Review Article

Azelnidipine in Hypertension Management: A Review of Analytical Techniques, Degradation Profiling, and Green Chemistry Approaches

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ABSTRACT

Azelnidipine is a third-generation dihydropyridine calcium channel blocker that is frequently used to treat essential hypertension because of its cardiometabolic profile, excellent vascular selectivity, and long-acting antihypertensive action. However, during pharmaceutical development, quality control, and regulatory evaluation, its substantial plasma protein binding, low water solubility, and vulnerability to oxidative and photolytic degradation serious analytical problems. This article offers a thorough summary of the analytical techniques used to determine azelnidipine both qualitatively and quantitatively in pharmaceutical dosage forms, biological matrices, fixed-dose combination products, and bulk drug substances. Emphasis is placed on spectrophotometric, reverse-phase high-performance liquid chromatographic (RP-HPLC), ultra-performance liquid chromatographic (UPLC), high-performance thin-layer chromatographic (HPTLC), and liquid chromatography–tandem mass spectrometric (LC–MS/MS) techniques. Stability-indicating methods, forced degradation studies, impurity profiling, and enantioselective analyses are critically discussed in accordance with ICH and regulatory guidelines. In addition, recent advancements in analytical quality by design (AQbD) and green analytical chemistry approaches aimed at improving method robustness, environmental sustainability, and regulatory compliance are highlighted. The review also identifies current limitations, research gaps, and future perspectives related to analytical standardization, bioanalytical sensitivity, and sustainable method development. Overall, this article underscores the pivotal role of validated, sensitive, and environmentally responsible analytical methodologies in ensuring the quality, safety, and therapeutic efficacy of azelnidipine throughout its product lifecycle.

Keywords: Stability-indicating methods, RP-HPLC and UPLC, LC-MS/MS, Bioanalytical method validation Analytical Quality by Design (AQbD), Green analytical chemistry.

INTRODUCTION

Azelnidipine is a third-generation dihydropyridine (DHP) calcium channel blocker with selective affinity for L-type voltage-dependent calcium channels and is widely used in the management of essential hypertension[1]. It was originally developed in Japan and exhibits a slow onset and long-acting antihypertensive effect, which contributes to effective blood pressure control with minimal reflex tachycardia compared to earlier DHP calcium channel blockers[1,2]. This favourable hemodynamic profile is attributed to its high vascular tissue selectivity and sustained receptor binding[2].

Clinical studies have demonstrated that azelnidipine significantly reduces both systolic and diastolic blood pressure in patients with mild-to-moderate hypertension[1,3]. In addition to its antihypertensive efficacy, azelnidipine has been reported to exert cardioprotective and antioxidant effects, including suppression of oxidative stress and improvement of vascular endothelial function, as evidenced in both experimental and clinical studies[3,4].

Beyond blood pressure reduction, emerging evidence suggests that azelnidipine may offer metabolic advantages, such as improved insulin sensitivity and anti-inflammatory effects, distinguishing it from other calcium channel antagonists and supporting its potential role in patients with hypertension associated with metabolic disorders[5].

Physicochemical properties relevant to analysis of Azelnidipine

The physicochemical characteristics of azelnidipine play a crucial role in determining its analytical behaviour, method development, sample preparation, and chromatographic performance. These properties significantly influence solubility, stability, extraction efficiency, and detection sensitivity, which are critical parameters for reliable qualitative and quantitative analysis.

Azelnidipine is a crystalline dihydropyridine calcium channel blocker with the molecular formula $C_{33}H_{34}N_4O_6$ and a molecular weight of approximately 582.7 g/mol. It appears as a yellow to off-white powder and exhibits poor aqueous solubility, a characteristic common to highly lipophilic dihydropyridine derivatives[1,2]. Due to its low solubility and high membrane permeability, azelnidipine is categorized as a Biopharmaceutics Classification System (BCS) Class II drug, which has direct implications for dissolution behaviour and analytical sample preparation[6].

Structurally, azelnidipine contains ester functional groups, a dihydropyridine ring, and a substituted aromatic moiety, all of which contribute to its UV absorbance characteristics and chromatographic retention behaviour[1]. These

functional groups also render the molecule susceptible to hydrolytic and oxidative degradation, making stability-indicating analytical methods essential during formulation development and quality control[7].

Azelnidipine exhibits a melting point in the range of 120–126°C and has a pKa of approximately 7.8–8.0, indicating partial ionization near physiological pH[1,2]. This pKa value influences its ionization efficiency in LC–MS analysis and extraction behaviour in biological matrices. The drug is sparingly soluble in water, slightly soluble in alcohols, and freely soluble in organic solvents, which guides solvent selection for analytical method development[6,7].

