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Chromatographic Advances in Antihypertensive Drug Analysis: A Comprehensive Review

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Abstract

Hypertension remains a leading cause of cardiovascular morbidity and mortality worldwide, necessitating the development of effective therapeutic agents and robust analytical methods to ensure their quality and efficacy. This review focuses on chromatographic advancements for the estimation of key antihypertensive drugs: Indapamide, Amlodipine, Atenolol, and Azilsartan. These agents represent diverse pharmacological classes, including diuretics, calcium channel blockers, beta-blockers, and angiotensin II receptor blockers, each with unique mechanisms of action and analytical challenges.Chromatographic techniques, particularly high-performance liquid chromatography (HPLC) and ultra-performance liquid chromatography (UPLC), have become indispensable in the qualitative and quantitative analysis of these drugs. The review highlights single-drug estimation, simultaneous analysis in fixed-dose combinations, stability-indicating methods, and bioanalytical applications. Recent advancements, including the use of modern stationary phases, green chromatography practices, and coupled detection techniques such as LC-MS/MS, have enhanced the sensitivity, specificity, and environmental sustainability of these methods.This comprehensive review aims to provide insights into the chromatographic methodologies applied to Indapamide, Amlodipine, Atenolol, and Azilsartan, addressing analytical challenges, regulatory requirements, and future directions. It serves as a valuable resource for researchers and pharmaceutical scientists engaged in the development and validation of innovative analytical approaches for antihypertensive drugs.

Keywords: Analytical method, Review on analytical method, Antihypertensive agent, HPLC method, HPTLC method

1. Introduction

The prevalence of hypertension, commonly referred to as high blood pressure, is a significant global health concern affecting millions of individuals worldwide. Characterized by persistently elevated arterial pressure, hypertension is a major risk factor for cardiovascular diseases, including heart attack, stroke, and kidney failure. The management of hypertension often involves the use of antihypertensive agents, which target various physiological pathways to reduce blood pressure and mitigate associated risks. Among these, indapamide, amlodipine, atenolol, and azilsartan have emerged as crucial drugs due to their distinct pharmacological actions and efficacy in diverse patient populations[1].

Indapamide, a thiazide-like diuretic, is widely prescribed for its ability to promote diuresis and sodium excretion, thus lowering blood pressure. It is often favored for its dual effects on blood pressure reduction and minimal impact on serum lipid levels, making it suitable for patients with metabolic syndrome[2,3]. Amlodipine, a calcium channel blocker, is extensively used for its potent vasodilatory effects, which reduce systemic vascular resistance and improve arterial compliance[4,5]. Atenolol, a beta-adrenergic blocker, functions by decreasing cardiac output and sympathetic stimulation, making it particularly effective in patients with coexisting cardiac arrhythmias[6]. Azilsartan, an angiotensin II receptor blocker (ARB), represents a newer generation of antihypertensive agents that effectively inhibit the renin-angiotensin-aldosterone system (RAAS), a key regulator of blood pressure and vascular tone[7].

Given the critical role of these antihypertensive agents in managing hypertension and associated comorbidities, the development and validation of robust analytical methods for their quantification in pharmaceutical formulations and biological matrices are of paramount importance. Accurate and reliable estimation of these drugs is essential for quality control, pharmacokinetic studies, and ensuring therapeutic efficacy and safety. Chromatographic techniques, particularly high-performance liquid chromatography (HPLC), have become the gold standard in the analytical landscape due to their precision, sensitivity, and versatility[8–11].

Chromatographic techniques, including high-performance liquid chromatography (HPLC) and ultra-performance liquid chromatography (UPLC), have emerged as powerful tools for the qualitative and quantitative analysis of drugs. Their precision, sensitivity, and versatility make them the preferred choice for analyzing antihypertensive agents. Moreover, these techniques have undergone significant advancements over the years, enabling the simultaneous estimation of multiple drugs in fixed-dose combinations, stability studies under various stress conditions, and the detection of impurities at trace levels[12,13].

This review aims to provide a comprehensive overview of chromatographic methods developed for the estimation of indapamide, amlodipine, atenolol, and azilsartan. Emphasis is placed on the evolution of these methods, highlighting innovations in stationary phases, mobile phase compositions, detection techniques, and method validation parameters. Furthermore, the review underscores the importance of stability-indicating methods and forced degradation studies in ensuring the robustness of analytical procedures under various stress conditions.

2. Chromatographic Techniques in Antihypertensive Drug Analysis

The quantification of pharmaceutical compounds often requires sophisticated analytical techniques capable of resolving complex mixtures and detecting trace-level analytes. Chromatography, a separation technique based on the differential partitioning of analytes between stationary and mobile phases, is widely employed in pharmaceutical analysis. High-performance liquid chromatography (HPLC) and ultra-performance liquid chromatography (UPLC) have become indispensable tools due to their superior resolution, shorter analysis times, and ability to handle diverse analyte chemistries.

