A Review on Analytical Method Development and Validation for Simultaneous Estimation of Perindopril and Indapamide in Bulk and Pharmaceutical Dosage Form by RP-HPLC

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ABSTRACT

Perindopril and Indapamide, a fixed-dose combination medication, are utilized for the management of hypertension by integrating the properties of an angiotensin-converting enzyme (ACE) inhibitor with a thiazide-like diuretic. The detection of Indapamide, Perindopril, and its active metabolite perindoprilat in human plasma or whole blood was achieved through hyphenated ultra-performance liquid chromatography-mass spectrometry (UPLC-MS/MS). Internal standards included indapamide-d3, perindopril-d4, and perindoprilat-d4. The chromatography was conducted at a column temperature of 50°C with a flow rate of 0.6 mL/min using isocratic elution, and UV detection was performed at 215 nm. The method demonstrated acceptable linearity, accuracy, and precision across concentration ranges of 1-5µg/mL for Perindopril and 10-15µg/mL for Indapamide. A statistical comparison of the proposed chromatographic method against reference methods was conducted using one-way analysis of variance, with Beer-Lambert's range established at 0-60 µg/mL.

The most commonly used mobile phases are methanol and acetonitrile, whereas the stationary phase used is a Phenomenex Luna C18 column (250 mm × 4.6 mm, 10 µm). Various parameters are collected, including LOD, LOQ, correlation coefficient and linearity, absorbance maxima, and retention time, which were within the limits specified by the ICH guidelines.

Keywords: RP-HPLC, Perindopril, Indapamide.

INTRODUCTION

Perindopril, also known chemically as (2S,3aS,7aS)-1-[(2S)-2-[[(2S)-1-ethoxy-1-oxopentan-2-yl]amino]propanoyl]-2,3,3a,4,5,6,7,7a-octahydroindole-2-carboxylic acid (fig. no. 1), is the active ingredient of an angiotensin-converting enzyme inhibitor (ACE-I). In addition, heart attacks, strokes, and kidney problems are among the various illnesses that can be treated with this[1]. It is poorly soluble in methylene chloride but easily soluble in water and 96% ethanol.

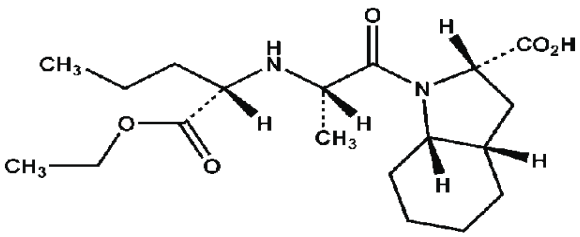

Fig No. 1: Structure of Perindopril

Indapamide, also known chemically as 4-chloro-N-(2-methyl-2, 3-dihydroindol-1-yl)-3-sulfamoylbenzamide (fig. no. 2), is a thiazide-like diuretic that has become a standard treatment for edema and hypertension associated with various cardiovascular diseases[2]. It reduces blood pressure and increases urine output by blocking the reabsorption of sodium by the kidneys distal convoluted tubules[3]. Water-insoluble, it dissolves in 96% ethanol, methanol, acetic acid, and ethyl acetate, and it dissolves very slightly in ether, chloroform, and benzene[4].

