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# ANALYTICAL APPROACHES FOR SIMULTANEOUS ESTIMATION OF AMLODIPINE BESYLATE, TELMISARTAN AND INDAPAMIDE: A COMPREHENSIVE REVIEW

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## ABSTRACT

Hypertension is a major chronic cardiovascular disorder affecting large portion of global population. It is characterized by consistently increased force of blood against artery walls. For the long-term management of the hypertension there are multiple single or combination drugs therapy available. Consequently, a triple combination drug containing Amlodipine Besylate (Calcium channel blocker), Telmisartan (Angiotensin II receptor blocker) and Indapamide (Thiazide like Diuretic) is developed. There are formal analytical methods like HPLC, UV, HPTLC, LCMS, UHPLC-UV developed for the estimation of these compounds in single or with other combination dosage form, but not for this particular combination. Which indicates requirement of accurate, precise and sensitive analytical method for the quantitation of the active pharmaceutical compound in pharmaceutical preparation. A well-validated method contributes significantly in maintaining of product quality, safety and therapeutic efficacy. The following study represent the review on official and reported methods available for the antihypertensive drugs Amlodipine besylate, Telmisartan and Indapamide.

**KEYWORDS:** Hypertension, Amlodipine besylate, Telmisartan, Indapamide, RP-HPLC, Chromatographic method, Simultaneous Estimation.

## INTRODUCTION

Hypertension is a cardiovascular disorder in which the arterial blood pressure is persistently high, typically 140/90 mmHg or higher. Global estimate indicates that approximately 1.4 billion individual adults aged 30-79 years were living with hypertension, nearly two-third of adults.[1]

For the management of Hypertension, Lifestyle modifications plays important role. Conservative management approaches include reducing dietary sodium intake, maintenance of healthy body weight, adoption of a balanced diet rich in fruits and vegetables, Smoking cessation, physical activity, stress management, limitation of alcohol consumption contribute significantly to improve overall cardiovascular health.[2] However, this interventions may not be sufficient for many patient to maintain blood the blood pressure. Under these circumstances, pharmacological therapy required to achieve optimal blood pressure level. A Variety of antihypertensive medications available such as ACE inhibitors, ARBs, Beta-blocker, calcium channel blocker, Diuretics, Vasodilators. Fixed-dose combination therapies of antihypertensive drugs used to enhance effectiveness and patient compliance.[3] Among this Amlodipine besylate, Telmisartan and Indapamide is widely used for the management of hypertension either as monotherapy or combination with other drugs. Their first triple combination is approved by FDA in June, 2025.[4] This developed combination is new and entails development of analytical method for simultaneous estimation of each pharmaceutical agent in combination. It is Crucial in quality control for accurately determining active pharmaceutical ingredient in combination. Accordingly the present review shows the existing analytical methods available for these agents.

### Drug profile

#### Amlodipine Besylate[5]

Amlodipine besylate belongs to the class of dihydropyridine group of calcium channel blocker. Chemically it is benzenesulfonic acid, 3-O-ethyl 5-O-methyl 2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate and chemical formula is $C_{20}H_{25}ClN_2O_6$. $C_6H_6O_3S$ having molecular weight about 408.879 g/mol. It is lipophilic drug as its Log P value is 2.96. Its melting point is 195-204°C which is high due to anhydrous besylate salt form. Amlodipine besylate is poorly soluble in water and demonstrates moderate solubility in ethanol or methanol. It acts by blocking the movement of calcium ions across the cell membranes of vascular smooth and cardiac muscle, leading to

muscle relaxation and a decrease in vascular resistance. It may cause complications like headache, dizziness, flushing, palpitations, ankle swelling (edema).