Due to its high lipophilicity and extensive plasma protein binding, azelnidipine demonstrates strong tissue affinity and slow pharmacokinetic distribution. These characteristics can pose analytical challenges during bioanalytical estimation, necessitating optimized extraction procedures and sensitive detection techniques[8].

Bioanalytical methods of Azelnidipine

Bioanalytical methods play a crucial role in the determination of azelnidipine in biological matrices such as human plasma and serum for pharmacokinetic, bioavailability, and bioequivalence studies. Due to the low circulating concentrations and high plasma protein binding of azelnidipine, highly sensitive and selective analytical techniques are required. Liquid chromatography coupled with tandem mass spectrometry (LC–MS/MS) is the most widely employed bioanalytical approach, offering excellent sensitivity, specificity, and rapid analysis. Validated LC–MS/MS methods using protein precipitation or liquid–liquid extraction have demonstrated good linearity, accuracy, and precision over a wide concentration range, making them suitable for clinical pharmacokinetic studies[8,9]. Earlier bioanalytical studies also employed liquid chromatography–based methods with non-tandem detection for the determination of azelnidipine in human plasma for pharmacokinetic evaluation; however, these approaches exhibited lower sensitivity and longer chromatographic run times compared with modern LC–MS/MS techniques[10].

Enantioselective bioanalytical methods have been developed to quantify azelnidipine enantiomers in plasma, providing insight into stereoselective pharmacokinetics[11]. These bioanalytical methods have been successfully applied to assess absorption, distribution, metabolism, and elimination characteristics of azelnidipine in both preclinical and clinical settings, supporting dose optimization and therapeutic monitoring[12]. Overall, LC–MS/MS-based bioanalytical methods remain the gold standard for azelnidipine quantification in biological samples.

UV–visible spectrophotometric detection in Azelnidipine

UV detection is one of the most widely employed techniques in reversed-phase high-performance liquid chromatography (RP-HPLC) and ultra-performance liquid chromatography (UPLC) methods for the analysis of azelnidipine, owing to its strong UV-absorbing characteristics. Azelnidipine exhibits significant absorbance in the wavelength range of 254–260 nm, primarily due to the presence of aromatic rings and conjugated systems in its molecular structure, which confirms its UV-active nature and enables sensitive and reliable detection during chromatographic separation. Several validated stability-indicating analytical methods have utilized UV detection to quantify azelnidipine and investigate its degradation behaviour under oxidative, acidic, alkaline, and photolytic stress conditions, highlighting the effectiveness of UV-based detection in monitoring assay values, degradation kinetics, and photostability profiles for routine quality control and regulatory analysis[13,14]. Furthermore, UV detection has been successfully applied in the analysis of combination drug products, including the simultaneous estimation of azelnidipine with other antihypertensive agents such as Olmesartan, Medoxomil and Telmisartan, where adequate sensitivity, reproducibility, and robustness were achieved for assay determination and content uniformity testing[13,15]. Even in advanced analytical approaches such as chiral LC–MS, UV detection continues to play a supportive role during method development and preliminary screening, underscoring its continued relevance in analytical workflows[8].

In addition to chromatographic techniques, UV–visible spectrophotometric methods for azelnidipine have been extensively documented as simple, rapid, cost-effective, and dependable techniques for the quantitative determination of antihypertensive drugs in pharmaceutical formulations. A validated UV spectrophotometric method for azelnidipine was established by scanning in the wavelength range of 200–400 nm, wherein azelnidipine was found to be moderately soluble in methanol and freely soluble in acetone, exhibiting maximum absorbance at approximately 257 nm when acetone was used as the diluent. The method demonstrated linearity over a concentration range of 2–14 µg/mL and was validated in accordance with ICH guidelines for linearity, range, accuracy, precision, specificity, robustness, limit of detection (LOD), and limit of quantification (LOQ), with acceptable percent relative standard deviation (%RSD) values observed in both intra- and inter-day precision studies and satisfactory recoveries at 50%, 100%, and 150% levels[12].

