrate; Eplerenone; Type 2 diabetes mellitus; Cardio-renal syndrome; Chronic kidney disease; Fixed-dose combination.

INTRODUCTION

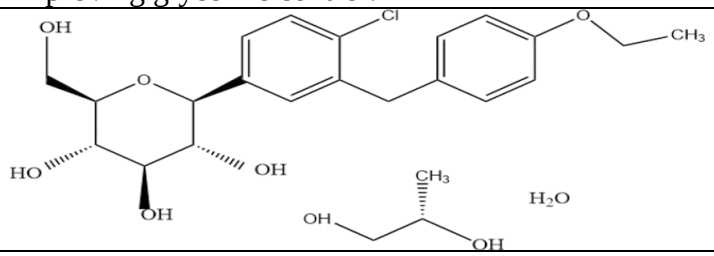
Type 2 diabetes mellitus represents a major public health concern due to its strong association with long-term cardiovascular and renal complications. Persistent metabolic imbalance in diabetic individuals promotes structural and functional alterations in multiple organ systems, particularly the heart and kidneys, resulting in increased morbidity and mortality.[1] These interrelated conditions often progress simultaneously, underscoring the need for therapeutic approaches that address shared pathophysiological mechanisms.

Recent therapeutic advances have highlighted the role of renal-targeted interventions in modifying systemic disease progression. Dapagliflozin reduces renal glucose reabsorption by inhibiting sodium–glucose cotransporter-2 activity in the proximal tubule. This mechanism promotes glucosuria and natriuresis, contributing to improved metabolic status, reduced circulatory volume, and attenuation of renal stress.[2] Clinical evidence supports its beneficial impact on renal outcomes and cardiovascular function in patients with chronic kidney disease. In addition to metabolic factors, excessive aldosterone activity has been implicated in the progression of cardiac and renal damage through its effects on sodium retention, inflammation, and fibrotic remodeling. Eplerenone selectively blocks mineralocorticoid receptors, thereby limiting these deleterious processes while minimizing endocrine-related adverse effects.[2,3] Its established role in cardiovascular therapy supports its use in conditions involving fluid overload and tissue remodeling.

The combination of dapagliflozin and eplerenone offers a rational therapeutic strategy by simultaneously modulating proximal tubular sodium handling and downstream aldosterone-mediated effects. Evidence from clinical and experimental studies indicates that this dual approach may enhance reductions in albuminuria, improve cardiac performance, and limit fibrotic progression compared with individual agents.[2,3] This review focuses on the mechanistic rationale and clinical relevance of this fixed-dose combination as an emerging option in the management of cardio-renal complications associated with metabolic disease.

Introduction to Drug Profile

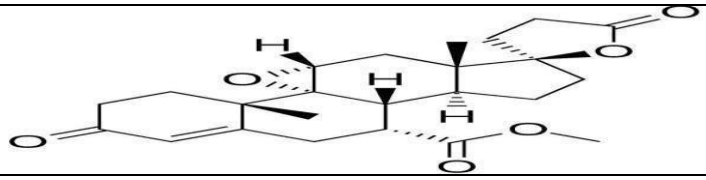
Drug Profile for Dapagliflozin Propanediol Monohydrate[56]

Drug Information	
Therapeutic category	Antidiabetic (SGLT-2 inhibitors)
Therapeutic Indication	Dapagliflozin propanediol monohydrate is indicated for the treatment of type 2 diabetes mellitus and for lowering the risk of cardiovascular and renal complications.
Mechanism of action	Dapagliflozin propanediol monohydrate acts by blocking SGLT2 in the kidneys, promoting urinary glucose excretion and improving glycemic control.
Chemical Structure	

Nomenclature	
International Union of Pure and Applied Chemistry (IUPAC) Name	(2S)-propane-1,2 diol (2S, 3R, 4R, 5S, 6R)-2-{4-chloro-3-[(4-ethoxyphenyl) methyl] phenyl}-6-(hydroxymethyl) oxane-3,4,5- triol hydrate
Empirical formula	C24H35ClO9
Molecular weight	502.99 g/mol
Chemical Abstracts Service (CAS) Number	960404-48-2
Approval Status	Approved by FDA, CDSCO and European union.(IP,USP)
BCS Class	Class III Drug (High solubility,Low permeability)
Physicochemical Properties	
Appearance	White powder
Solubility	Soluble in ethanol, DMSO, and dimethyl formamide. Sparingly soluble in aqueous buffers and water.
Melting point	69 °C to 74 °C
Log p	2.7
pKa value	12.57

Drug Profile of Eplerenone[57,58]

Drug Information	
Therapeutic category	Anti-hypertensive Agent
Therapeutic Indication	Used to treat high blood pressure and to improve survival in patients with heart failure.
Mechanism of action	Eplerenone selectively antagonizes mineralocorticoid receptors, reducing aldosterone-mediated sodium retention and cardiovascular stress.
Chemical Structure	

