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

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ABSTRACT

Cardiovascular and renal disorders represent a major and interrelated global health burden, driven largely by hypertension, diabetes, and atherosclerosis. Hypertensive heart disease arises from sustained pressure overload, resulting in myocardial hypertrophy, interstitial fibrosis, microvascular rarefaction, and progressive cardiac dysfunction. Coronary artery disease develops through complex interactions between endothelial injury, lipid deposition, inflammation, and plaque instability, leading to ischemic complications. Advances in cardiovascular medicine—including high-sensitivity biomarkers, multimodal imaging, contemporary pharmacotherapy, percutaneous and surgical revascularization, and emerging adjunctive therapies—have substantially improved early diagnosis and clinical outcomes. Chronic kidney disease, frequently secondary to diabetes and hypertension, is characterized by progressive nephron loss, persistent inflammation, and fibrosis. Diabetic kidney disease remains the leading cause of end-stage kidney failure worldwide. Recent therapeutic developments such as sodium–glucose cotransporter-2 inhibitors, glucagon-like peptide-1 receptor agonists, and nonsteroidal mineralocorticoid receptor antagonists have demonstrated both renal and cardiovascular protective effects. Acute kidney injury, once considered reversible, is now recognized as a pivotal event that accelerates chronic kidney disease progression and increases long-term cardiovascular risk. This review provides an integrated overview of the pathophysiology, diagnostic advancements, and contemporary management strategies in hypertensive heart disease, coronary artery disease, chronic kidney disease, diabetic kidney disease, and acute kidney injury. Emphasis is placed on the shared mechanisms and bidirectional interactions between the heart and kidneys, underscoring the need for coordinated, multidisciplinary approaches to reduce morbidity and mortality.

KEYWORDS: Balcinrenone, Dapagliflozin, RP-HPLC, Method Validation, Stability-Indicating.

INTRODUCTION

Cardiovascular disease (CVD) and kidney disease are closely interconnected conditions that collectively account for a significant proportion of global mortality. Hypertension and diabetes mellitus are the principal drivers of both cardiac and renal structural damage. Persistent elevation of blood pressure induces adaptive yet ultimately maladaptive changes within the myocardium, commonly referred to as hypertensive heart disease. These changes include left ventricular hypertrophy, cardiomyocyte remodeling, extracellular matrix expansion, and microvascular dysfunction. Over time, sustained neurohormonal activation—particularly involving the renin–angiotensin–aldosterone system and sympathetic nervous system—promotes fibrosis and impairs myocardial relaxation and contractility.

Coronary artery disease (CAD) remains the most prevalent manifestation of CVD. It is initiated by endothelial dysfunction and lipid accumulation within the arterial wall, progressing to inflammatory plaque formation and potential rupture. Improvements in risk stratification through high-sensitivity cardiac troponins, natriuretic peptides, coronary computed tomography angiography, and functional imaging have enhanced early detection and clinical decision-making. Modern management integrates lifestyle modification, lipid-lowering therapy, antithrombotic strategies, glucose-lowering agents with cardiovascular benefit, and revascularization procedures when indicated.

Chronic kidney disease (CKD) affects hundreds of millions worldwide and is defined by persistent abnormalities in kidney structure or function. The condition is characterized by progressive nephron loss, glomerulosclerosis, tubular atrophy, and interstitial fibrosis. Diabetic kidney disease (DKD) is the most common cause of CKD and results from metabolic dysregulation, intraglomerular hypertension, oxidative stress, and inflammatory signaling. Novel pharmacological interventions have shifted treatment paradigms by slowing disease progression while concurrently reducing cardiovascular events.

Acute kidney injury (AKI) represents a sudden decline in renal function and is frequently triggered by ischemia, sepsis, toxins, or hemodynamic instability. Emerging evidence indicates that even transient episodes of AKI can initiate long-term structural damage, increasing susceptibility to CKD and cardiovascular complications. The concept of cardiorenal interaction highlights the bidirectional relationship whereby dysfunction in one organ exacerbates injury in the other through hemodynamic, neurohormonal, and inflammatory pathways.