Reverse-Phase HPLC methods for the analysis of Azelnidipine

Reverse-phase high-performance liquid chromatography (RP-HPLC) has emerged as a robust, reliable, and widely accepted analytical technique for the quantitative determination of azelnidipine in bulk drug and pharmaceutical dosage forms[15,16]. However, validated stability-indicating RP-HPLC methods, particularly for azelnidipine in combination formulations, remain limited[16,17]. Early stability-indicating RP-HPLC methods demonstrated efficient chromatographic performance using a C18 column with a mobile phase composed of

acetonitrile and methanol (30:70 v/v), delivered at a flow rate of 1.0 mL/min, and UV detection at 280 nm. These methods exhibited good linearity over the concentration range of 20–80 ppm, with high correlation coefficients and compliance with ICH Q2(R1) requirements for linearity, accuracy, precision, specificity, and robustness. Recovery studies in tablet formulations showed percent relative standard deviation (%RSD) values below 1%, confirming excellent accuracy, precision, and reproducibility[16].

Forced degradation studies conducted under acidic, basic, thermal, and oxidative stress conditions revealed that azelnidipine remained stable under acidic, basic, and thermal environments, while significant degradation was observed only under oxidative stress[7,16]. The developed RP-HPLC methods demonstrated effective separation of azelnidipine from its degradation products, confirming their stability-indicating capability and suitability for stability assessment[15,16]. Method implementation using a Shimadzu HPLC system equipped with an LC-20AD pump, SPD-20A photodiode array detector, and SIL-20ACHT injector further supported method robustness. Validation studies showed strong linearity over the 5–30 µg/mL range ($r^2 \approx 0.99$), acceptable sensitivity with defined limits of detection and quantification, and solution stability for at least 5 h at room temperature. System suitability parameters, including column efficiency, resolution, and peak symmetry, were within acceptable limits, confirming the reliability and reproducibility of the analytical system[16].

More recently, Analytical Quality by Design (AQbD)–guided RP-HPLC methods have been developed to enhance method robustness, regulatory compliance, and environmental sustainability for the determination of azelnidipine alone or in fixed-dose combination with chlorthalidone[17]. These approaches involve systematic definition of the Analytical Target Profile (ATP), identification of critical quality attributes (CQAs), and evaluation of critical method parameters (CMPs) using structured risk assessment tools such as Ishikawa fishbone analysis, failure mode and effect analysis (FMEA), Plackett–Burman screening, and central composite design optimization. Multivariate modeling identified mobile phase composition, flow rate, and modifier concentration as the most influential factors governing chromatographic performance.

Optimized AQbD-based RP-HPLC methods typically employ a C18 column with a simple isocratic mobile phase consisting of acetonitrile combined with methanol or aqueous acidic modifiers, operating at a flow rate of approximately 1.0 mL/min, resulting in sharp and symmetrical azelnidipine peaks with retention times around 3.2 min[17]. Forced degradation studies confirmed the stability-indicating nature of these methods under acidic, basic, oxidative, thermal, hydrolytic, and photolytic conditions, with particular sensitivity observed under oxidative stress[17,18]. Furthermore, the application of Green Analytical Chemistry (GAC) principles, evaluated using tools such as the AGREE metric, demonstrated reduced solvent consumption, simplified mobile phase composition, and lower waste generation[17].

In addition to conventional stability-indicating assays, specialized chromatographic approaches such as chiral RP-HPLC and bioanalytical LC methods have been reported for the enantiomeric separation and plasma quantification of azelnidipine, further extending its analytical characterization[8,11].

Collectively, these conventional, AQbD-guided, stability-indicating, and advanced RP-HPLC methods provide fast, sensitive, reproducible, and environmentally sustainable analytical approaches for routine quality control, assay determination, stability evaluation, and pharmacokinetic analysis of azelnidipine-containing pharmaceutical formulations[8,16].

Analytical methods for combination products of Azelnidipine

In addition to individual drug analysis, various analytical methodologies have been developed for the concurrent estimation of azelnidipine in fixed-dose combination (FDC) products with other antihypertensive agents, thereby ensuring quality control of multicomponent formulations. One of the most frequently cited methods is a validated stability-indicating RP-HPLC technique for the simultaneous determination of azelnidipine and olmesartan. This method achieves effective chromatographic separation and resolution of both drugs and their degradation products, with quantitation based on UV detection at 260 nm and excellent validation parameters such as linearity, precision, and specificity[15].

For the simultaneous measurement of telmisartan and azelnidipine in tablet formulations, an ultra-performance liquid chromatography (UPLC) method has also been described. This approach has demonstrated high efficiency, excellent linearity, and robust accuracy, supporting UPLC–UV as a potent tool for combination medication analysis[14].

