A Review -Development and Validation of Stability-Indicating RP-HPLC Methods for Simultaneous Estimation of Amlodipine and Telmisartan

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***Abstract*—Long-acting calcium channel blockers like amlodipine and Telmisartan are frequently used in conjunction with other antihypertensive medications to treat hypertension and angina pectoris. Its stability evaluation and quality control depend on precise and trustworthy analytical techniques. The active pharmaceutical ingredient (API) must be separated from its breakdown products created under stress settings using stability-indicating techniques. Because of its excellent sensitivity, selectivity, and repeatability, reverse phase high performance liquid chromatography (RP-HPLC) has become the most popular method. The development and validation of stability-indicating RP-HPLC techniques for the simultaneous measurement of amlodipine in pharmaceutical dosage forms are the main topics of this review. A critical discussion is held on method development methodologies, forced degradation studies, validation parameters in accordance with ICH guidelines, and stated analytical conditions.**

***Index Terms*—Amlodipine, Telmisartan, RP-HPLC, Stability-indicating method, Simultaneous estimation, Method validation**

I. INTRODUCTION

Dihydropyridine calcium channel blockers like amlodipine and telmisartan baseplate are widely used to treat cardiovascular conditions like hypertension and persistent stable angina. There is a great demand for analytical techniques that can simultaneously estimate amlodipine and co-formulated medications because it is often used in fixed-dose combinations with medications like hydrochlorothiazide, valsartan, atenolol, indapamide, and atorvastatin.

Stability-indicating analytical techniques guarantee the identity, potency, quality, and purity of pharmaceutical goods over the course of their shelf life, they are essential to pharmaceutical development. ICH rules state that these techniques must be able to differentiate the API from its degradation products that are created under stress. Because to its robustness, high resolution, and UV detection compatibility, RP-HPLC is commonly used for this purpose.

II. STABILITY-INDICATING METHODS

A stability-indicating method is an analytical procedure that accurately measures the active ingredient without interference from degradation products, process impurities, excipients, or other potential contaminants. Forced degradation studies are essential to demonstrate the specificity of the method and to understand degradation pathways.

2.1 Forced Degradation Conditions

Amlodipine and Telmisartan is subjected to various stress conditions, including:

- Acidic hydrolysis
- Alkaline hydrolysis
- Oxidative degradation
- Thermal degradation
- Photolytic degradation

The developed RP-HPLC method should resolve the amlodipine peak from all degradation peaks with

adequate resolution, confirming its stability-indicating nature.

III. DRUG PROFILE

1. Amlodipine

1.1 General Information

- Generic Name: Amlodipine
- Chemical Name: 3-Ethyl-5-methyl (4RS)-2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
- Molecular Formula: $C_{20}H_{25}ClN_2O_5$
- Molecular Weight: 408.88 g/mol
- Category: Calcium channel blocker (Dihydropyridine)
- Dosage Form: Tablets (alone or in combination)

1.2 Mechanism of Action

Amlodipine inhibits the influx of calcium ions into vascular smooth muscle and cardiac muscle by blocking L-type calcium channels. These results in peripheral vasodilation, reduced vascular resistance, and decreased blood pressure.

1.3 Pharmacokinetics

- Absorption: Well absorbed orally
- Bioavailability: 60–65%
- Peak Plasma Time (Tmax): 6–12 hours
- Half-life: 30–50 hours
- Metabolism: Hepatic (CYP3A4)
- Elimination: Primarily via urine as inactive metabolites

1.4 Indications

- Hypertension
- Chronic stable angina
- Vasospastic angina

1.5 Chemical Properties

- Appearance: White to pale yellow crystalline powder
- Solubility: Slightly soluble in water, freely soluble in methanol
- pKa: ~8.6
- Log P: ~3.0

1.6 Stability

Amlodipine is sensitive to light and susceptible to degradation under acidic, alkaline, oxidative, thermal, and photolytic conditions, making it suitable for stability-indicating analytical studies.

2. Telmisartan

2.1 General Information

- Generic Name: Telmisartan
- Chemical Name: 4′-[(1,4′-dimethyl-2′-propyl[2,6′-bi-1H-benzimidazol]-1′-yl)methyl]-[1,1′-biphenyl]-2-carboxylic acid
- Molecular Formula: $C_{33}H_{30}N_4O_2$
- Molecular Weight: 514.63 g/mol
- Category: Angiotensin II receptor blocker (ARB)
- Dosage Form: Tablets (alone or in combination)

2.2 Mechanism of Action

Telmisartan selectively blocks angiotensin II type 1 (AT_1) receptors, preventing vasoconstriction and aldosterone secretion. This leads to vasodilation and reduced blood pressure.