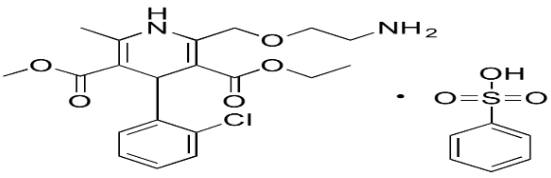

**Fig.1: Structure of Amlodipine Besylate.**

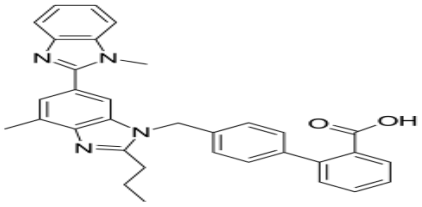

**Fig. 2: Structure of Telmisartan.**

**Telmisartan**[6]

Telmisartan is an angiotensin II receptor blocker (ARB). Its IUPAC name is 2-(4-{[4-Methyl-6-(1-methyl-1H-1,3-benzodiazol-2-yl)-2-propyl-1H-1,3-benzodiazol-1-yl]methyl}phenyl)benzoic acid and the chemical formula is $C_{33}H_{30}N_4O_2$. Telmisartan possesses molecular weight of 514.63 g/mol. It has high melting point of about 261-263°C because of strong crystal lattice structure. Have Log P value 3.2 which indicates the compound is lipophilic in nature. It is an antihypertensive drug with very low water solubility, which limits its bioavailability. It dissolves better in alkaline media and certain organic solvents. The drug exerts its effect by selectively blocking angiotensin II from binding to AT1 receptor. Angiotensin II promotes vasoconstriction and aldosterone release, its inhibition leads to vasodilation, reduced vascular resistance and lower blood pressure, while also enhancing blood and oxygen supply to the heart.

**Indapamide**[7]

Indapamide classified as a sulfonamide diuretic with significant antihypertensive activity. According to IUPAC nomenclature, the compound is named 4-chloro-N-(2-methyl-2,3-dihydro-1H-indol-1-yl)-3-sulfamouylbenzamide. The chemical composition of the compound corresponds to the molecular formula $C_{16}H_{16}ClN_3O_3S$ and molecular weight about 365.835 g/mol. It melts at 160-162°C. It is amphiphilic compound having Log P value 2.2. Indapamide exhibit poor water solubility but dissolves readily in organic compound. It is soluble in methanol, acetic acid, ethyl acetate and alkaline aqueous solutions. The antihypertensive action of indapamide is attributed to both its diuretic and vascular effects. It acts in a thiazide-like manner by inhibiting the sodium-chloride cotransporter in the distal convoluted tubule of the kidney, leading to enhanced urinary excretion of sodium and water. Moreover, indapamide exerts direct vasodilatory effects by lowering peripheral vascular

resistance, possibly through reduced calcium influx into vascular smooth muscle cells and diminished responsiveness to vasoconstrictors.

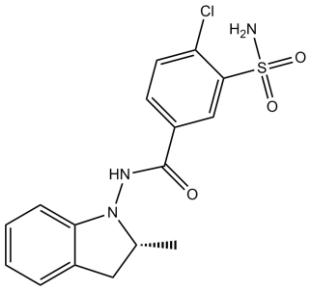


**Figure 3: Structure of Indapamide.**

**Literature Review**

**Amlodipine besylate**

**Table 1: Official methods for Amlodipine Besylate.**

| Sr. No. | Official in | Method | Description | Ref. No. |
|---|---|---|---|---|
| **1** | **BP** | **RP- HPLC** | **Column:** stainless steel column (10 cm × 4.6 mm) packed with octadecylsilyl silica gel for chromatography (2.6 µm) (Kinetex C18 is suitable). **Mobile phase:** A 45 volumes of 0.03M potassium dihydrogen orthophosphate, adjusted to pH 3.0 with orthophosphoric acid, and 55 volumes of methanol. Mobile phase B 30 volumes of 0.03M potassium dihydrogen orthophosphate, adjusted to pH 3.0 with orthophosphoric acid, and 70 volumes of methanol. **Flow rate:** 0.6 ml/min **Detection:** 238 nm | [14] |
| **2** | **USP** | **RP- HPLC** | **Column:** 3.9-mm × 15-cm; 4 **Mobile phase:** Add 7.0 mL of triethylamine into a 1000-Ml ask containing 900 mL of water. Adjust the solution with phosphoric acid to a pH of 3.0 Dilute with water to volume, and mix well. Mobile phase: Methanol, acetonitrile, and Buffer (35:15:50) **Flow rate:** 1.0 ml/min **Detection:** 237 nm | [15] |
| **3** | **IP** | **RP- HPLC** | **Column:** a stainless steel column 15 cm x 3.9 mm, packed with octadecylsilane bonded to porous silica (5 iim) **Mobile phase:** a mixture of 15 volumes of acetonitrile, 35 volumes of methanol and 50 volumes of a solution prepared by dissolving 7.0 | [16] |