In addition to individual drug analysis, several analytical techniques have been developed for the simultaneous estimation of azelnidipine in fixed-dose combination products. For instance, high-performance thin-layer chromatography (HPTLC) has been effectively used to simultaneously quantify azelnidipine and chlorthalidone in synthetic mixtures, offering a cost-effective and reliable method for quality control[19]. This approach ensures accurate quantification even in the presence of multiple components, highlighting the versatility of HPTLC in combination product analysis.

Likewise, multianalyte systems, such as azelnidipine and its metabolites, have been subjected to enhanced impurity profiling using LC–MS/MS, suggesting that mass spectrometric detection after chromatographic separation remains crucial for complex combination products[9]. Finally, although less common, bioanalytical methods involving tandem mass spectrometry have also been adapted for

multianalyte quantification in biological matrices, reflecting the evolving landscape of combination drug analysis[8].

Method validation and regulatory considerations of Azelnidipine

Analytical method validation is a critical aspect of the pharmaceutical development and regulatory assessment of azelnidipine. It ensures that analytical procedures yield reliable, reproducible, and accurate results suitable for quality control, stability studies, and pharmacokinetic evaluations. Validation parameters encompass specificity, linearity, accuracy, precision, limits of detection and quantification, robustness, and system suitability testing, as delineated by internationally recognized guidelines such as ICH Q2(R1)[20].

For azelnidipine, stability-indicating chromatographic methods have been developed and validated to differentiate the drug from its degradation products under stress conditions, including acid, base, oxidative, thermal, and photolytic exposure. These methods exhibit selectivity, accuracy, and precision across relevant concentration ranges, affirming their suitability for routine analysis and regulatory compliance[15]. Forced degradation studies further elucidate the degradation pathways of azelnidipine, thereby supporting method specificity and ruggedness during long-term stability assessments and shelf-life determination.

In bioanalytical applications, LC–MS/MS and LC–ESI–MS methods have been validated for the quantification of azelnidipine in biological matrices such as human plasma. These methods typically demonstrate low limits of quantitation, good linearity, and acceptable intra- and inter-assay precision and accuracy, rendering them suitable for pharmacokinetic, bioavailability, and clinical research studies[9]. These bioanalytical validations are generally conducted in accordance with regulatory guidelines from agencies such as the FDA, EMA, and ICH, which emphasize rigorous evaluation of matrix effects, recovery, and stability under various sample handling conditions.

Regulatory frameworks necessitate comprehensive documentation of all validation experiments, including analytical conditions, results, statistical evaluations, and justifications for acceptance criteria. Such documentation supports regulatory submissions, batch release certification, and post-approval modifications to analytical methods[10]. Ultimately, strict adherence to validated analytical procedures and regulatory expectations ensures high-quality azelnidipine products and safeguards patient safety by ensuring accurate drug quantification throughout the production process.

Comparative assessment of analytical methods of Azelnidipine

Numerous analytical methodologies have been developed and validated for both the qualitative and quantitative assessment of azelnidipine in pharmaceutical formulations and biological matrices. These methodologies vary in terms of sensitivity, specificity, complexity of sample preparation, throughput, and regulatory compliance suitability. High-performance liquid chromatography (HPLC) methods are extensively utilized for routine quality control of azelnidipine in bulk drug and dosage forms due to their simplicity, reproducibility, and cost-effectiveness. Reversed-phase HPLC with UV detection offers acceptable sensitivity and linearity, rendering it suitable for assay determination, stability studies, and degradation profiling[15]. However, these methods may lack adequate sensitivity for trace-level quantification in biological matrices.

Liquid chromatography–tandem mass spectrometry (LC–MS/MS) methods provide significantly enhanced sensitivity and selectivity, facilitating accurate quantification of azelnidipine in complex biological samples such as human plasma. These methods are particularly valuable for pharmacokinetic, bioavailability, and bioequivalence studies, where low detection limits and minimal matrix interference are essential[9]. Liquid chromatography coupled with mass spectrometric detection has also been employed for the enantioselective and stereospecific determination of azelnidipine, allowing precise quantification at low concentration levels while enhancing analytical specificity. Such methods are advantageous for understanding drug disposition and stereochemical behaviour in biological systems[8].

Ultra-performance liquid chromatography (UPLC) has emerged as a rapid and efficient alternative to conventional HPLC, offering shorter run times, improved resolution, and reduced solvent consumption. UPLC-based methods have demonstrated excellent performance in the simultaneous estimation of azelnidipine in fixed-dose combinations, making them suitable for high-throughput pharmaceutical analysis[14].