Nomenclature	
International Union of Pure and Applied Chemistry (IUPAC) Name	methyl (1R,2S,9R,10R,11S,14R,15S,17R)-2,15-dimethyl-5,5'-dioxospiro[18-oxapentacyclo[8.8.0.01,17.02,7.011,15]octadec-6-ene-14,2'-oxolane]-9-carboxylate
Empirical formula	$C_{24}H_{30}O_6$
Molecular weight	414.49 g/mol
Chemical Abstracts Service (CAS) Number	107724-20-9
Approval Status	Official in IP, BP
BCS Class	Class II Drug(Low solubility, High permeability)
Physicochemical Properties	
Appearance	White colored powder
Solubility	Soluble in organic solvent (Ethanol, Chloroform)
Melting point	245 °C to 250 °C
Log p	1.34
pKa value	Strongest Acidic- 16.44 Strongest Basic- -4.2

Review of official and reported methods for Dapagliflozin Propanediol Monohydrate

Official method for Dapagliflozin

Sr. No.	Drugs	Matrix	Method	Brief Introduction	Reference
1.	Dapagliflozin	Bulk Drug	RP-HPLC	Column:C^{18}(150mm×4.6mm, 3.5µm) Mobile Phase:Trifluoroacetic acid: ACN (85:15% v/v) Flow rate: 1ml/min λmax: 220 nm	[4]

Reported methods for Dapagliflozin

Sr. No.	Drugs	Matrix	Method	Brief Introduction	Ref.
1.	Dapagliflozin	Tablet	UV	Solvent:Methanol λmax:224 nm-UV	[5]
2.	Dapagliflozin	Bulk Drug and Tablet	UV	Solvent:Methanol:water (15:85% v/v) λmax: 220 nm	[6]
3.	Dapagliflozin	Bulk Drug and Tablet	RP-HPLC	Column:Waters C^{18} (250mm×4.6mm,5µm) Mobile Phase:Phosphate buffer:ACN (60:40%v/v) Flow rate: 1 ml/min	[7]

				λmax:237 nm Run time: 6.0 minutes Retention time: 3.461minutes	
4.	Dapagliflozin	Bulk Drug and Tablet	RP-HPLC	Column:C^{18}(250mm×4.6mm, 10µm) MobilePhase:0.1%Triethylmne(pH-5.0):ACN (50:50% v/v), Flowrate:1ml/min λmax: 224 nm Run time: 6 minutes Retention time : 5.163 minutes	[8]
5.	Dapagliflozin	Bulk Drug and Tablet	Stability Indicating RP-HPLC	Column:C^{18} (250mm × 4.6mm, 5µm) Mobile Phase:Acetonitrile and 0.1% orthophosphoric acid in water (70:30%v/v) Flow rate: 1 ml/min λmax: 230 nm RunTime:6minutes Retention Time: Approximately 5.16 minutes	[9]
6.	Dapagliflozin	Bulk Drug and Tablet	Stability Indicating RP-HPLC	Column: Agilent C^{18} (250mm × 4.6mm,10µm) Mobile Phase:ACN: di-potassium hydrogen phosphate with pH-6.5 adjusted with OPA (40:60% v/v) Flow rate: 1 ml/min λmax: 222 nm Run Time ~ 6 min Retention time For API: ~3.160 min; for tablet: ~3.067 min	[10]
7.	Dapagliflozin	Bulk and Pharmaceutical Dosage form	UV	Wavelength: 233.65 nm Solvent: Ethanol: Phosphate buffer (1:1%v/v)	[11]
8.	Dapagliflozin	API	RP-HPLC and UV	Column: BDS Mobile phase: Acetonitrile: Ortho phosphoric acid (55-45%v/v) Flow rate: 1.2 ml/min Wavelength: 203 nm Retention time: 2.072 min	[12]
9.	Dapagliflozin	Bulk and Pharmaceutical	RP-HPLC	Column: C^{18} Mobile phase: Buffer (potassium hydrogen	[13]

		Dosage form		orthophosphate): Methanol (65:35%v/v) Flow rate: 1.0 ml/min Wavelength: 225 nm Retention time: 2.93min	
10.	Dapagliflozin	Forced Degradation Studies	RP-HPLC	Column: BDS Mobilephase:Buffer:Acetonitrile (60:40 %v/v) Flow rate: 1.0 ml/min Wavelength: 245 nm Retention time: 2.789 min	[14]
11.	Dapagliflozin	Bulk and Tablet Dosage form	RP-HPLC	Column: C^{18} Mobile phase: Methanol: Acetonitrile: 1%OPA(75:25:05%v/v/v) Flow rate: 1.0 ml/min Wavelength: 246 nm Retention time: 2.797 min	[15]
12.	Dapagliflozin	Bulk and Pharmaceutical Dosage form	RP-HPLC	Column: C^{18} Mobile phase: Phosphate Buffer: Methanol (35:65%v/v) Flow rate: 1.0 ml/min Wavelength: 215 nm	[16]
13.	Dapagliflozin	Bulk and Tablet formulation	RP-HPLC	Column: BDS Mobile phase: Ortho phosphoric acid Buffer: Acetonitrile (50:50 %v/v) Flow rate: 1.0 ml/min Wavelength: 245 nm Retention time: 2.226 min	[17]
14.	Dapagliflozin	Tablet form	RP-HPLC	Column:C^{18} Mobile phase: Acetonitrile:0.1% Triethylamine (50:50%v/v) Flow rate: 1.0 ml/min Wavelength: 224 nm Retention time: 5.163 min	[18]
15.	Dapagliflozin	API	RP-HPLC	Column: BDS Mobile phase: Ortho phosphate acid: Acetonitrile (45:55%v/v) Flow rate: 1.0 ml/min Wavelength: 245 nm Retention time: 2.963 min	[19]
16.	Dapagliflozin	API and Pharmaceutical Dosage form	RP-HPLC	Column: C^{18} Mobile phase: Acetonitrile: Dipotassium hydrogen phosphate (40:60%v/v) Flow rate: 1.0 ml/min	[20]