HPLC techniques for antihypertensive drugs often employ reverse-phase configurations, where a non-polar stationary phase (e.g., C18 columns) is used in conjunction with a polar mobile phase. The choice of mobile phase is critical and typically involves a combination of aqueous buffers and organic solvents such as acetonitrile or methanol. Gradient elution techniques are often employed to achieve optimal separation of drug components and their impurities. Detection methods such as UV-Vis spectrophotometry, fluorescence detection, and mass spectrometry (MS) further enhance the sensitivity and selectivity of chromatographic analyses[14,15].

2.1 Indapamide[16,17]

Indapamide is a thiazide-like diuretic used primarily for the treatment of hypertension and edema associated with heart failure. Its dual action as a diuretic and vasodilator contributes to its antihypertensive efficacy. The drug exhibits a high degree of lipophilicity, allowing it to penetrate vascular smooth muscle cells effectively. Analytical challenges for Indapamide arise from its low therapeutic dose and the need to detect impurities and degradation products.Indapamide’s analytical profile is characterized by its relatively low molecular weight and hydrophilic nature, making it amenable to chromatographic separation using reverse-phase HPLC. Studies have focused on optimizing mobile phase pH and ionic strength to achieve sharp peak resolution. Stability-indicating methods have been developed to assess the degradation of indapamide under acidic, alkaline, oxidative, and thermal stress conditions. Forced degradation studies are particularly valuable in understanding the stability profile of indapamide and ensuring the reliability of its pharmaceutical formulations. The HPLC and HPTLC method for the estimation of antihypertensive agent shown in Table 1 and table 2 respectively.

2.2 Amlodipine[4,5,18]

Amlodipine, a dihydropyridine calcium channel blocker, is widely prescribed for hypertension and angina. It works by inhibiting calcium ion influx in vascular smooth muscle and cardiac muscle, leading to vasodilation and reduced cardiac workload[19]. Amlodipine's stability profile, including its susceptibility to photo and oxidative degradation, necessitates stability-indicating chromatographic methods for its analysis.As a calcium channel blocker with a long half-life, amlodipine presents unique challenges in analytical quantification due to its susceptibility to photodegradation. Chromatographic methods often incorporate photostability testing to evaluate its degradation products under UV light exposure. Mobile phase optimization, including the use of buffers like phosphate or acetate, plays a critical role in achieving consistent retention times and peak shapes. Dual-wavelength detection techniques are sometimes employed

to differentiate amlodipine from its impurities and degradation products[5].The HPLC and HPTLC method for the estimation of antihypertensive agent shown in Table 1 and table 2 respectively.

2.3 Atenolol[3,6]

Atenolol, a cardioselective beta-1 adrenergic receptor blocker, is frequently used for managing hypertension, angina, and arrhythmias. Its hydrophilic nature and renal elimination make it distinct from other beta-blockers. Analytical methods for Atenolol often involve detecting its metabolites and ensuring its stability under various conditions, as degradation can compromise therapeutic efficacy.Atenolol, a hydrophilic beta-blocker, is frequently analyzed using HPLC with UV detection. The polar nature of atenolol necessitates careful selection of mobile phase components to ensure adequate retention and resolution. Methods using ion-pairing agents such as tetrabutylammonium bromide have been explored to enhance chromatographic performance. Atenolol's stability under oxidative and thermal conditions is a key consideration in method validation, with forced degradation studies providing insights into its degradation pathways.The HPLC and HPTLC method for the estimation of antihypertensive agent shown in Table 1 and table 2 respectively.

2.4 Azilsartan[7,20]

Azilsartan medoxomil, an angiotensin II receptor blocker (ARB), is a newer addition to the antihypertensive drug class. It is notable for its potent antihypertensive action and favorable pharmacokinetic properties. Azilsartan's analysis requires methods capable of distinguishing it from its prodrug form and potential impurities, given its recent introduction and evolving quality standards.Azilsartan, a relatively newer antihypertensive agent, poses analytical challenges due to its complex molecular structure and potential for multiple degradation pathways. HPLC methods for azilsartan often utilize gradient elution techniques to separate the drug from its related substances and excipients. The incorporation of advanced detection technologies, such as tandem mass spectrometry (MS/MS), has enabled the precise quantification of azilsartan in biological matrices and pharmaceutical dosage forms. Stability-indicating methods are essential for evaluating azilsartan's behavior under stress conditions, including hydrolysis, oxidation, and photolysis.The HPLC and HPTLC method for the estimation of antihypertensive agent shown in Table 1 and table 2 respectively.