2.3 Pharmacokinetics

- Absorption: Rapid after oral administration
- Bioavailability: ~50%
- Peak Plasma Time (Tmax): 0.5–1 hour
- Half-life: ~24 hours
- Metabolism: Minimal hepatic metabolism
- Elimination: Primarily via feces

2.4 Indications

- Hypertension
- Cardiovascular risk reduction

2.5 Chemical Properties

- Appearance: White to off-white crystalline powder
- Solubility: Practically insoluble in water, soluble in methanol
- pKa: ~4.5
- Log P: ~7.7

2.6 Stability

Telmisartan shows good stability under thermal conditions but may undergo degradation under acidic, alkaline, and oxidative stress, which must be monitored during stability studies.

3. Amlodipine–Telmisartan Combination

Rationale for Combination Therapy

- Complementary mechanisms of action
- Enhanced antihypertensive efficacy
- Reduced dose-related side effects
- Improved patient compliance

This combination is widely used in fixed-dose formulations and commonly analyzed using stability-indicating RP-HPLC methods for quality control and regulatory compliance.

4. Analytical Relevance

Both drugs:

- Absorb strongly in the UV range (230–240 nm)
- Are amenable to RP-HPLC analysis using C18 columns
- Require stability-indicating methods to separate degradation products

IV. RP-HPLC METHOD DEVELOPMENT FOR AMLODIPINE & TELMISARTAN DRUGS

4.1 Selection of Column

Most reported methods employ C18 reversed-phase columns due to their compatibility with moderately lipophilic drugs like amlodipine. These columns provide good peak symmetry and resolution.

4.2 Mobile Phase Selection

The mobile phase typically consists of:

- Aqueous buffer (phosphate buffer adjusted to acidic pH)
- Organic modifier such as methanol or acetonitrile

An acidic pH (around 3–4) is commonly preferred to improve peak shape and retention behaviour of amlodipine.

4.3 Detection Wavelength

UV detection is generally carried out in the range of 230–240 nm, where amlodipine shows maximum absorbance and good sensitivity.

V. SIMULTANEOUS ESTIMATION OF AMLODIPINE AND TELMISARTAN DRUGS

Several RP-HPLC methods have been reported for the simultaneous estimation of amlodipine with other drugs such as:

- Hydrochlorothiazide
- Atorvastatin
- Indapamide
- Chlorthalidone
- Valsartan
- Atenolol

These methods demonstrate effective separation, linear response, and compatibility with stability studies. The use of isocratic or gradient elution depends on the polarity and retention characteristics of the combined drugs.

VI. METHOD VALIDATION ACCORDING TO ICH GUIDELINES

Validation of RP-HPLC methods is performed as per ICH Q2(R1) guidelines and includes the following parameters:

6.1 Specificity

Ability of the method to assess the analyse in the presence of degradation products and excipients.

6.2 Linearity

Demonstrated over a suitable concentration range with a high correlation coefficient ($r^2 \geq 0.999$).

6.3 Accuracy

Evaluated by recovery studies, typically within 98–102%.

6.4 Precision

Includes repeatability and intermediate precision, expressed as %RSD, which should be less than 2%.

6.5 Limit of Detection (LOD) and Limit of Quantitation (LOQ)

Indicate the sensitivity of the method.

6.6 Robustness

Assesses the effect of small deliberate variations in chromatographic conditions.

VII. ADVANTAGES OF RP-HPLC STABILITY-INDICATING METHODS

- High sensitivity and selectivity
- Capability to separate degradation products
- Suitable for routine quality control
- Compliance with regulatory requirements

VIII. CHALLENGES AND FUTURE PERSPECTIVES

Although RP-HPLC methods are well established, challenges such as co-elution in multi-component formulations and degradation product identification remain. Advanced techniques like LC-MS may be integrated for structural elucidation of degradation products and improved sensitivity.

IX. CONCLUSION

Stability-indicating RP-HPLC methods are essential tools for the simultaneous estimation of amlodipine and Telmisartan in pharmaceutical formulations. Proper method development and validation ensure accurate quantification, regulatory compliance, and product safety. The reviewed literature confirms that RP-HPLC remains the most reliable and widely used analytical technique for stability studies of amlodipine and its combinations.

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