				Wavelength: 222 nm Retention time: 3.16 min	
17.	Dapagliflozin	Bulk and Tablet Dosage form	RP-HPLC	Column: BDS Mobile phase: Ortho phosphoric acid buffer: Acetonitrile (50:50%v/v) Flow rate: 1.0 ml/min Wavelength: 245 nm Retention time: 2.226 min	[21]
18.	Dapagliflozin	Bulk and Tablet	RP-HPLC	Column: C^{18} Mobile phase: Methanol: Acetonitrile:1%OPA(75:25:05%v/v/v) Flow rate: 1.0 ml/min Wavelength: 246 nm Retention time: 2.797 min	[22]
19.	Dapagliflozin and Saxagliptin	Bulk Drug	RP-HPLC	Column: Phenomenex Luna C^{18} (250mm × 4.6mm,10µm) Mobile Phase:10mM phosphate buffer (pH 6.8): ACN (40:60% v/v) Flow rate: 1 ml/min λmax: 260 nm	[23]
20.	Dapagliflozin and Saxagliptin	Bulk and Tablet	Stability indicating RP-HPLC	Column: Xterra RP^{18} (150mm × 4.6mm, 5µm) Mobile Phase: ACN: Water (60:40% v/v) Flow rate: 1 ml/min λmax: 248 nm Run time: close to ~5 min Retention times(RT): Dapagliflozin ~ 2.091 min; Saxagliptin ~ 3.249 min	[24]
21.	Dapagliflozin,Empagliflozin and Canagliflozin	Bulk and Tablet	Stability indicating RP-HPLC	Column:Hypercil C^{18} (250mm × 4.6mm, 10µm) Mobile Phase: acetonitrile and 0.1% formic acid buffer, pH 3.7 (60:40%v/v) Flow rate: 1 ml/min λmax: 230 nm for empagliflozin and dapagliflozin; 290 nm for canagliflozin Run time:~7 minutes Retention times ~7 min	[25]
22.	Dapagliflozin and Linagliptin	Bulk Drug and Tablet	Stability indicating RP-HPLC	Column: Eclipse Plus C^{18} (150mm × 4.6mm, 5µm) Mobile Phase: 0.1 % v/v Formic acid and ACN (40:60% v/v)	[26]

				Flow rate: 0.7 ml/min λmax: 260 nm	
23.	Dapagliflozin and Empagliflozin	Bulk Drug and Tablet	RP-HPLC	Column: C^{18} (250mm × 4.6mm, 5µm) Mobile Phase: ACN: Water (30:70% v/v) Flow rate: 1.2 ml/min λmax: 230, 250 nm Run time: 4 minutes total run Retention times: 4 minutes	[27]
24.	Dapagliflozin and Vildagliptin	Bulk Drug and Tablet	QbD based RP-HPLC	Column: Hypercil C^{18} (250mm × 4.6mm, 10µm) Mobile Phase: Ethanol: Water (70:30% v/v) Flow rate: 1 ml/min λmax: 250 nm	[28]
25.	Dapagliflozin and Metformin	Bulk Drug and Tablet	QbD based RP-HPLC	Column: Hypercil C^{18} (250mm × 4.6mm, 10µm), Mobile Phase: Ethanol: Water (70:30% v/v) Flowrate: 1 ml/min λmax: 250nm	[28]
26.	Dapagliflozin and Metformin hydrochloride	Synthetic Mixture	UV	Wavelength: Dapagliflozin-225nm , Metformin - 237 nm Solvent: Methanol	[29]
27.	Dapagliflozin and Metformin hydrochloride	Synthetic Mixture	UV	Wavelength: Dapagliflozin-235nm , Metformin - 272 nm Solvent: Methanol	[30]
28.	Dapagliflozin and Metformin	Pharmaceutical Dosage Form Tablet	RP-HPLC	Column-C^{18} Mobile phase – Acetonitrile:0.05 m potassium dihydrogen phosphate buffer (65:35% v/v) Flow rate-1ml/min UV wavelength-212nm Retention time: MET- 1.898 min DAPA-3.560 min	[31]
29.	Dapagliflozin and Metformin	Pharmaceutical Dosage Form Tablet	RP-HPLC	Column: C^{18} Mobile phase: 0.1Mdipotassium hydrogen phosphate: Acetonitrile: Methanol (60:30:10%v/v/v) Flow rate: 1.2 ml/min UV Wavelength: 285 nm Retention time: DAPA:2.847min	[32]