3. Key Considerations in Method Development

The development of chromatographic methods for antihypertensive agents involves several critical steps, including the selection of suitable chromatographic conditions, validation of analytical performance, and assessment of method robustness. The International Council for Harmonisation (ICH) guidelines serve as a framework for method validation, outlining parameters such as accuracy, precision, specificity, linearity, limit of detection (LOD), and limit of quantification (LOQ)[21,22].

Forced degradation studies are a cornerstone of stability-indicating method development, providing insights into the degradation behavior of drugs under various stress conditions. These studies not only aid in method validation but also support regulatory compliance by ensuring the stability and efficacy of pharmaceutical products throughout their shelf life. The application of statistical tools for method optimization and robustness testing further enhances the reliability of chromatographic analyses.

Table 1: HPLC method for the estimation of antihypertensive agent

Sr. No.	Title	Details	Ref. No.
1	Study of the Acidic, Basic, and Thermal Degradation Kinetics of Three Antihypertensive Drugs—Individually and in Combination	The degradation processes were studied using the previously developed reverse phase high-performance liquid chromatographic (RP-HPLC) method after exposing each drug individually, as well as the combinations of two/three drugs, to different stress factors, such as light, oxidation, acidic, basic, or neutral pH values at different temperatures. Results: The results show that PER is most unstable under basic conditions and that AML displays a negative, while IND displays a positive effect, on PER stability when combined. AML is most affected by basic conditions and oxidation, and its stability is affected by both drugs positively; IND undergoes extreme photolysis, which is positively affected by AML but negatively by PER.	[23]
2	Multivariate Analysis and Response Surface Modeling to Green Analytical Chemistry–Based RP-HPLC-PDA Method for Chromatographic Analysis of Vildagliptin and Remogliflozin Etabonate	The multivariate analysis has been carried out for the identification of critical method risk parameters (CMRPs) and critical method performance attributes (CMPAs) using principal component analysis (PCA). The identified CMRPs and CMPAs were linked with each other for optimization of the RP-HPLC-PDA method using DoE-based response surface modeling. The analytical design space (ADS) has been explored for robust chromatographic analysis of VDG and RGE. Results: The chromatographic analysis of VDG and RGE has been carried out using Shim-Pack C18 column (250 mm L, 4.6 mm	[24]

		ID, 5.0 mm PS) and isopropyl alcohol–0.1% (v/v) formic acid (FA) in water (45 + 55, v/v, pH -3.5). The developed method has been validated in accordance with ICH Q2 (R1) guidelines.	
3	Analytical Method Development and Validation for Simultaneous Estimation of Amlodipine Besylate and Indapamide by using UV VIS Spectrophotometry and RPHPLC in Bulk and Dosage Form	C-18 column with UV-detection. Acetonitrile: acetate buffer pH-5 (40: 60 % v/v) with 1.2 mL / min flow rate was selected as mobile phase.	[25]
4	A new RP–HPLC method for simultaneous quantification of perindopril erbumine, indapamide, and amlodipine besylate in bulk and pharmaceutical dosage form	The Phenomenex C-18 column (250 mm × 4.6 mm, 5 µm) was used as a stationary phase, and acetonitrile: methanol: water (30:20:50, v/v/v) was found to be optimized mobile phase which was further adjusted to pH 3.0 by utilizing 1.0% orthophosphoric acid; the flow rate kept was 1 ml/min and experiments were performed using PDA detector. The common detection wavelength for all the three APIs was found to be 215.0 nm.	[18]
5	UV-Spectrophotometric and Stability Indicating RP-HPLC Method for the Simultaneous Estimation of Amlodipine Besylate and Indapamide	For the RP-HPLC; Chromatography was carried on Shimadzu LC-20AT series HPLC; C-18 ODS bonded column (25 cm × 4.60 mm, 10 µl, 40°C) used as stationary phase; methanol: water (95:5% v/v) as mobile phase. The retention time of the AMDB and INDA were 8.780 and 2.850 min, respectively; detection at λmax 238 nm for both of drug (overlain spectra).	[26]
6	Simultaneous estimation of amlodipine besylate and indapamide in a pharmaceutical formulation by a high-performance liquid	A Brownlee C-18, 5 µm column with a mobile phase containing 0.02 M potassium dihydrogen phosphate-methanol (30+70, v/v) total pH-adjusted to 3 using o-phosphoric acid was used.	[27]