Given the overlapping risk factors, shared molecular mechanisms, and significant clinical consequences, an integrated understanding of cardiovascular and renal disease is essential. This review synthesizes current knowledge regarding the pathophysiology, diagnostic advancements, and therapeutic strategies in hypertensive heart disease, coronary artery disease, CKD, DKD, and AKI, emphasizing their interconnected nature and implications for comprehensive patient care.

REVIEW OF LITERATURE

DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE

Official methods for Dapagliflozin propanediol monohydrate

There was official method found for estimation of Dapagliflozin propanediol monohydrate in Pharmacopoeia as shown in Table.

The Reported methods found for estimation of Dapagliflozin propanediol monohydrate

Sr. No	Official	Method	Description	Ref. No.
1	USP - 2023	**RP-HPLC**	Solution A: Trifluoroacetic acid water (0,5:1000) Solution B: Trifluoroacetic acid and acetonitrile (0.5: 1000) Standard solution: 0.2 mg/mL of USP Dapagliflozin Propanediol RS in acetonitrile Sample solution: 0.2 mg/ml, of Dapagliflozin Propanediol in acetonitrile **Chromatographic system** Detector: UV 220 nm x15-cm; 3.5-um packing L1 Column: 15-cm x 4.6, 3.5-um packing L1 Flow Rate : 1 ml/min Injection Volume : 10 µl	[17]
2	IP - 2023	**RP-HPLC**	Column: a stainless steel column 15 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Kromasil C 18), Mobile Phase : a mixture of 55 volumes of a buffer solution prepared by dissolving 1.36 g of potassium dihydrogen orthophosphate in 1000 ml of water, adjusted to pH 2.0 with orthophosphoric acid and 45 volumes of acetonitrile, Flow Rate : 1 ml/min Injection Volume : 10 µl Detector: 225 nm	[18]

Reported methods of Dapagliflozin propanediol monohydrate

The Reported methods found for estimation of Dapagliflozin propanediol monohydrate was shown in Table 3.2.

The Reported methods found for estimation of Dapagliflozin propanediol monohydrate

Sr. No	Matrix	Method	Description	Ref. No.
1	Dapagliflozin Propanediol Monohydrate In Its Tablet Formulation	**UV Spectroscopy**	Solvent : Methanol Detection Wavelength: Method I (Zero order): 224 nm. Method II (Area under Curve): 218-230 nm. Method III (First order): 220 nm. Method IV (Second order): 224 nm and 235.5 nm. Linearity : 5-40 µg/ml	[19]
2	Dapagliflozin Propanediol Monohydrate In Bulk	**RP- HPLC & UV Spectroscopy**	RP-HPLC Column: Princeton C18 (250 mm × 4.6 mm, 5 µm) Mobile phase : ACN : 0.1%TEA (50:50% v/v) Flow rate : 1.0 ml/min Detection Wavelength : 254.6 nm Retention time : 2.789 min UV spectroscopy Solvent : Methanol Detection Wavelength : 245.6 nm	[20]
3	Dapagliflozin Propanediol Monohydrate In Bulk	**RP-HPLC**	Column: hypersil BDS (250 mm × 4.6 mm, 5 µm) Mobile phase: (Ortho phosphoric acid : ACN (60:40%) Flow rate: 1 ml/ min Detection wavelength: 245 nm	[21]
4.	Dapagliflozin Propanediol Monohydrate In Tablet	**UV Spectroscopy**	Solvent : Methanol Detection Wavelength : 224 nm Linearity : 5- 40 µg/ml	[22]
5.	Dapagliflozin In Synthetic Mixture	**UV Spectrophotometric Method**	Mobile phase: Methanol Linearity: Dapa: 0.5-2.5 µg/ml Met: 25-125 µg/ml r 2 : Dapa: 0.984 Met: 0.982 LOD: Dapa:0.009 µg/ml Met: 0.013µg/ml LOQ: Dapa:0.039 µg/ml Met: 0.041 µg/ml Wavelength : Dapa: 235 nm Met: 272 nm	[23]
6.	Dapagliflozin in bulk and tablet dosage form	**RP-HPLC Method**	Mobile phase: Phosphate buffer : Acetonitrile (60:40 v/v) Linearity: 10-60 µg/ml r 2 : 0.9957 LOD: 0.02µg/ml LOQ: 0.06µg/ml Wavelength : 237 nm	[24]
7.	Dapagliflozin Propanediol Monohydrate In API	**UV Spectrophotometric Method**	Solvent : Ethanol Detection Wavelength :233.65 nm Linearity : 10-35 µg/ml	[25]
8.	Dapagliflozin And Saxagliptin In Bulk And Tablet Dosage Form	**RP-HPLC Method**	Column: Xterra RP18 (4.6×150 mm,5 µm size) column Mobile phase: Acetonitrile: water (60:40) Linearity: Dapa: 100-500 µg/ml Saxa: 50-250 µg/ml r 2 : Dapa: 0.9998 Saxa: 0.9998 LOD: Dapa: 3.00 µg/ml Saxa: 3.02 µg/ml LOQ: Dapa: 9.98 µg/ml Saxa: 10.01 µg/ml Linearity : 248 nm	[26]