				MET: 3.804 min	
30.	Dapagliflozin and Metformin hydrochloride	Pharmaceutical Dosage Form Tablet	RP-HPLC	Column: C^{18} Mobile phase: 0.05 M Potassium dihydrogen orthophosphate buffer: Acetonitrile (50:50%v/v) Flow rate: 1 ml/min Retention time: Dapaglifiozin: 2.633 min Metformin: 5.620 min	[33]
31.	Dapagliflozin and Metformin hydrochloride	Tablet Dosage Form	RP-HPLC	Column-BDS Mobile phase – phosphatebuffer: Methanol: Acetonitrile(50:30:20 %v/v/v) Flow rate-1ml/min Retention time- DAPA-3.647 min MET -2.475 min UV wavelength- 240 nm	[34]
32.	Dapagliflozin and Metformin	Tablet Form	RP-HPLC	Column: C^{18} Mobile phase: Buffer: Acetonitrile (60:40%v/v) Flow rate: 1 ml/min UV wavelength: 266 nm Retention time: Metformin: 2.330 min Dapaglifolizin:3.098 min	[35]
33.	Dapagliflozin and Metformin	Bulk and Pharmaceutical Dosage form	RP-HPLC	Column: C^{18} Mobile phase: Acetonitrile: Phosphate buffer (70:30%v/v) Flow rate: 1ml/min Retention time: MET: 2 .463 min DAPA: 3.760min	[36]
34.	Dapagliflozin and Metformin	Bulk and Pharmaceutical Dosage form	RP-HPLC	Column: C^{18} Mobile phase: 0.1M Orthophosphoric acid: Acetonitrile: Methanol (35:40:25%v/v/v) UV Wavelength: 234nm Retention time: MET: 2.102min DAPA: 4.105min	[37]
35.	Dapagliflozin and Metformin hydrochloride	Bulk Drug and Tablet Dosage Form	RP-HPLC	Column: C^{18} Mobile phase: Buffer: Acetonitrile (50:50 %v/v) Flow rate: 1 ml/min Retention time: MET: 2.791 min	[38]

				DAPA: 3.789 min	
36.	Dapagliflozin and Metformin hydrochloride	Degradation Product	RP-HPLC	Column- C^{18} Mobile phase -0.05M Potassium Dihydrogen Phosphate Buffer: Acetonitrile: methanol.(5:4:1%v/v/v) Flow rate-0.5ml/min UV wavelength-236 Retention time- DAPA-8.314±0.05 min MET-2.274±0.04min	[39]
37.	Dapagliflozin and Metformin	Pharmaceutical Tablet Formulation	RP-HPLC	Column: C^{18} Mobilephase:Acetonitrile:0.1 M Ortho phosphoric acid buffer (70:30%v/v)	[40]
38.	Dapagliflozin and Metformin	Bulk and Synthetic Mixture	RP-HPLC	Column: C^{18} Mobile phase: Acetonitrile: Water (75:25%v/v) UV Wavelength: 285nm Flow rate: 0.5 ml/min Retention time: Metformin:3.2 min Dapagliflozin-5.4min	[41]

Review of official and reported methods for Eplerenone

Official methods for Eplerenone

Sr.No.	Drugs	Matrix	Method	Brief Introduction	Ref.
1.	Eplerenone	Bulk Drug	HPLC	Column: Stainless steel ODS (150mm × 4.6mm, 5 µm) Mobile Phase: 10 mM ammonium acetate, pH 7.4 and ACN (60:40% v/v) Flow rate: 1 ml/min λmax: 214 nm	[42]
2.	Eplerenone	Bulk Drug	HPLC	Column: ODS (150mm × 4.6 mm, 5 µm) Mobile Phase: 0.1 % Phosphoric acidA and Phosphoric acid : ACN : MethanolB (0.1: 40:60% v/v) (A:B 54 : 46 % v/v) Flow rate: 1 ml/min λmax: 240 nm	[43]

