Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 11, 2024

Original Article

Amlodipine: A Comprehensive Review Of Reported Analytical Methods

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Abstract:
Amlodipine, a widely used calcium channel blocker, is essential in the management of hypertension and angina pectoris. Accurate and reliable analytical methods are crucial for the quality control and therapeutic monitoring of amlodipine. This review presents a comprehensive examination of the reported analytical methods for the determination of amlodipine in various matrices, including pharmaceutical formulations and biological samples. Techniques such as high-performance liquid chromatography (HPLC), spectrophotometry, capillary electrophoresis, and mass spectrometry are discussed in detail. The review also addresses method validation parameters, such as sensitivity, specificity, linearity, accuracy, precision, and robustness. Emphasis is placed on recent advancements in analytical techniques and their application in routine quality control and research settings. By providing an in-depth analysis of the strengths and limitations of each method, this review aims to guide researchers and practitioners in selecting the most appropriate analytical approach for amlodipine.

Keywords: Amlodipine, HPLC, HPTLC, UV Spectrophotometric

Introduction

Amlodipine is a calcium channel blocker used as an anti-hypertensive agent. Calcium channel blockers (CCBs) were first introduced over 35 years ago initially for coronary heart disease (CHD), but they soon gained wide recognition for their efficacy in hypertension (HTN).[(1)]

Amlodipine is an angioselective calcium channel blocker and inhibits the movement of calcium ions into vascular smooth muscle cells and cardiac muscle cells which inhibits the contraction of cardiac muscle and vascular smooth muscle cells. Amlodipine inhibits calcium ion influx across cell membranes, with a greater effect on vascular smooth muscle cells. This causes vasodilation and a reduction in peripheral vascular resistance, thus lowering blood pressure. Its effects on cardiac muscle also prevent excessive constriction in the coronary arteries.[(2)]

Drug Profile[(3-4)]

- **Drug Name**: Amlodipine
- **Chemical Name**: dialkyl 1,4-dihydropyridine-3,5-dicarboxylate derivative
- **Molecular Formula**: $C_{20}H_{25}ClN_2O_5$
- **Molecular Weight**:408.9 g/mol

- **Drug Class**: Calcium Channel Blocker
- **Solubility**: Slightly soluble in water
- **Storage**: Should be stored in a refrigerator at 2°c to 8°c
- **Pharmacokinetics:**
- **Absorption**: Peak plasma concentrations between 6 and 12 hours.
- **Distribution**: Widely distributed, with a volume of distribution of approximately 21 L/kg
- **Metabolism**: Extensively metabolized in the liver
- **Elimination**: Primarily excreted renally, with a terminal half-life of approximately 30 to 50 hours.

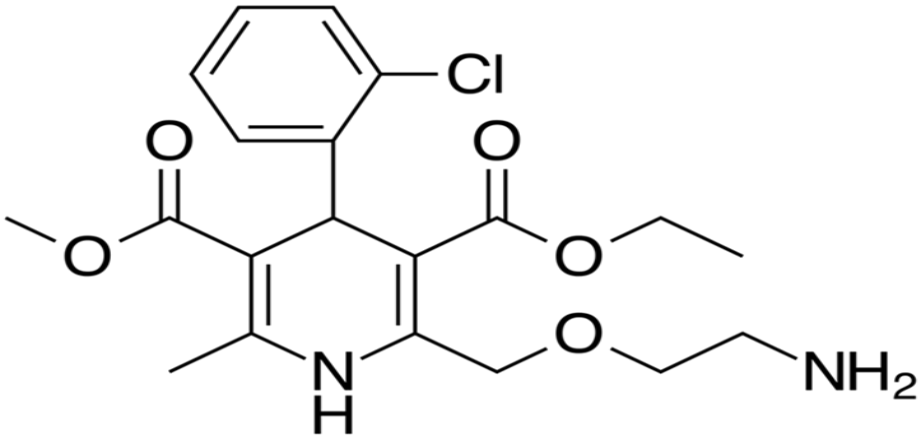

Figure 1. Structure of Amlodipine[4]