	chromatographic (RP-HPLC) method	The flow rate was 1.0 mL min -1 and effluents were monitored at 242 nm.	
7	Stability indicating RP-HPLC studies for the estimation of irbesartan and amlodipine besylate in pharmaceutical formulations and identification and characterization of degradants using LC-MS	The chromatographic separation was achieved on a Zorbax CN column using a mixture of 1 mM potassium dihydrogen phosphate (pH 3.0) and acetonitrile (70:30, v/v) as the mobile phase at a flow rate of 0.9 mL/min. Detection was carried out at 240 nm.	[28]
8	RP HPLC estimation of atenolol and indapamide in bulk and pharmaceutical dosage form simultaneously	Separation was achieved with anphenomenex C18 coloumn, 250mm x 4.6mm (particles with 5µm).A mixture of methanol and HPLC water (50:50)as mobile phase at a flow rate of 1 ml/min and the column temperature was maintained at 25˚c. Dual wavelength detector was performed at 231 nm with a run time of 10 minutes.	[29]
9	A Versatile Stability-indicating Liquid Chromatographic Method for the Simultaneous Determination of Atenolol, Hydrochlorothiazide and Chlorthalidone	In this method, the separation was accomplished through an Inertsil (R) ODS-3V C18 column (250 mm x 4.6 mm, 5 mu m), the mobile phase used was 25 mM aqueous potassium dihydrogen orthophosphate solution adjusted to pH 6.8 by using 0.1M sodium hydroxide and acetonitrile (77 : 23, v/v), the flow rate used was 1 ml/min and detection was achieved at 235 nm using UV	[30]
10	Validated RP-HPLC Method for the Determination of Indapamide in Bulk and Tablet Dosage Form	Separation was achieved on C18 column (250X4.6mm i.d.,5µm) in isocratic mode using Acetonitrile:Methanol:Water in the ratio of 40:50:10 (v/v/v) as mobile phase, pumped in to the column at flow rate of 1.0 mL min-1and the detection of eluent from the column was carried out using variable wavelength UV detector at 242 nm.	[31]
11	A validated RP-HPLC method for	Waters C18 column (250×4.6 mm, 5 µ	[32]

	simultaneous estimation of atenolol and indapamide in pharmaceutical formulations	particle size) using a mobile phase, methanol and water (adjusted to pH 2.7 with 1% orthophosphoric acid) in the ratio of 80:20. The flow rate was 1 mL/min and effluent was detected at 230 nm.	
12	Development & validation of stability indicating High Performance Liquid Chromatographic method for simultaneous estimation of atenolol & indapamide in tablet dosage form	Waters HPLC system on a L1 column (Hypersil Gold: 250mm x 4.6 mm, 5µm) using a mixture of 0.1% Triethyl Amine in water of pH 3.0 & Methanol in the ratio 30:70 v/v as mobile phase in an isocratic elution mode at a flow rate of 1.0 ml/min, at 30ºC with a load of 20µl. The detection was carried out at 240 nm.	[33]
13	Development and Validation of Stability Indicating Chromatographic Methods for Determination of Azilsartan Medoxomil in Pharmaceutical Formation	In RP-HPLC, separation was performed with Hiber® C-18 column (250 mm X 4.6 mm, 5 µm), using mobile phase methanol: acetonitrile: water (88:8:4 v/v/v) at a flow rate of 0.5 ml/min. The analyte was detected at 254 nm over a concentration range of 20 - 70 µg/ml with correlation coefficient of 0.999. In HPTLC, separation was carried out with silica gel G60 F254 aluminum sheet using acetone: toluene: ammonia (8.2:1.7:0.1 v/v/v) as a developing system	[34]
14	Stability indicating RP-HPLC method for determination of azilsartan medoxomil in pharmaceutical dosage form	The quantification was carried out using Hypersil BDSC18, 250X4.6 mm, 5µ, enhanced polar selectivity column and mobile phase comprised of potassium dihydrogen phosphate buffer pH adjusted to 4.0 ± 0.5 with orthophosphoric acid and acetonitrile in proportion of ratio 60:40 and degassed under ultrasonication. The flow rate was 1.0mL/min and the effluent was monitored at 248nm.	[35]
15	Method Development and Validation for the Determination	Separation of impurities at satisfactory level is achieved in Acquity UPLC BEH	[36]

	of Potential Impurities Present in Azilsartan medoxomil Tablets by Reverse Phase-Ultra Performance Liquid Chromatography	C18, 100 mm length x 2.1 mm id with 1.7 µm particle size column. Mobile phase A consists of 0.1% ortho phosphoric acid in water adjusted the pH to 3.0 with dilute sodium hydroxide and acetonitrile as Mobile phase B using gradient elution mode. Flow rate was kept at 0.5 mL.min-1 with a monitoring wavelength of 215 nm	