Reported methods for Eplerenone

Sr. No.	Drugs	Matrix	Method	Brief Introduction	Ref.
1.	Eplerenone	Tablet	UV	Solvent: 0.05 N HCl λmax: 245 nm	[44]
2.	Eplerenone	Tablet	UV	Solvent: Potassium dihydrogen orthophosphate, pH 2.0 λmax: 245 nm	[45]
3.	Eplerenone	Bulk Drug and Tablet	Stability indicating RP-HPLC	Column: C^{18} (250mm × 4.6 mm, 5 µm) Mobile Phase: 50 mM ammo nium acetate buffer (pH 7) and ACN (55:45% v/v) Flow rate: 1 ml/min λmax: 240 nm	[46]
4.	Eplerenone	Spiked Human Plasma	RP-HPLC	Column: HiQSil C-18HS (250mm × 4.6mm, 5 µm), Mobile Phase: ACN and Water (50:50%v/v) Flow rate: 1 ml/min λmax: 241 nm	[47]
5.	Eplerenone	Human Plasma	LC-MS	Column: Zorbax XDB C^{8} (250mm × 4.6mm,10µm), Mobile Phase: ACN: Water 10 mM ammonium acetate (pH 7.4) (40:60% v/v) Flow rate: 1 ml/min λmax: 246 nm Run Time: 5 minutes per injection	[48]
6.	Eplerenone	Bulk Drug	Stability indicating UPLC	Column: Waters UPLC BEH C^{18} (50mm ×2.1 mm, 1.7µm) Mobile Phase: 10 mmol/L ammonium acetate adjusted to pH 4.5: methanol: ACN Flow rate: 0.3 ml/min λmax: 245 nm	[49]
7.	Eplerenone	Human Urine	LC-MS/MS	Column: Zorbax XDB C^{8} (50mm × 2.1mm, 5µm) Mobile Phase: ACN: Water (40:60% v/v) containing 10 mM ammonium acetate (pH 7.4) Flow rate: 1 ml/min λmax: 245 nm Run Time: 5 minutes per injection	[50]
8.	Eplerenone	Tablet	RP-HPLC	Column: Waters Symmetry C^{18} (250mm × 4.6mm,5µm) Mobile Phase: Triethyl ammo nium phosphate buffer (pH 2.3) : ACN (40:60% v/v)	[51]

				Flow rate: 1 ml/min λmax: 240 nm Retention Time: 3.63 minutes	
9.	Eplerenone	Tablet	Stability indicating RP-HPLC	Column: C^{18} (250mm × 4.6mm, 5µm), Mobile Phase: 50 mM ammonium acetate buffer (pH 7): ACN (55:45% v/v) Flow rate: 1 ml/minλmax: 240 nm	[52]
10.	Eplerenone	Tablet	Stability indicating RP-HPLC	Column: HiQ sil C-18HS (250mm × 4.6mm, 5µm) Mobile Phase: Methanol and water (70:30% v/v) Flow rate: 1 ml/min λmax: 241 nm	[53]
11.	Eplerenone and Torsemide	Tablet	RP-HPLC	Column: Sheisedo C^{18} (250mm × 4.6mm, 5µm) Mobile Phase: ACN: Methanol: water (30:50:20%v/v/v) Flow rate: 1 ml/min λmax: 268 nm Retention Time: Eplerenone: 3.200 minutes,Torsemide: 5.023 minutes	[54]
12.	Eplerenone and Torsemide	Tablet	QbD based RP-HPLC	Column: C^{18} (250mm × 4.6mm, 5µm) Mobile Phase: ACN : water: methanol (50:30:20%v/v/v) Flow rate: 1 ml/min Run Time: Less than 5 minutes.	[55]

Summary of Review of Literature

Sr. No	Dapagliflozin	Number of Methods	Eplerenone	Number of Methods
1.	Official method in the pharmacopoeia		Official method in the pharmacopoeia	
	RP-HPLC	1	HPLC	2
2.	Reported methods (Single drug)		Reported methods (Single drug)	
	RP-HPLC	13	RP-HPLC	2
	UV	4	UV	2
	Stability Indicating RP-HPLC	2	Stability Indicating RP-HPLC	3
			LC-MS/LC-MS/MS	2
			Stability Indicating UPLC	1
3.	Reported methods for the combination with other drugs		Reported methods for the combination with other drugs	

	RP-HPLC	13	RP-HPLC	1
	QbD based RP-HPLC	2	QbD based RP-HPLC	1
	Stability Indicating RP-HPLC	3		
	UV	2		

CONCLUSION

A comprehensive examination of previously published research articles revealed the absence of a validated reverse-phase high-performance liquid chromatographic method for the concurrent quantification of Eplerenone and Dapagliflozin Propanediol Monohydrate. This analytical gap highlights the need for the establishment of a novel method capable of accurately determining both compounds when present together.

Accordingly, the present investigation is directed toward the design and validation of a new RP-HPLC analytical procedure for the measurement of Eplerenone and Dapagliflozin Propanediol Monohydrate in a laboratory-prepared mixture. The study emphasizes the systematic selection and refinement of chromatographic parameters to ensure clear resolution and reproducible performance. The proposed method is rigorously validated in compliance with ICH Q2 (R2) requirements and subsequently employed for the quantitative estimation of both active pharmaceutical ingredients in their synthetic combination.