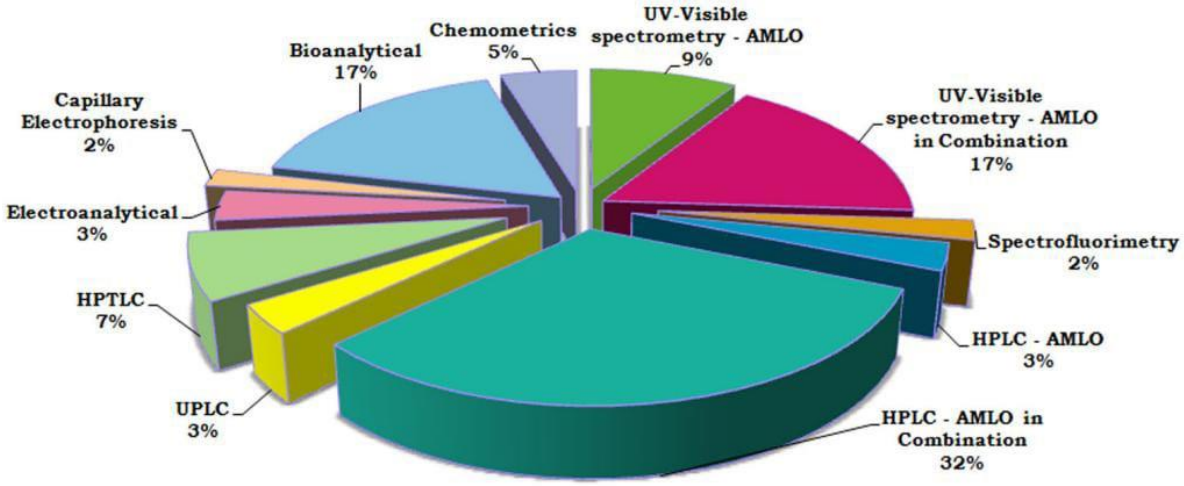

Figure 2. Proportion of analytical method available for the estimation of amlodipine[5]

Method of Analysis[6-8]

UV spectrophotometric: UV specrophotometric method based on simultaneous equation method and area under curve has been reported. Apart from these uv spectrophotometric by chemometric approach has also been reported. Simultaneous equation method is based upon solving simultaneous equation constructed using the absorbance measured at 3 wavelengths 236.5, 254 and 271nm, which are the absorption maxima of corresponding drugs. In the area under the curve method range of wavelength in which anyone of the drug has substantial absorption was selected. Area in this range is used for theestimation of the particular drug, accordingly 231.5-241.5nm for AML. [6]

High Performance Liquid Chromatography (HPLC): Chromatography is an analytical method that finds wide application for the separation, identification and determination of chemical

components in complex mixtures. This technique is based on the separation of components in a mixture (the solute) due to the difference in migration rates of the component through a stationary phase by a gaseous or liquid mobile phase. The almost all the method flow rate was kept at the 1ml/min. The most of the method detector wavelength used is about 200-230nm.[7]

High Performance Thin Layer Chromatography (HPTLC): HPTLC is a fast separation technique and flexible and to analyze a wide variety of samples. This technique is very advantageous it is simple to handle and requires a short time to analyze. It is suitable for qualitative and quantitative analysis. Chromatographic with the advancement of the technique, high performance thin layer chromatography (HPTLC) emerged as an important instrument in technique method.[8]

Sr. No	Official.in	Method	Description	Ref. No
1	IP-2022	Liquid Chromatography	**Stationary phase:** Stainless steel column(150mm x 3.9mm), 5 µm silica **Mobile phase:** Acetonitrile ,methanol, triethylamine (15:35:50)v/v **Detection Wavelength:** 237nm **Flow rate :** 1ml/min	9
2	IP-2018	Liquid Chromatography	**Stationary phase :** C18(150 x 3.9mm),5µm **Mobile phase:** acetonitrile:methanol(35:50v/v) **Detection wavelength:** 237nm **Flow rate:** 1ml/min	10

OFFICIAL IP METHODS OF AMLODIPINE[9-10]