Table 2: HPTLC method for the estimation of antihypertensive agent

Sr. No.	Title	Details	Ref. No.
1	High performance thin layer chromatographic estimation of atenolol and indapamide from pharmaceutical dosage form	Atenolol and indapamide were separated on the plate coated with silica gel 60G F254 using a mixture of toluene:ethanol:acetone:acetic acid (7:2.5:3:0.3 v/v) as mobile phase. Quantification was carried out by the use of densitometer in absorbance mode at 266 nm	[37]
2	Simultaneous determination of amlodipine besylate and azilsartan mixture in human plasma utilizing high-performance thin-layer chromatography with ultraviolet detection	Reflectance/absorbance densitometry was conducted using toluene–ethyl acetate–methanol–acetone–acetic acid (6:1.5:1:0.5:1, V/V) as the mobile phase, and separation was achieved on a precoated silica gel HPTLC plate.	[38]
3	HPTLC-Densitometric Estimation of Anti-hypertensive Drug Combination Azilsartan Medoxomil and Cilnidipine in Combined Dosage Form	Pre-coated silica gel- G60 F254 aluminum sheet (100 × 100 mm, 0.2 mm layer thickness) were used as stationary phase and Ethyl Acetate: Toluene: Glacial Acetic Acid (5: 4.9: 0.1 %v/v/v) in the mixture was used as mobile phase.	[39]
4	Simultaneous estimation of azilsartan medoxomil and chlorthalidone by chromatography method using design of experiment and quality risk	Chromatographic separation was performed using silica gel GF254 as the stationary phase and toluene–methanol–ethyl acetate–formic acid (7:2:1:0.2, V/V) as the mobile phase	[40]

	management based quality by design approach	in twin-trough chamber keeping a saturation time of 15 min.	
5	Application of Chemometry and Design of Experiments to Green HPTLC Method for Synchronous Estimation of Multiple FDCs of Cilnidipine	The chromatographic separation was performed using silica gel G60 F254 as the stationary phase and toluene-ethyl acetate-methanol (6.5+2+1.5, v/v) as the mobile phase. The method was validated as per the International Council for Harmonization Q2 (R1) guideline.	[20]
6	Development and validation of HPTLC method for simultaneous determination of amlodipine besylate and metoprolol succinate in bulk and tablets	The method employed HPTLC aluminum plates precoated with silica gel 60F-254 (10×10) as the stationary phase. The solvent system consisted of toluene:ethyl acetate:methanol:triethylamine (4:1:1:0.4 v/v/v). The system was found to give a compact spot for amlodipine besylate (R f = 0.39±0.02) and metoprolol succinate (R f = 0.59±0.02). Densitometric analysis of amlodipine besylate and metoprolol succinate was carried out in the absorbance mode at 254 nm.	[41]
7	Development and validation of HPTLC method for the simultaneous estimation of amlodipine besylate and atorvastatin calcium in combined dosage form	Chromatographic separation of the drugs were performed on aluminum plates precoated with silica gel 60 F254 used as stationary phase and the chromatogram was developed using Ethyl acetate: Methanol: Ammonia (7.5: 2: 0.5 %v/v/v) as mobile phase. Amlodipine besylate and Atorvastatin calcium showed Rf values 0.50 ± 0.02 and 0.26 ± 0.02 respectively. Densiometric analysis of both the drugs was carried out in the absorbance mode at 365 nm.	[42]
8	Simultaneous HPTLC analysis of atenolol and indapamide in tablet formulation	Chromatographic separation was achievedon aluminum foil plates precoated with silica gel 60F254, with toluene: ethyl acetate: methanol: ammonia5:3:3:0.1 (v/v) as mobile phase.	[43]

		Detection was performed densitometrically at 229 nm.	
9	Validated HPTLC methods for determination of some selected antihypertensive mixtures in their combined dosage forms	For Mixture II, the mobile phase was chloroform–methanol–ammonia in the volume ratio 8:2:0.1. Detection was performed at 254nm for valsartan and hydrochlorothiazide, and at 365nm for amlodipine.	[44]
10	Development and validation of stability-indicating HPTLC method for the estimation of perindopril and Indapamide	The method was based on the separation of two drugs on plates precoated with silica gel 60 F254using Dichloromethane: Methanol: Glacial acetic acid in the ratio of 9.5:0.5:0.1 v/v/v as mobile phase followed by scanning in absorbance mode at 215 nm.	[45]
11	Simultaneous determination of amlodipine besylate and azilsartan mixture in human plasma utilizing high-performance thin-layer chromatography with ultraviolet detection		

3.1 Emerging Trends and Future Perspectives

Advances in chromatographic technology, including the development of superficially porous particles (SPPs) and core-shell columns, have revolutionized the analytical landscape. These innovations enable faster analyses with improved resolution and reduced solvent consumption. The integration of chromatographic techniques with hyphenated systems such as HPLC-MS/MS and HPLC-FTIR has expanded the scope of pharmaceutical analysis, allowing simultaneous quantification and structural elucidation of analytes.