REFERENCES

1. Olokoba AB, Obateru OA, Olokoba LB, “Type 2 diabetes mellitus: a review of current trends”. Oman Med., Journal 2012; 27(4): 269-273.
2. Provenzano M, Puchades MJ, Garofalo C, Jongs N, D’Marco L, Andreucci M, De Nicola L, Gorriz JL. “Albuminuria-lowering effect of dapagliflozin, eplerenone, and their combination in patients with chronic kidney disease: a randomized crossover clinical trial.” Journal of the American Society of Nephrology. 2022; 33(8): 1569-80.
3. Soulié M, Stephan Y, Durand M, Lima-Posada I, Palacios-Ramírez R, Nicol L, Lopez-Andres N, Mulder P, Jaisser F. “Benefit of combination therapy with dapagliflozin and eplerenone on cardiac function and fibrosis in rats with non diabetic chronic kidney disease.” Scientific Reports. 2024 Oct; 14(1): 23955.
4. United States Pharmacopoeia, National Formulary, 2024; 1364-1365.
5. Mante GV, Gupta KR, Hemke AT. “Estimation of dapagliflozin from its tablet formulation by UV-spectrophotometry.” Pharm Methods. 2017; 8(2): 102-7.

6. Vadla S, Putta V, Nadipudi S, Bilakanti S, Kudumula N. “Estimation Method for Dapagliflozin in Bulk and Marketed Dosage Form: Development and Validation by UV-pectroscopy.” International Journal of Pharmaceutical and Phytopharmacological Research (eIJPPR). 2023; 13(4): 1-6.
7. Debata J, Kumar S, Jha SK, Khan A. “A New RP-HPLC method developmentand validation of dapagliflozin in bulk and tablet dosage form.” Int. Journal Drug Dev., Res., 2017; 9(2): 48-51.
8. Mante GV, Hemke AT, Umekar MJ. “RP-HPLC method for estimation of dapagliflozin from its tablet.” International Journal of Chem., Tech., Research. 2018; 11(01): 242-8.
9. Manoharan G, Ismaiel AM, Ahmed ZM. “Stability-indicating RP-HPLC method development for simultaneous determination and estimation of dapagliflozin in raw and tablet formulation.” Chem., Res., Journal 2018; 3(2): 159-64.
10. Verma MV, Patel CJ, Patel MM. “Development and stability indicating HPLC method for dapagliflozin in API and pharmaceutical dosage form.” International Journal of Applied Pharmaceutics. 2017; 9(5): 33-41.
11. Karuna Priya Chitra, M. China Eswaraiah & M. V. Basaveswara Rao, Unic UV Spectrophotometric method for reckoning of dapagliflozin in bulk & pharmaceutical dosage forms. Journal of Chemical & Pharmaceutical Research, 2015; 7(9): 45-49.
12. Sanagapati Manasa, Dhanalakshmi k, Nagarjuna Reddy G, Sreenivasa S, Method development & validation of dapagliflozin in API by RP-HPLC & UV- Spectroscopy. Int., J. Pharm., Sci., Drug Res., 2014; 6(3): 250-252.
13. Santhosh Illendula, B. Niranjan, K. Pavan Kumar, G. Koteswar Rao, K.N. Rao, K. Rajeswar Dutt, Development & validation of stability indication quantitative estimation of dapagliflozin in bulk & pharmaceutical dosage form by RP-HPLC. IAJPS, 2018; 05(01): 615-620.
14. Shakir Basha S, Sravanthi P, Development & validation of dapagliflozin by reversed – phase high – performance liquid chromatography method & its forced degradation studies. Asian J. Pharm., Clin., Res., 2017; 10(11): 101-105.
15. Subrata Sarkar, Vipul P Patel, Method development & validation of dapagliflozin drug in bulk and tablet dosage form by RP-HPLC. Int J. Pharma Res., Health Sci., 2017; 5(4): 1755-59.
16. Dr. Sanjeev Kumar Subudhi, Bonagani Naresh, Vadicherla Swarnalatha, Merugu Mahesh, Stability indicating RP-HPLC method development & validation of dapagliflozin in bulk & pharmaceutical dosage form. Indo American Journal of Pharmacy, 2017; 3(6): 321-329.