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| | | | ml of triethylamine in 1000 ml of water and adjusting the pH to 3.0 with orthophosphoric acid, - flow rate: 1 ml per minute<br>**Flow rate:** 1.0 ml/min<br>**Detection:** 237 nm | |

**Table 2: Reported methods of Amlodipine Besylate.**

| Sr. no. | Matrix | Analytical method | Characteristics | Ref. No. |
|---|---|---|---|---|
| 1 | **Amlodipine besylate and Losartan potassium in Tablet dosage form** | **UV Spectroscopy method** | **Solvent**: Methanol<br>**Linearity**: 2-20 µg/ml.<br>**Detection**: 237.5 nm | [11] |
| 2 | **Amlodipine besylate and Nebivolol hydro-chloride in Tablet dosage form** | **UV Spectroscopy method** | **Solvent**: Methanol<br>**Linearity**: 2-20 µg/ml.<br>**Detection**: 238 nm and 360 | [12] |
| 3 | **Amlodipine besylate and Atenolol in Tablet dosage form** | **HPTLC** | **Stationary phase** :- Merck HPTLC plates (0.2 mm thickness) pre-coated with 60F254 silica gel on aluminium sheet<br>**Mobile phase**:- methylene chloride: methanol: ammonia solution (25% NH3) (8.8:1.3:0.1; v: v).<br>**Detection**:- 230 nm | [13] |
| 4 | **Amlodipine besylate and Valsartan in Bulk drug and dosage form.** | **HPTLC** | **Stationary phase** :- aluminium plates pre-coated with silica gel 60 F254.<br>**Mobile phase**:- toluene: methanol: acetic acid 7:3:0.1 (v/v/v)<br>**Detection**:- 244 nm | [14] |
| 5 | **Amlodipine besylate and Indapamide in Pharmaceu-tical Formulation** | **RP-HPLC Quality by Design (AQbD) approach** | **Column**: Shimpack C18 column (250 × 4.6 mm, 5 µm)<br>**Mobile phase**: methanol and phosphate buffer (pH 4.5, adjusted with OPA) in a 45:55 ratio<br>**linearity** : 0.25–8 µg/mL for **indapamide** and 0.75–24 µg/mL for **amlodipine besylate** | [15] |
| 6 | **Amlodipine and Ramipril in Tablet** | **RP-HPLC** | **Column**:- Inertsil ODS-3 column (250 mm×4.0 mm, 3 µm).<br>**Mobile phase**:- 60 mM sodium perchlorate buffer (containing 7.2 mM triethylamine)-acetonitrile (60:40, v/v) and mobile phase B was 60 mM sodium perchlorate buffer (containing 7.2 mM | [16] |

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| | | | triethylamine)-acetonitrile (20:80, v/v). The apparent pH adjusted to 2.6 with phosphoric acid.<br>**Flow rate**:- 1.0 ml/min<br>**Detection**:- 210 nm | |
| 7 | **Amlodipine besylate Tablet** | **RP-HPLC** | **Column** :WATERS C18 column 250 mm × 4.6 mm (5µm)<br>**Mobile phase**:-acetonitrile: 70mM potassium dihydrogen orthophosphate buffer: methanol (15:30:55) pH adjusted to 3.0<br>**Flow rate**:- 1.0 ml/min<br>**Detection**:- 240 nm | [17] |
| 8 | **Amlodipine and benazepril Tablet** | **RP-HPLC and UV - spectrophotometry** | **Column** : Shodex-RP C18 5e column (250 × 4.6 mm, 5 µm)<br>Mobile phase:- potassium dihydrogen phosphate buffer: Acetonitrile (55:45 v/v)<br>**Flow rate**:- 1.0 ml/min<br>**Detection**: 237nm<br>UV Spectroscopy method<br>**Solvent** : 0.01 N HCl<br>**Concentration range**: 2- 24 µg/ml | [18] |
| 9 | **Amlodipine besylate, Rovustatin calcium and Telmisartan Tablet** | **HPLC** | **Column**:- Luna C18 100Å column (250 mm × 4.6 mm i.d., particle size 5 µ)<br>**Mobile phase**:- ethanol and acetonitrile (pH 3.5 adjusted by ortho-phosphoric acid) (60:40 v/v)<br>**Flow rate**:- 1.0 ml/min<br>**Detection**:- 242 nm | [19] |