As the field of analytical chemistry continues to evolve, the focus is shifting towards green analytical chemistry (GAC) principles, which emphasize the reduction of hazardous chemicals and waste in analytical processes. The use of eco-friendly solvents and miniaturized chromatographic systems aligns with the broader goals of sustainability and environmental stewardship.

4. Conclusion

The estimation of antihypertensive agents such as indapamide, amlodipine, atenolol, and azilsartan through chromatographic methods is a critical aspect of pharmaceutical research and quality control. Advances in chromatographic techniques and method validation protocols have significantly enhanced the accuracy and reliability of drug analysis. This review underscores the importance of stability-indicating methods and highlights emerging trends that promise to shape the future of analytical methodologies. By bridging the gap between analytical innovation and therapeutic application, chromatographic methods continue to play a pivotal role in ensuring the safety and efficacy of antihypertensive drugs.

5. Reference:

[1] Basile J, Bloch MJ, Bakris GL, White WB, Kunins L, John P Forman. Overview of hypertension in adults - UpToDate. Up To Date 2019:1–56.

[2] Indapamide | C16H16ClN3O3S | CID 3702 - PubChem n.d.

[3] Divitiis O De, Somma S Di, Petitto M, Fazio S, Ligouri V. Indapamide and atenolol in the treatment of hypertension: Double-blind comparative and combination study. Curr Med Res Opin 1983;8:493–500. https://doi.org/10.1185/03007998309109788.

[4] Carey RM, Moran AE, Whelton PK. Treatment of Hypertension: A Review. JAMA 2022;328:1849–61. https://doi.org/10.1001/jama.2022.19590.

[5] Shah JP, Akabari AH, Patel S, Surati J. Amlodipine: A Review of Characteristics, Properties, Analytical Methods and Impact in the Green Chemistry. Int J Pharm Sci Invent 2022;11:30–8.

[6] Rehman B, Sanchez DP, Patel P, Shah S. Atenolol. XPharm Compr Pharmacol Ref 2024:1–6. https://doi.org/10.1016/B978-008055232-3.61259-0.

[7] Angeloni E. Azilsartan medoxomil in the management of hypertension: An evidence-based review of its place in therapy. Core Evid 2016;11:1–10. https://doi.org/10.2147/CE.S81776.

[8] Umang Shah, Ashok Akabari, Amit Kumar Baser AP. Complete Companion for GPAT and Other Entrance Examination in Pharmacy | With Previous Years Solved Question Paper | Fourth Edition | By Pearson. Pearson Education India; 2019.

[9] Akabari AH, Mistry P, Patel SK, Surati J, Patel SP, Shah U. Simultaneous Estimation of Fimasartan potassium trihydrate and Atorvastatin calcium with Greenness Assessment using HPLC and UV Spectrophotometric Methods. Green Anal Chem 2023;6:100067. https://doi.org/10.1016/j.greeac.2023.100067.

[10] Patel MM, Patel D, Shah U, Kachhiya HM. A Simple, Precise, and Sensitive RP-HPLC Method for Quantification of Teneligliptin Hydrobromide and Metformin Hydrochloride: Development and Validation. Res J Pharm Technol 2023;16:495–501. https://doi.org/10.52711/0974-360X.2023.00084.

[11] Shah U, Patel S, Raval M. Stability Indicating Reverse Phase HPLC Method for Estimation of Rifampicin and Piperine in Pharmaceutical Dosage Form. Curr Drug Discov Technol 2017;15:54–64. https://doi.org/10.2174/1570163814666170619092224.

[12] Lalhriatpuii T. HPTLC fingerprint in herbal drug formulations. Herb. Med. India Indig. Knowledge, Pract. Innov. its Value, Springer Singapore; 2019, p. 337–62. https://doi.org/10.1007/978-981-13-7248-3_22.

[13] Nikolin B, Imamović B, Medanhodzić-Vuk S, Sober M. High perfomance liquid chromatography in pharmaceutical analyses. Bosn J Basic Med Sci 2004;4:5–9. https://doi.org/10.17305/BJBMS.2004.3405.

[14] Akabari AH, Surati J, Patel S, Pathak B, Patel A, Patel C, et al. Development and validation of high-performance thin layer chromatographic method for simultaneous quantitation of novel combination perindopril erbumine and moxonidine hydrochloride. Sep Sci Plus 2023:2300051. https://doi.org/10.1002/SSCP.202300051.