Additionally, stability-indicating chromatographic methods incorporating forced degradation studies play a crucial role in identifying degradation pathways and ensuring method robustness. These validated approaches support regulatory compliance and ensure consistent quality throughout the product lifecycle[20].

Forced degradation, impurity profiling, and stability evaluation of Azelnidipine

Forced degradation and impurity profiling studies of azelnidipine (AZD), conducted in accordance with ICH guidelines, play a crucial role in assessing its intrinsic stability, identifying degradation pathways, and establishing stability-indicating analytical methods. AZD bulk drug and tablet formulations have been subjected to acidic, alkaline, oxidative, hydrolytic, thermal, and photolytic stress conditions. Acidic and alkaline degradation using dilute hydrochloric acid and sodium hydroxide, respectively, along with hydrolytic stress at elevated temperatures, demonstrated chemical instability under extreme pH and moisture conditions. Oxidative

degradation using hydrogen peroxide, as well as thermal and photolytic exposure, further confirmed the susceptibility of AZD to multiple degradation pathways, as evidenced by a reduction in the parent drug peak and the appearance of additional chromatographic peaks[7,18].

High-performance liquid chromatography (HPLC) has been extensively employed to separate AZD from its impurities and degradation products, while hyphenated techniques such as LC–MS and LC–MS/MS have enabled structural elucidation of degradation products and mechanistic understanding of degradation pathways. Oxidative degradation predominantly follows radical-initiated mechanisms, leading to ester cleavage and oxidation of the dihydropyridine ring, with degradation products characterized using mass spectrometric fragmentation patterns[7,20]. Photostability studies revealed significant light sensitivity of azelnidipine, highlighting the need for light-protective formulations and validated impurity monitoring[18].

Chemical kinetic studies under acidic and alkaline conditions provided insights into the rate and extent of degradation, supporting stability profiling and shelf-life estimation. Oxidative stress resulted in the formation of a dehydrogenated degradation product, which was synthesized, isolated, and structurally characterized using mass spectrometry[20]. Quantification of AZD was achieved using validated calibration curves with good linearity, and tablet analysis was performed following methanolic extraction. The analytical methods were validated in compliance with ICH Q2(R1) guidelines, demonstrating acceptable accuracy, precision, sensitivity, robustness, and specificity. Additionally, enantioselective chromatographic techniques have been applied to study stereochemical impurities and chiral behaviour, further emphasizing the complexity of azelnidipine impurity profiling[8,11].

Collectively, these studies provide essential data for defining acceptable impurity limits, ensuring quality control, supporting formulation development, and enabling long-term stability assessment of azelnidipine pharmaceutical products.

Green analytical chemistry approaches for Azelnidipine

Green analytical chemistry (GAC) emphasizes the development of environmentally benign, safe, and sustainable analytical methods while maintaining analytical performance. In the analysis of azelnidipine, recent approaches have focused on minimizing solvent consumption, replacing hazardous organic solvents, reducing energy usage, and simplifying sample preparation without compromising sensitivity or accuracy[21]. These principles are increasingly relevant for routine quality control and stability studies in pharmaceutical analysis.

Eco-friendly reversed-phase HPLC methods have been developed for azelnidipine by employing greener solvents such as ethanol or reduced proportions of acetonitrile, along with shorter run times and lower flow rates. Such modifications significantly decrease solvent waste and analyst exposure while maintaining adequate resolution and reproducibility[20]. Stability-indicating green chromatographic methods further align with regulatory expectations by enabling accurate quantification of azelnidipine in the presence of degradation products using optimized, less hazardous mobile phases[15].

Additionally, green bioanalytical strategies incorporate simplified sample preparation techniques, such as protein precipitation with minimal solvent volumes, reducing sample handling steps and waste generation. The integration of green principles into bioanalytical LC methods enhances sustainability while preserving sensitivity for pharmacokinetic evaluations of azelnidipine[8]. The adoption of green metrics, including analytical eco-scale and greenness assessment tools, has further facilitated objective evaluation of analytical methods, encouraging the transition toward sustainable pharmaceutical analysis[22]. Overall, green analytical chemistry approaches provide a viable and responsible framework for the analytical evaluation of azelnidipine, balancing environmental considerations with regulatory and analytical requirements.

Limitations, research gaps, and challenges of Azelnidipine

One of the major challenges associated with azelnidipine is its poor aqueous solubility and extensive first-pass metabolism, which result in low and variable oral bioavailability, thereby limiting dissolution, gastrointestinal absorption, and consistent therapeutic performance[23]. This physicochemical limitation necessitates the development of advanced formulation strategies to enhance drug absorption.