17. Jeyabaskaran. M, Prof. Rambabu. C & Dhanalakshmi. B, RP-HPLC method development & validation of dapagliflozin in bulk & tablet formulation. IJPAR, 2013; 2(4): 221-226.
18. G. V. Mante, A. T. Hemke & M.J. Umekar, RP-HPLC method for estimation of dapagliflozin form its tablet. International Journal of Chem., Tech., Research, 2018; 11(01): 242-248.
19. Manasa. Sanagapati, K. Dhanalakshmi, G. Nagarjunareddy & S. Sreenivasa, Development & validation of a RP-HPLC method for the estimation of dapagliflozin in API. International Journal of Pharmaceutical Sciences & Research, 2014; 5(12): 5394-5397.
20. Dr. C. J. Patel, Mitali V. Verma & Dr. M. M. Patel, Simultaneous estimation of dapagliflozin in API & pharmaceutical dosage form by development & stability indicating HPLC method. World Journal of Pharmacy & Pharmaceutical Sciences, 2017; 6(7): 1618-1632.
21. Jeyabaskaran. M, Prof. Rambabu. C & Lakshmi. Maneka S., Stability indicating RP- PLC method for estimation of dapagliflozin in bulk & tablet form. Intercontiental Journal of Pharmaceutical investigation & Research, 2015; 2(4).
22. Vrushali Ravindra Harnaskar, P. A. Datar, R. V. Shete, Sonali Gire, A review on analysis of dapagliflozin. Current Pharma Research, 2018; 8(2): 15-27.
23. Rao BR, Rao VV, Venkateswarlu BS. "RP-HPLC method for simultaneous estimation of dapagliflozin and saxagliptin in bulk samples." Journal of Pharmaceutical Sciences and Research. 2019; 11(1): 254-7.
24. Deepan T, Dhanaraju MD. "Stability indicating HPLC method for the simultaneous determination of dapagliflozin and saxagliptin in bulk and tablet dosage form." Current Issues in Pharmacy and Medical Sciences. 2018; 31(1): 39-43.
25. Sharif S, Bashir R, Adnan A, Mansoor S, Ahmad I, Ch AR, Tahir MS. "Stability Indicating, pH and p K a Dependent HPLC–DAD Method for the Simultaneous Determination of Weakly Ionizable Empagliflozin, Dapagliflozin and Canagliflozin in Pharmaceutical Formulations." Chromatographia. 2020; 83(12): 1453-65.
26. Siddique W, Zulcaif, Umar H, Junaid Usmani S, Waqas M, Gul M, Gul., M. "Method development and validation of Metformin HCL and Dapagliflozin by using RP-HPLC." Acta Chromatographica. 2025; 37(2): 176-82.
27. Kladi E, Zerva M, Dotsikas Y. "A novel HPLC method for the simultaneous determination of empagliflozin and dapagliflozin: Development, validation, robustness testing and greenness assessment." Archives of Pharmacy. 2024; 74(2): 267-80.

28. Prajapati P, Rana B, Pulusu VS, Shah S. “Simultaneous chromatographic estimation of vildagliptin and dapagliflozin using hybrid principles of white analytical chemistry and analytical quality by design.” Journal of AOAC International. 2024; 107(1): 212-22.
29. Jain BR, Shah KV, Kapupara PP, Development & validation of UV-Spectroscopic method for simultaneous estimation of dapagliflozin & metformin hydrochloride in synthetic mixture, International Journal of Research & Development in Pharmacy & Life Sciences, 2015; 4(3): 1569-1576.
30. Jain BR, Shah KV, Kapupara PP, Development & validation of UV-Spectroscopic first derivative method for simultaneous estimation of dapagliflozin & metformin hydrochloride in synthetic mixture. Journal of Bioequivalence Studies, 2015; 1(1): 102.
31. Ghadir A Khalil, Ismail Salama, Mohammed S Gomaa1 and Mohammed A Helal, Validated RP-HPLC Method For Simultaneous determination Of Canagliflozin, Dapagliflozin, Empagliflozin And Metformin. IJBPAS, 2018; 8(1): 1-13.
32. K. Lakshmi Prameela, P. Rama Krishna Veni P. V.V. Satyanarayana, B. Hari babu, Development and validation of stability indicating reverse phase high performance liquid chromatography method with photodiode array detection for the simultaneous estimation of hypoglycemic agents, dapagliflozin and Metformin. Int J. Pharma Bio Sci., 2017 July; 8(3): 328-336.
33. Khyati J. Patel, Ankit B. Chaudhary, Shweta M. Bhadani and Ruchi J. Raval, Stability indicating RP-HPLC method development and validation for estimation of dapagliflozin and metformin HCL. World Journal of Pharmacy & Pharmaceutical Sciences, 2017; 6(9): 796-809.
34. Shyamala, Nidhi B, Kavitha M, Pooja and JVC Sharma, Validated RP-HPLC method for simultaneous estimation of Metformin Hydrochloride and Dapagliflozin in tablet dosage form. American Journal of Biological And Pharmaceutical Research, 2015; 2(2): 109-113.
35. Syed Abdul Hadi and Bharath Rathna Kumar P., Simultaneous estimation of metformin and dapagliflozin tablets by RP-HPLC. World Journal of Pharmacy and Pharmaceutical Sciences, 2017; 6(11): 1188-1199.
36. Syeda Kulsum, G. Vidyasagar, Tasneem Mohammed, A Simple and Validated RP-HPLC Method for the Simultaneous Estimation of Metformin and Dapagliflozin in Bulk and Pharmaceutical Dosage Forms. Journal of Pharmaceutical and Medicinal Chemistry, 2015; 1(2): 99-104.