[15] Akabari AH, Gajiwala H, Patel SK, Surati J, Solanki D, Shah K V, et al. Stability-Indicating TLC-Densitometric and HPLC Methods for Simultaneous Determination of Teneligliptin and Pioglitazone in Pharmaceutical Dosage Forms with Eco-Friendly Assessment. J Chromatogr Sci 2024. https://doi.org/10.1093/CHROMSCI/BMAE038.

[16] Mandić-Kovačević N, Kasagić-Vujanović I, Popović Bijelić A. Analysis of Fixed-Dose Combination of Three Antihypertensive Drugs by a Green and Quality by Design Approach. J Chromatogr Sci 2023;61:256–68. https://doi.org/10.1093/CHROMSCI/BMAC044.

[17] Sassard J, Bataillard A, McIntyre H. An overview of the pharmacology and clinical efficacy of indapamide sustained release. Fundam Clin Pharmacol 2005;19:637–45. https://doi.org/10.1111/j.1472-8206.2005.00377.x.

[18] Patel KP, Chhalotiya UK, Kachhiya HM, Patel JK. A new RP–HPLC method for simultaneous quantification of perindopril erbumine, indapamide, and amlodipine besylate in bulk and pharmaceutical dosage form. Futur J Pharm Sci 2020 61 2020;6:1–9. https://doi.org/10.1186/S43094-020-00092-4.

[19] Meghna P, Nehal S, Ashok A, Saralai M, Sutariya K. Simultaneous Estimation of Amlodipine Besylate and Indapamide using Multi-Component Mode of Analysis. Inven Rapid Pharm Anal Qual Assur 2013.

[20] Prajapati P, Tailor P, Shahi A, Acharya A, Shah S. Application of Chemometry and Design of Experiments to Green HPTLC Method for Synchronous Estimation of Multiple FDCs of Cilnidipine. J AOAC Int 2022;105:1491–501. https://doi.org/10.1093/jaoacint/qsac056.

[21] Nivetha V, Vijey Aanandhi, M Gandhimathi R. Validation of a new analytical method for the RP-HPLC quantitative analysis of recombinant human insulin. Ann Phytomedicine 2023;12:560–4.

[22] Biswas P, Chaithanya Sudha P, Ranganath M, Varun H, Eresh Kumaran P, Kavitha. A novel stability indicating RP-HPLC method for the simultaneous determination of dapagliflozin and vildagliptin in tablet dosage forms. Ann Phytomedicine 2023;12:874–81.

[23] Mandić-Kovacević N, Kasagić-Vujanović I, Gatarić B, Škrbić R, Bijelić AP. Study of the Acidic, Basic, and Thermal Degradation Kinetics of Three Antihypertensive Drugs—Individually and in Combination. Pharmaceutics 2024;16:1410. https://doi.org/10.3390/PHARMACEUTICS16111410.

[24] Prajapati P, Prajapati B, Pulusu VS, Shah S. Multivariate Analysis and Response Surface Modeling to Green Analytical Chemistry–Based RP-HPLC-PDA Method for Chromatographic Analysis of Vildagliptin and Remogliflozin Etabonate. J AOAC Int 2023;106:601–12. https://doi.org/10.1093/jaoacint/qsad013.

[25] Kumari TP, Kumar BT, Malothu N. Analytical Method Development and Validation for Simultaneous Estimation of Amlodipine Besylate and Indapamide by using UV VIS Spectrophotometry and RPHPLC in Bulk and Dosage Form. J Pharm Res Int 2021;33:3205–39. https://doi.org/10.9734/jpri/2021/v33i60b34998.

[26] Mahant B Das, Rajoriya V, Jain RK, Kashaw V. UV-Spectrophotometric and Stability Indicating RP-HPLC Method for the Simultaneous Estimation of Amlodipine Besylate and Indapamide. Anal Chem Lett 2016;6:354–70. https://doi.org/10.1080/22297928.2016.1217787.

[27] Patel DB, Mehta FA, Bhatt KK. Simultaneous estimation of amlodipine besylate and indapamide in a pharmaceutical formulation by a high performance liquid chromatographic (RP-HPLC) method. Sci Pharm 2012;80:581–90. https://doi.org/10.3797/scipharm.1203-07.

[28] Bodapati K, Vaidya JR, Siddiraju S, Gowrisankar D. Stability indicating RP-HPLC studies for the estimation of irbesartan and amlodipine besylate in pharmaceutical formulations and identification and characterization of degradants using LC-MS. J Liq Chromatogr Relat Technol 2015;38:259–70. https://doi.org/10.1080/10826076.2014.903851.

[29] Babu MS, N S, N H. RP HPLC estimation of atenolol and indapamide in bulk and pharmaceutical dosage form simultaneously. Int Clin Med Case Reports J Res Artic 2023;2:1–23.