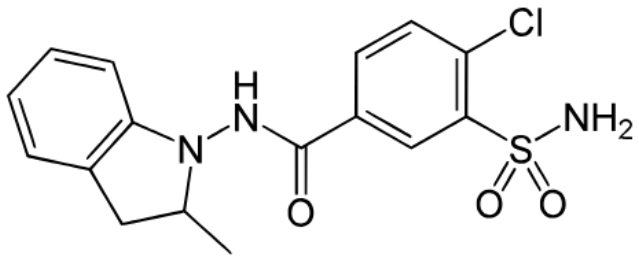

Fig. No. 2: Structure of Indapamide

Table.No.1: Analytical methods for Perindopril and Indapamide

S.No.	Author Name	Title	Name of the Journal	Chromatographic Conditions	Results
1	Jain P s[5]	RP-HPLC Assay Method for Simultaneous Determination of Perindopril Erbumine and Indapamide Combination in Bulk and Tablet Dosage Form	Journal of Pharmaceutical Research,2012	Mobile Phase:Acetonitrile: Buffer pH 2.8 (40: 60 % v/v) Stationary phase: Phenomenex Luna C18 column (250mm × 4.6mm, 10µm)λmax- 225nm Flow rate-1 .2ml/min	Perindopril R_t - 3.150min LOD- 0.120 µg/ml LOQ-0.365 µg/ml Indapamide R_t – 10 min LOD- 0.606µg/ml LOQ-1.8µg/ml R.S.D= <2.0%
2	P.S.R.CH.N .P. Varma D[6]	Validated Stability Indicating Reverse Phase HPLC Method for The Simultaneous Estimation of Perindopril and Indapamide in Pharmaceutical Dosage Forms	International Journal of Pharmacy,2013	Mobile phase: methanol = 65:35 v/v pH 3.5±0.05 Stationary phase:Hypersil BDS C18 column λmax- 215nm Flow rate-1 ml/min	Perindopril R_t - 3.53min LOD- 0.120 µg/ml LOQ-0.365 µg/ml Indapamide R_t – 4.09 min LOD- 0.606µg/ml LOQ-1.839 µg/ml Linearity range 160 to 480 µg/mL
3	B. Siva Sai Kiran[7]	Stability Indicating isocratic RP-HPLC Method Development and Validation for Indapamide and Perindopril Erbumine in pure and its combined tablet dosage Form	International Journal of Pharmaceutical Sciences and Research,2014	Mobile phase: pH 2.5 acetonitrile :60:40 v/v Stationary phase: YMC Column (150 x 4.6mm, 3µ particle size) λmax- 230nm Flow rate-0.8ml/min	Perindopril R_t -1.5min LOD- 0.07 µg/ml LOQ-0.23 µg/ml Indapamide R_t – 0.5 min LOD-2.8µg/ml LOQ-8.48 µg/ml
4	Kirtan P. Patel[8]	A new RP–HPLC method for simultaneous quantification of	Future Journal of Pharmaceutical Sciences,2020	Mobile phase: acetonitrile: methanol: water (30:20:50, v/v/v) Stationary	Perindopril linearity range 0.400–7.600 µg/ml LOD- 0.065 µg/ml

		perindopril erbumine, indapamide, and amlodipine besylate in bulk and pharmaceutical dosage form		phase:Phenomenex C-18 column (250 mm × 4.6 mm, 5 µm) pH 3.0 λmax- 215nm Flow rate-1 ml/min	LOQ-0.198 µg/ml Indapamide LOD- 0.019µg/ml LOQ-0.056µg/ml
5	Naser F AlTannak[9]	UHPLC-UV Method for Simultaneous Determination of Perindopril Arginine and Indapamide Hemihydrates in Combined Dosage Form: A Stability-Indicating Assay Method	Scientia Pharmaceutica, 2018	Mobile phase:0.01% v/v formic acid in water Stationary phase: BEH C18 (1.7 µm, 2.1 × 50 mm) λmax– 227nm Flow rate -0.3 ml/min.	Perindopril& Indapamide linearity range (20–450 g/mL) LOD- 3:1 LOQ-10:1 Relative Standard Deviation (%RSD) -0.63%
6	Yi Tao[10]	Simultaneous determination of indapamide, perindopril and perindoprilat in human plasma or whole blood by UPLC-MS/MS and its pharmacokinetic application	Journal of Pharmaceutical Analysis,2018	Mobile phase: Thermo BDS Hypersil Stationary phase: C18 column (4.6mm 100mm, 2.4mm)	Perindopril Linearity range 0.2–20ng/ml Indapamide Linearity range 1–250ng/ml
7	Pawar Seemarani[11]	Development and Validation of UV Spectrophotometric Estimation of Perindopril Erbumine and Indapamide in Bulk and Tablet Dosage by using Area Under Curve Method	London Journal of Medical and HealthResearch, 2023	Perindopril λmax-208-214 nm Indapamide λmax- 239-244 nm	Perindopril Concentration range 1-5 µg/ml Indapamide Concentration range 10-50 µg/ml Recovery study 99-101%
8	Erica Alves[12]	Development and Validation of a Novel UV Spectrophotometric Method for Simultaneous Analysis of Amlodipine, Indapamide and Perindopril	Indian journal of pharmaceutical analysis,2020	Perindopril λmax=204nm Indapamide λmax=245 nm Beer Lambert's range0-60 µg/ml	Perindopril LOD- 1.860µg/ml LOQ-5.60µg/ml Indapamide LOD-0.630µg/ml LOQ-1.920 µg/ml Correlation coefficient (r2) of ≥0.999.
9	John Chalmers[13]	Effects of Combination of Perindopril, Indapamide, and Calcium Channel Blockers in Patients with Type 2 Diabetes Mellitus	Ahajournals, 2025	perindopril–indapamide (4/1.25 mg) CCB at baseline compared with 5% (−12% to 20%)	CCB at baseline compared with 5% (−12% to 20%)among those without CCB (P homogeneity 0.02)
10	Xin Zheng[14]	Simultaneous determination of	Journal of Chromatography	Stationary phase: X-terra MS	Perindopril ion transitions

		indapamide, perindopril and its active metabolite perindoprilat in human plasma using UPLC-MS/MS method	B, 2021	C_{18} (2.1 mm × 150 mm, 3.5 μm) with isocratic elution Linearity range: 0.250-50.0 ng/mL	at *m/z* 369.165 → 172.0 Indapamide 366.010 → 132.100
11	Nevin Erk[15]	Comparison of Spectrophotometric and an LC method for the determination perindopril and indapamide in pharmaceutical formulations	Journal of Pharmaceutical and Biomedical Analysis, 2001	Mobile Phase: phosphate buffer pH 2.4 and acetonitrile (7:3 v/v) Linearity range for Perindopril and Indapamide was 5.0–70.0 and 8.0–35.0 μg ml^{-1}	Linear calibration graphs of first derivative values at 225.7 and 255.4 nm for Perindopril and Indapamide

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