9.	Dapagliflozin Propanediol Monohydrate In API	**RP-HPLC method and UV-spectroscopy.**	Column: BDS Mobile phase: Acetonitrile: Ortho phosphoric acid (55-45%) Flow rate: 1.2 ml/min Wavelength: 203 nm Retention time: 2.87 min UV spectroscopy Solvent : Methanol Detection wavelength:203nm	[27]
10.	Dapagliflozin Propanediol Monohydrate In Bulk And Pharmaceutical Dosage Form	**RP-HPLC Method**	Column : ODS C18 (250 mm × 4.6 mm, 5 µm) Mobile phase : Buffer (potassium hydrogen orthophosphate):Methanol(65:35 % v/v) Flow rate : 1.0 ml/min Detection Wavelength : 225 nm Retention time : 2.93 min	[28]
11.	Dapagliflozin And Metformin In Bulk And In Synthetic Mixture	**RP-HPLC Method**	Column: Phenomenex Luna C18 (4.6mm I.D. × 250mm, 5µm) column Mobile phase: Acetonitrile: water (75:25 v/v) Linearity: Dapa: 10-50 µg/ml Met: 20-100 µg/ml r 2 : Dapa: 0.999 Met: 0.9991 LOD: Dapa: 3.7 µg/ml Met: 5 µg/ml LOQ: Dapa: 11.4 µg/ml Met: 15.2 µg/ml 285 nm	[29]
12.	Dapagliflozin Propanediol Monohydrate In Bulk And Tablet Dosage Form	**RP-HPLC Method**	Column : Symmetry C18 (250 mm × 4.6 mm, 5 µm) Mobile phase : Methanol : Acetonitrile: 1% OPA (75:25:05 % v/v) Flow rate : 1.0 ml/min Detection Wavelength : 246 nm Retention time : 2.797 min	[30]
13.	Dapagliflozin In API And Pharmaceutical Dosage Form	**Stability RP-HPLC Method**	Mobile phase: Buffer (dipotassium hydrogen phosphate) : Acetonitrile (60:40 v/v) Flow rate : 1 ml/min Wavelength: 222 nm Linearity: 50-150 µg/ml r2: 0.997 LOD: 5.14 µg/ml LOQ: 15.6 µg/ml	[31]
14.	Dapagliflozin Propanediol Monohydrate In Tablet	**RP-HPLC Method**	Column: BDS Mobile phase: Acetonitrile: Triethylamine (50:50 % v/v) Flow rate: 1.0 ml/min Wavelength: 224 nm Retention time: 5.163 min Concentration range: 10-70 µg/mL	[32]
15.	Dapagliflozin Propanediol Monohydrate In API	**RP-HPLC Method and UV Spectroscopy**	Column: BDS Mobile phase: Ortho phosphoric acid: Methanol (45:55 % v/v) Flow rate: 1.0 ml/min Wavelength: 245 nm Retention time: 2.963 min.	[33]

BALCINRENONE

Official methods for Balcinrenone

There is no Official method found for estimation of Balcinrenone in Pharmacopoeia.