Sr. No	Drug	Method	Brief Introduction	Ref. No
1	Amlodipine besylate	RP-HPLC	**Stationary phase:** 60 RP column (250mm x 4 mm), 5µm **Mobile phase:**0.04M sodium dihydrogen phosphate monohydrate:ethanol(60:40 v/v) **Flow rate:** 1 ml/min **Detection wavelength:** 237 nm	11
2	Amlodipine, Hydrochloro thiazide and Telmisartan	RP-HPLC	**Stationary phase:** C8(150mm x 0.46 mm), 5µm **Mobile phase:** Acetonitrile: Methanol(50:50 v/v) **Flow rate:** 1.5 ml/min **Detection wavelength:** 240 nm	12
3	Amlodipine and Perindopril	HPLC	**Stationary phase:** Inertsil C18 (250mm x 4.6 mm), 5µm **Mobile phase:** Buffer: Acetonitrile(55:45 v/v) **Flow rate:** 1 ml/min **Detection wavelength:** 215 nm	13

4	Amlodipine and Atorvastatin	HPLC	**Stationary phase:** C18(150mm x 4.5mm) 5µm **Mobile phase :** Phosphate buffer : Acetonitrile: Methanol (53:43:4 v/v) **Flow rate:** 1 ml/min **Detection wavelength:** 246 nm	14
5	Amlodipine And Olmesartan	HPTLC	**Mobile phase:** Acetonitrile:water; Toluene (6:3:1 v/v/v) **Detection wavelength:** 270 nm	15
6	Amlodipine	UV Spectrophotometric	**Detection wavelength:** 246 nm **Solvent:** Methanol , Chloroform **Concentration range:** 5-25 µg/ml	16
7	Amlodipine	UV Spectrophotometric	**Detection wavelength:** 355 nm **Solvent:** Methanol **Concentration range:** 5-25 µg/ml	17
8	Amlodipine And Ramipril	RP-HPLC	**Stationary phase :** BDS C_{18}(250mm x 4.6mm),5µm **Mobile phase:** buffer:acetonitrile (45:55v/v) **Flow rate:**1ml/min **Detection wavelength:**230nm	18
9	Amlodipine Besylate And Indapamide	RP-HPLC	**Stationary phase :** Phenomenex C_{18}(250mm x 4.6mm),5µm **Mobile phase:** methanol:water(95:5v/v) **Flow rate:** 1.0ml/min **Detection wavelength:** 238nm	19
10	Amlodipine Besylate And Olmesaratan Medoxomil	HPTLC	**Mobile phase:** chloroform: methanol (9:1 v/v) **Detection wavelength:** 254nm	20
11	Amlodipine	HPTLC	**Mobile phase:** Acetonitrile:0.025 M Buffer (45:55 v/v) **Detection wavelength:** 365 nm	21
12	Amlodipine Besylate And Benazepril	UV Spectrophotometric	**Detection wavelength:** 227 nm **Solvent:** Methanol **Concentration range:** 4-20 µg/ml	22
13	Amlodiopine And Atenolol	HPLC	**Stationary phase :** shim-pack CLC, ODS C_{18}(25cm x 4.6mm),0.5µm **Mobile phase:** glacial acetic acid: acetonitrile:methanol(35:30:35v/v/v) **Detection wavelength:** 237nm **Flow rate:** 1.5ml/min	23
14	Amlodipine Besylate and Metoprolol Succinate	HPTLC	**Mobile phase:** toluene:ethyl acetate:methanol:triethylamine (4:1:1:0.4 v/v/v) **Detection wavelength:**254nm	24
15	Amlodipine Besylate And Telmisartan	UV Spectrophotometric	**Detection wavelength:** 298-360 nm **Solvent**: Methanol **Concentration range:** 15-75 µg/ml	25