37. N. Padmaja and G. Veerabhadram, Stability–indicating RP-HPLC method for the determination of Metformin and Dapagliflozin in bulk and pharmaceutical dosage form.journal de Afrikana, 2017; 4(2): 409-425.
38. Mohammad Yunoos, Gowri sankar D., A validated stability indicating high-performance liquid chromatographic method for simultaneous determination of metformin hcl and dapagliflozin in bulk drug and tablet dasage form. Asian J. Pharm., Clin., Res., 2015; 8(3): 320-326.
39. Sherif A. Abdel-Gawad, Abdul Malik S. Al-Tamimi, Elsadig H.K. Adam, Chromatographic Simultaneous Quantification Of Dapagliflozin And Metformin Hydrochloride In Presence Of Their Degradation Products. IJBPAS, 2017; 6(10): 2007-2021.
40. T. Deepan, M.V. Basaveswara Rao and M.D., Dhanaraju, Development of Validated Stability Indicating Assay Method for Simultaneous Estimation of Metformin and Dapagliflozin by RP- HPLC. European Journal of Applied Sciences, 2017; 9(4): 189-199.
41. Afshan Urooj, P. Shyam Sundar1, R. Vasanthi, M. Alagar Raja, K. Rajeswar Dutt, K. N. V. Rao and H. Ramana, Development And Validation of RP-HPLC method for simultaneous estimation of dapagliflozin and metformin in bulk and in synthetic mixture. World Journal of Pharmacy and Pharmaceutical Sciences, 2017; 6(7): 2139-2150.
42. Indian Pharmacopoeia, Government of India ministry of health and family welfare, Indian Pharmacopoeia Commission, Ghaziabad , 2022; 2: 2250-2251.
43. British Pharmacopoeia, Monographs: Medicinal and Pharmaceutical Substances, 2024, 2765.
44. Shailaja B, Swarna K, Afreen M, Kumar A. “A rapid assay method development and validation for the estimation of Eplerenone in tablets by UV spectrophotometry.” Int. Journal Pharm., Pharm., Sci., 2015; 7(9): 327-30.
45. Manasa P, Jaffer SK, Ashwini M, Kumar AA. “A simple and a cheap UV assay method development and validation for the estimation of eplerenone in a tablet.” Int. Journal Pharm Pharm., Sci., 2015; 7(10): 348-51.
46. Rane VP, Patil KR, Sangshetti JN, Yeole RD, Shinde DB. “Stability-indicating RP-HPLC method for analysis of eplerenone in the bulk drug and in a pharmaceutical dosage form.” Acta Chromatographica. 2009; 21(4): 619-29.
47. Gide P, Sonawane S, Chitnis A. “Development and validation of RP-HPLC method for estimation of eplerenone in spiked human plasma.” Journal of pharmaceutical analysis. 2012; 2(5): 390-3.

48. Zhang JY, Fast DM, Breau AP. "Development and validation of a liquid chromatography–tandem mass spectrometric assay for eplerenone and its hydrolyzed metabolite in human plasma." Journal of Chromatography B. 2003; 787(2): 333-44.
49. Du M, Pan C, Chen J, Song M, Zhu T, Hang T. "A validated stability-indicating ultra performance liquid chromatography method for the determination of potential process-related impurities in eplerenone." Journal of Separation Science. 2016; 39(15): 2907-18.
50. Zhang JY, Fast DM, Breau AP. "A validated SPE–LC-MS/MS assay for Eplerenone and its hydrolyzed metabolite in human urine." Journal of pharmaceutical and biomedical analysis. 2003; 31(1): 103-15.
51. Kumar DV, Srinivas S, Kumar AA. "A Rapid Rp-hplc Method Development And Validation For The Quantitative Estimation Of Eplerenone In Tablets." International Journal of Pharmacy and Pharmaceutical Sciences. 2015; 360-4.
52. Sangshetti JN, Shinde D, Ma BA. "Stability-Indicating RP-HPLC Method for Analysis of Eplerenone in the Bulk Drug and in a Pharmaceutical Dosage", Acta Chromatographica. 2009; 21(4): 619-29.
53. Sonawane S, Gide P. "An experimental design approach for the forced degradation studies and development of a stability-indicating LC method for eplerenone in tablets." Journal of liquid chromatography & related technologies. 2011; 34(17): 2020-31.
54. Patel KS, Bendale A, Luhar SV, Narkhede SB. "Development and validation of RP-HPLC method for the simultaneous estimation of eplerenone and torsemide in pharmaceutical dosage form." Journal Pharm Sci., Bio.,-Sci., Res., 2016; 6(3): 283-90.
55. Hinge MA, Patel D. "Optimization of HPLC method using central composite design for estimation of Torsemide and Eplerenone in tablet dosage form." Brazilian Journal of Pharmaceutical Sciences. 2022; 58: e20219.
56. Drug Profile for Dapagliflozin Propanediol Monohydrate, Drugbank Online,https://go.drugbank.com/drugs/DB06292,Accessed on 02/09/2025.
57. Drug Profile for Eplerenone, Drugbank Online, https://go.drugbank.com/drugs/DB00700 , Accessed on 03/09/2025.
58. Drug Profile for Eplerenone, PubChem Online, https://pubchem.ncbi.nlm.nih.gov/compound/Eplerenone#section=ChEBI-ID, Accessed on 03/09/2025.