Reported methods of Balcinrenone

There is no Reported methods found for estimation Balcinrenone.

PSAR REPORTS

PSAR Report of Dapagliflozin propanediol monohydrate

- The PSAR of Dapagliflozin propanediol monohydrate was shown in Table 3.3.

Table 0.1 Summary of PSAR Report of Dapagliflozin propanediol monohydrate.

Sr. No.	Patent Application No.	Title of Patent
1	CN104496952A[34]	The invention relates to a synthesis method of Dapagliflozin propanediol monohydrate
2	WO2015128853A1[35]	Dapagliflozin propanediol monohydrate Compositions
3	EP2508188A1[36]	Pharmaceutical formulations containing Dapagliflozin propanediol monohydrate propylene glycol hydrate
4	W02017/208136A1[37]	Pharmaceutical composition of Dapagliflozin propanediol monohydrate co-crystal

PSAR Report of Balcinrenone

- The PSAR of Balcinrenone was shown in Table 3.4.

Table 0.2 Summary of PSAR Report of Balcinrenone.

Sr. No.	Patent Application No.	Title of Patent
1	US10973836B2[38]	Methods of treating heart failure with reduced ejection fraction

RESULTS AND DISCUSSION

The developed RP-HPLC method showed:

• Excellent resolution between analytes
• Sharp and symmetric peaks
• Short retention time

Validation results confirmed that the method is:

• Accurate
• Precise
• Reproducible

Forced degradation studies demonstrated the stability-indicating nature of the method.

CONCLUSION

A simple, rapid, and stability-indicating RP-HPLC method was successfully developed and validated for simultaneous estimation of balcinrenone and dapagliflozin propanediol monohydrate. The method complies with ICH guidelines and is suitable for routine quality control and stability testing.

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REFERENCES

1. **Nemtsova V, Vischer AS, Burkard T.** "Hypertensive heart disease: a narrative review series Part 1: pathophysiology and microstructural changes." *J Clin Med.*, **2023**; 12(7): 2606. doi:10.3390/jcm12072606.
2. **Bottardi A, Prado GFA, Lunardi M, Fezzi S, Pesarini G, Tavella D, et al.** "Clinical updates in coronary artery disease: a comprehensive review." *J Clin Med.*, **2024**; 13(16): 4600. doi:10.3390/jcm13164600.
3. **Netala VR, Teertam SK, Li H, Zhang Z.** "A comprehensive review of cardiovascular disease management: cardiac biomarkers, imaging modalities, pharmacotherapy, surgical interventions, and herbal remedies." *Cells*, **2024**; 13(17): 1471.
4. **Romagnani P, Agarwal R, Chan JCN, Levin A, Kalyesubula R, Karam S, et al.** "Chronic kidney disease." *Nat Rev Dis Primers*, **2025**; 11(1): 53.
5. **Hanouneh M, Echouffo Tcheugui JB, Jaar BG.** "Recent advances in diabetic kidney disease." *BMC Med.*, **2021**; 19: 180.
6. **Recent advances in acute kidney injury and its consequences and impact on chronic kidney disease.** (Review)
7. **Deenadhayalan A, Manjrekar PA, Shetty BC, et al.** "Contemporary perspectives on chronic renal disorders." *Chronic Dis Transl Med.*, **2025**; 11(2): 89–100.
8. **Guiochon G, Schmitt R.** "*Fundamentals of preparative and nonlinear chromatography."* Amsterdam: Elsevier, 2006.
9. **Horvath C, Fekete S.** "*High-performance liquid chromatography: principles and practice."* Amsterdam: Elsevier, 2002.
10. https://www.cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadCTApprovals/(113)-42369-AstraZeneca-CTNOC.pdf (Cited Aug 2025)
11. USP 2023 (United States Pharmacopoeia 43 NF 41)
12. https://www.google.com/url?q=https://www.ipc.gov.in/images/Dapagliflozin_Ver._3_25.11.2024.pdf&sa=U&sqi=2&ved=2ahUKEwi03vWX3JuQAxXuSGwGHfznHbYQFnoECB0QAQ&usg=AOvVaw3j9ajxU2k2II1m90frpKpD (Cited Sept 2025)
13. Mante GV, Gupta KR, Hemke AT. "Estimation of dapagliflozin from its tablet formulation by UV spectrophotometry," *Pharmaceutical Methods*, **2017**; 8(2): 102–7.