Another significant limitation is the susceptibility of azelnidipine to degradation, particularly under oxidative and photolytic conditions. Stability studies have demonstrated that azelnidipine undergoes considerable degradation when exposed to light and oxidative stress, posing challenges for formulation stability, packaging, and shelf-life management[7,18]. These degradation pathways demand robust stability-indicating analytical methods and protective formulation approaches.

From a research perspective, limited bioavailability and pharmacokinetic data are available for azelnidipine when incorporated into novel drug delivery systems, particularly nanocarriers and lipid-based formulations. While preliminary studies indicate improved performance, comprehensive in vivo and long-term clinical evaluations remain insufficient[24]. Additionally, although chiral analytical methods have been developed, the clinical relevance of stereochemical behaviour of azelnidipine remains underexplored, representing a notable research gap[8].

Furthermore, challenges persist in standardizing analytical methods across different matrices and dosage forms, particularly when addressing regulatory requirements for bioequivalence and post-approval changes. Collectively, these limitations highlight the need for further research focused on formulation optimization, advanced analytical

validation, long-term stability assessment, and comprehensive pharmacokinetic investigations to fully realize the therapeutic potential of azelnidipine.

Future perspectives of Azelnidipine

Future research on azelnidipine is expected to focus on overcoming its physicochemical and biopharmaceutical limitations to enhance therapeutic outcomes. One of the most promising directions involves the development of novel drug delivery systems such as solid lipid nanoparticles, self-micro emulsifying drug delivery systems, and gastroretentive formulations to improve solubility, bioavailability, and sustained drug release[24]. These advanced delivery platforms may help reduce dose variability and improve patient compliance in long-term antihypertensive therapy.

Another important future perspective lies in the integration of advanced analytical and bioanalytical techniques. Highly sensitive LC–MS/MS and stability-indicating HPLC methods will play a critical role in supporting pharmacokinetic studies, bioequivalence testing, and regulatory submissions, particularly for complex formulations and fixed-dose combinations[8]. The application of green analytical chemistry principles is also anticipated to expand, encouraging the development of eco-friendly, cost-effective, and regulatory-acceptable analytical methods[21].

Further investigation into the stereochemical behaviour of azelnidipine represents a valuable research opportunity. Although chiral analytical methods have been reported, the pharmacodynamic and clinical relevance of enantiomer-specific activity remains largely unexplored and may contribute to more targeted and effective therapy[11]. Additionally, future clinical studies evaluating long-term safety, cardiovascular outcomes, and comparative efficacy with newer antihypertensive agents are required to strengthen the clinical positioning of azelnidipine[20].

Overall, continued advances in formulation science, analytical methodologies, and clinical evaluation are expected to expand the therapeutic potential of azelnidipine, ensuring improved drug performance, regulatory compliance, and patient benefit.

CONCLUSION

Azelnidipine has emerged as an effective third-generation dihydropyridine calcium channel blocker; however, its successful pharmaceutical development and therapeutic application are highly dependent on robust analytical evaluation. Owing to its poor aqueous solubility and susceptibility to oxidative and photolytic degradation, precise and reliable analytical techniques are essential to ensure accurate quantification, stability assessment, and quality control of azelnidipine across various dosage forms.

High-performance liquid chromatography (HPLC) and its advanced variants have proven to be the most reliable analytical tools for the evaluation of azelnidipine. Stability-indicating HPLC methods enable effective separation of the drug from its degradation products, ensuring compliance with regulatory requirements and supporting shelf-life determination. Additionally, LC-MS/MS techniques provide superior sensitivity and selectivity, making them indispensable for bioanalytical applications such as pharmacokinetic and bioequivalence studies.

The growing application of chiral HPLC and green analytical chemistry approaches further highlights the evolution of analytical strategies for azelnidipine. Chiral methods offer insight into stereochemical behavior, while eco-friendly analytical practices contribute to sustainable and safer laboratory operations without compromising analytical performance. Together, these advancements demonstrate the adaptability and robustness of modern analytical methodologies. In conclusion, comprehensive analytical evaluation forms the cornerstone of azelnidipine research and development. Continued refinement of sensitive, stability-indicating, and environmentally sustainable analytical methods will be critical for supporting advanced drug delivery systems, ensuring regulatory compliance, and ultimately enhancing the clinical effectiveness and safety of azelnidipine.

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