[30] Elkady EF, Fouad MA, Faquih AAE. A Versatile Stability-indicating Liquid Chromatographic Method for the Simultaneous Determination of Atenolol, Hydrochlorothiazide and Chlorthalidone. Curr Pharm Anal 2020;16:1037–51. https://doi.org/10.2174/1573412915666190523122525.

[31] Pannu HKH, Mahajan MP, Sawant SD. Validated RP-HPLC Method for the Determination of Indapamide in Bulk and Tablet Dosage Form. Der Pharma Chem 2012;4:996–1002.

[32] Tulja Rani G, Gowri Sankar D, Kadgapathi P, Satyanarayana B. A validated RP-HPLC method for simultaneous estimation of atenolol and indapamide in pharmaceutical formulations. E-Journal Chem 2011;8:1238–45. https://doi.org/10.1155/2011/121420.

[33] Patel RA, Patel MP, Raj HA, Shah N. Development and Validation of Stability Indicating High Performance Liquid Chromatographic Method for Olmesartan Medoxomil and Indapamide in Tablet Dosage Form. Asian J Res Pharm Sci 2015;5:91. https://doi.org/10.5958/2231-5659.2015.00016.8.

[34] Kher M, Bhatt V, Jani A, Sheth N. Development and Validation of Stability Indicating Chromatographic Methods for Determination of Azilsartan Medoxomil in Pharmaceutical Formation. Anal Chem Lett 2020;10:387–401. https://doi.org/10.1080/22297928.2020.1784788.

[35] Masthanamma SK, Jahnavi P. Stability indicating RP-HPLC method for determination of azilsartan medoxomil in pharmaceutical dosage form. Res J Pharm Technol 2014;7:168–72.

[36] Mantena BPV, Rao S V., Appa Rao KMC, Ramakrishna K, Srikanth Reddy R. Method Development and Validation for the Determination of Potential Impurities Present in Azilsartan

medoxomil Tablets by Reverse Phase-Ultra Performance Liquid Chromatography. Anal Chem Lett 2014;4:287–301. https://doi.org/10.1080/22297928.2014.1000966.

[37] Gupta KR, Wankhede SB, Tajne MR, Wadodkar SG. High performance thin layer chromatographic estimation of atenolol and indapamide from pharmaceutical dosage form. Asian J Chem 2007;19:4183–7.

[38] Khorshed AA, Abdelnaeem FM, Derayea SM, Oraby M, Nagy DM. Simultaneous determination of amlodipine besylate and azilsartan mixture in human plasma utilizing high-performance thin-layer chromatography with ultraviolet detection. J Planar Chromatogr - Mod TLC 2024;37:261–9. https://doi.org/10.1007/s00764-024-00300-4.

[39] Solanki DP, Solanki KH, Desai J V., Shah DA, Chhalotiya UK. HPTLC-Densitometric Estimation of Anti-hypertensive Drug Combination Azilsartan Medoxomil and Cilnidipine in Combined Dosage Form. Anal Chem Lett 2023;13:82–94. https://doi.org/10.1080/22297928.2023.2195862.

[40] Prajapati P, Patel S, Mishra A. Simultaneous estimation of azilsartan medoxomil and chlorthalidone by chromatography method using design of experiment and quality risk management based quality by design approach. J Planar Chromatogr - Mod TLC 2020;33:631–46. https://doi.org/10.1007/s00764-020-00067-4.

[41] Jain PS, Patel MK, Bari SB, Surana SJ. Development and validation of HPTLC method for simultaneous determination of amlodipine besylate and metoprolol succinate in bulk and tablets. Indian J Pharm Sci 2012;74:152–6. https://doi.org/10.4103/0250-474X.103849.

[42] Rao NM, Sankar DG. Development and validation of HPTLC method for the simultaneous estimation of amlodipine besylate and atorvastatin calcium in combined dosage form. Eurasian J Anal Chem 2016;11:155–68. https://doi.org/10.12973/ejac.2016.129a.

[43] Rao JR, Yadav SS. Simultaneous HPTLC analysis of atenolol and indapamide in tablet formulation. Pharm Glob Int J Compr Pharm 2011;9:1–4.

[44] Shaalan RA, Belal TS, El Yazbi FA, Elonsy SM. Validated HPTLC methods for determination of some selected antihypertensive mixtures in their combined dosage forms. Bull Fac Pharmacy, Cairo Univ 2014;52:225–37. https://doi.org/10.1016/j.bfopcu.2014.07.001.

[45] Bhoir V, Hibare V, Damle MC. Development and validation of stability-indicating HPTLC method for the estimation of perindopril and Indapamide. Int J Pharm Pharm Sci 2014;6:621–5.