16	Amlodipine Besylate And Olmesartan Medoximil	HPTLC	**Mobile phase:** acetonitrile:water:toluene (6:3:1v/v/v) **Detection wavelength:** 270nm	26
17	Amlodipine And Valsartan	HPLC	**Stationary phase:**Agilent ODS 2, C18(200mm x 4.6mm) 10 µm **Mobile phase :** phosphate buffer (pH 3.6 , 0.01mol :acetonitrile:methanol (46:44:10 v/v/v) **Flow rate:** 1 ml/min **Detection wavelength:** 240 nm	27
18	Amlodipine Besylate	UV Spectrophotometric	**Detection wavelength:** 366 nm **Solvent:** Phosphoric acid , Distilled water **Concentration range:** 5-25 µg/ml	28
19	Amlodipine And Olmesartan	HPTLC	**Mobile phase:** Chloroform:Methanol:Toluene:Glacial acetic acid (8:1:1:0.1 v/v/v/v) **Detection wavelength:** 254 nm	29
20	Amlodipine And Valsartan	HPTLC	**Mobile phase:** Toluene:Methanol:Acetic acid (7:3:0.1 v/v/v) **Detection wavelength:** 244 nm	30
21	Amlodipine	UV Spectrophotometric (colorimetry)	**Detection wavelength:** 663 nm **Solvent:** Potassium permanganate in acidic condition and methylene blue **Concentration range:** 1-24 µg/ml	31
22	Amlodipine And Lisinopril	RP-HPLC	**Stationary phase:** Xterra C_{18} (150mmx4.6mm),5µm **Mobile phase:** phosphate buffer : acetonitrile(45:55v/v) **Flow rate :** 0.6ml/min **Detection wavelength:** 216nm	32
23	Amlodipine	UV Spectrophotometric (Visible)	**Detection wavelength:** 530 nm **Solvent:** Bromine/metanil yellow **Concentration range:** 1.25-7.5 µg/ml	33
24	Amlodipine	UV Spectrophotometric (Visible)	**Detection wavelength:** 417 nm **Solvent:** 10% volume/volume hydro alcoholic solution/methyl orange **Concentration range:** 1-10 µg/ml	34
25	Amlodipine and Atorvastatin	HPLC	**Stationary phase:** C8(150mm x 4.6 mm) 5µm **Mobile phase:** ethanol:0.02M sodium dihydrogen phosphate monohydrate(63:47 v/v) **Flow rate:** 0.8 ml/min **Detection wavelength:** 254 nm	35
26	Amlodipine And Benazepril	HPTLC	**Mobile phase:** Ethyl acetate:Methanol: Ammonia (8:5.0:1, v/v/v) **Detection wavelength:** 254 nm	36

27	Amlodipine	UV Spectrophotometric (Visible)	**Detection wavelength:** 580 nm **Solvent:** Chloroform **Concentration range:** 1-125 µg/ml	37
28	Amlodipine And Atenolo	HPTLC	**Mobile phase:** Methylene chloride: Methanol:25% Ammonia(8.8:1.3:0.1 v/v/v) **Detection wavelength:** 230 nm	38
29	Amlodipine	UV Spectrophotometric (Visible)	**Detection wavelength:** 409 nm **Solvent:** Chloroform/ bromophenol blue **Concentration range:** 1-80 µg/ml	39
30	Amlodipine	HPTLC	**Mobile phase:**Toluene:acetone:ethanol:ammonia (56:34.5:6:3.5 v/v/v/v) **Detection wavelength:** 366 nm	40

REPORTED ANALYTICAL METHODS OF AMLODIPINE[(11-40)]

Conclusion:

The comprehensive review of analytical methods for amlodipine highlights the significant progress made in the development and validation of various techniques for its quantification in pharmaceutical formulations and biological samples. High-performance liquid chromatography (HPLC) remains the gold standard due to its precision, accuracy, and versatility, while spectrophotometric methods offer simplicity and cost-effectiveness for routine analysis. Emerging techniques such as capillary electrophoresis and mass spectrometry provide enhanced sensitivity and specificity, making them valuable tools for advanced research and complex matrices.

Despite these advancements, the selection of an analytical method should be guided by the specific requirements of the application, including the need for sensitivity, the complexity of the matrix, and available resources. Method validation is critical to ensure the reliability of results, and ongoing improvements in analytical technologies will likely lead to even more robust and efficient methods in the future.

Overall, this review underscores the importance of continued innovation and rigorous validation in the development of analytical methods for amlodipine, ensuring high standards of quality control and therapeutic monitoring in clinical and pharmaceutical settings.

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