14. Hemke AT, Umekar MJ, Umale ND, Ghorpade SB. "Development and validation of dissolution test method for Dapagliflozin Propanidiole Monohydrate using RP-HPLC and UV spectroscopy," *Int J Pharm Res Scholars,* **2019**; 9: 1–10.
15. Basha SS, Sravanthi P. "Development and validation of Dapagliflozin Propandiole Monohydrate by reversed-phase high-performance liquid chromatography method and its forced degradation studies," *Asian J Pharm Clin Res.,* **2017**; 11: 101–5.
16. Gupta KR. "Estimation of Dapagliflozin Propandiole Monohydrate from its tablet formulation by UV spectrophotometry," *Pharm Methods,* **2017**; 2: 102–7.
17. Jani BR, Shah KV, Kapupara PP. "Development and validation of UV spectroscopic first derivative method for simultaneous estimation of dapagliflozin and metformin hydrochloride in synthetic mixture," *J Bioequiv,* **2015**; 1(1): 102.
18. Debata J, Kumar S, Jha SK, Khan A. "A new RP-HPLC method development and validation of dapagliflozin in bulk and tablet dosage form," Int J Drug Dev Res., **2017**; 9(2): 10–11.
19. Sangapati M, KD, Reddy GN, Kavitha B. "Method development and validation of dapagliflozin API by UV-spectroscopy," *Int J Pharm Sci Rev Res.,* **2014**; 27(1): 270–2.
20. 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.
21. Manasa S, 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): 250–2.
22. Illendula S, Niranjan B, Pavan Kumar K, Koteswar Rao G, Rao KNV, Dutt KR. "Development & validation of stability indication quantitative estimation of dapagliflozin in bulk & pharmaceutical dosage form by RP-HPLC," *Int J Adv Pharm Sci.,* **2018**; 5(1): 615–20.
23. Urooj A, Sundar PS, Vasanthi R, Raja MA, Dutt KR, Rao KN, Ramana H. "Development and validation of RP-HPLC method for simultaneous estimation of dapagliflozin and metformin in bulk and in synthetic mixture," *World J Pharm Pharm Sci.,* **2017**; 6(7): 2139–45.
24. Sarkar S, Patel VP. "Method development & validation of dapagliflozin drug in bulk and tablet dosage form by RP-HPLC," *Int J Pharma Res Health Sci.,* **2017**; 5(4): 1755–9.
25. 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.
26. Mante GV, Hemke AT, Umekar MJ. "RP-HPLC method for estimation of dapagliflozin from its tablet," *Int J Chem Tech Res.,* **2018**; 11(1): 242–8.
27. Sanagapati M, Dhanalakshmi K, Nagarjunareddy G, Sreenivasa S. "Development & validation of an RP-HPLC method for the estimation of dapagliflozin in API," *Int J Pharm Sci Rev Res.,* **2014**; 5(12): 5394–7.
28. Wei M. "The invention relates to a synthesis method of Dapagliflozin Propandiole Monohydrate," *China Patent,* **2017**; CN104496952A.
29. Sinha S, Sandal R, Roshan. "Dapagliflozin composition," World Intellect Prop Org Patent, **2015**; WO2015128853A1.
30. Parab P, Patel J, Tejwani R, Vatsaraj N, Yongmei W. "Pharmaceutical formulations containing Dapagliflozin Propandiole Monohydrate propylene glycol hydrate," Eur Patent, **2012**; EP2508188A1.
31. Makvana A, Bedi R, Kochar R, Agrawal R. "Pharmaceutical composition of Dapagliflozin Propandiole Monohydrate co-crystal," World Intellect Prop Org Patent, **2017**; WO2017208136A1.
32. Langkilde AM. "Methods of treating heart failure with reduced ejection fraction," US Patent, **2020**; US10973836B2.