**Telmisartan**

**Table 3: Official methods for Telmisartan.**

| Sr. No. | Official in | Analytic Method | Description | Ref. No. |
|---|---|---|---|---|
| 1 | **USP** | **RP-HPLC** | **Column:-** 4.0-mm × 4-cm; 5-µm packing L1<br>**Mobile phase:-** : Diluent: 0.005 N methanolic solution of sodium hydroxide Buffer: 2.0 g/L of ammonium dihydrogen phosphate. Adjust with 1 M phosphoric acid to a pH of 3.0.<br>Mobile phase: Methanol and Buffer (70:30)<br>**Flow rate:-** 0.7 ml/min<br>**Detection:-** 298 nm<br>**Injection volume :** 5µl | [20] |

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| 2 | **BP** | **RP-HPLC** | **Column:-** stainless steel column (12.5 cm × 4.0 mm) packed with octadecylsilyl silica gel for chromatography (5 µm) (Kromasil C18 is suitable).<br>**Mobile phase:-** : Mobile phase A Dissolve 2.0 g of potassium dihydrogen orthophosphate and 3.8 g of sodium pentanesulfonate monohydrate in 950 mL water, adjust to pH 3.0 with dilute orthophosphoric acid and dilute to 1000 mL with water.<br>Mobile phase B 20 volumes of methanol and 80 volumes of acetonitrile.<br>**Flow rate:-** 1.0 ml/min<br>**Detection:-** 230 nm<br>**Injection volume :** 10 µl | [21] |
| 3 | **IP** | **RP-HPLC** | **Column:-** A stainless steel Column 12.5 cm×4mm, packed with octadecylsilane bonded to porous silica (5 µm)<br>**Mobile phase:-** : A) Dissolve 2.0 g of Potassium Dihydrogen Phosphate and 3.8g of Sodium Pentane sulphonate monohydrate in water, adjust to pH 3 with orthophosphoric acid dilute to 1000ml with water. B) A Mixture of 20 Volume of Methanol and 80 Volume of Acetonitrile. (20 :80) v/v<br>**Flow rate:-** 1.0 ml/min<br>**Detection:-** 230 nm<br>**Injection volume :** 10 µl | [22] |

**Table 4: Reported methods for Telmisartan.**

| Sr. No. | Matrix | Analytic Method | Description | Ref. No. |
|---|---|---|---|---|
| 1 | **Telmisartan In Human Plasma** | **RP-HPLC Method** | **Column**:- Zorbax extend C18 column Mobile phase:- Methanol 10 mM ammonium acetate (85:15 v/v) to pH 4.5<br>**Flow rate**:- 1.0 ml/min<br>**Detection**:- Q-trap TM LC–MS/MS | [23] |
| 2 | **Telmisartan In Human Plasma** | **RP-HPLC Method** | **Column**:- Monolithic analytical column, Chromolith® (RP-18e 100mm × 4.6 mm, Merck, Germany) Mobile phase:- Acetonitrile and naproxen<br>**Flow rate**:- 3 ml/min<br>**Detection**:- Fluorescence detection λex 300 nm λem 385 nm | [24] |

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| 3 | **Telmisartan In Rat Plasma** | **RP-HPLC Method** | **Column**:- Phenomenex Luna® C8 column<br>**Mobile phase**:- Methanol and acetonitrile (70:30 v/v)<br>**Flow rate**:- 1.0 ml/min | [25] |
| 4 | **Telmisartan In Pure And Pharmaceutical Dosage Form** | **UV Spectroscopy method** | **Solvent**: Sodium Hydroxide<br>**Linearity**: 4-20 µg/mL<br>**Detection** : 295 nm | [26] |
| 5 | **Telmisartan In Tablet Dosage Form** | **UV Spectroscopy method** | **Solvent**: Bromocresol green<br>**Linearity**: 4-20 µg/mL<br>**Detection** : 440 nm | [27] |
| 6 | **Telmisartan In Bulk And Tablet Dosage Form** | **UV Spectroscopy method** | **Solvent**: NaOH, Distilled water<br>**Linearity**: 4-24 µg/mL<br>**Detection** : 234 nm | [28] |
| 7 | **Telmisartan In Bulk** | **UV Spectroscopy method** | **Solvent**: NaOH<br>**Linearity**: 2-12 µg/mL<br>**Detection** : 295 nm 327 nm | [29] |
| 8 | **Telmisartan In Tablet** | **UV Spectroscopy method** | **Solvent**: Sodium Hydroxide<br>**Linearity**: 1-8 µg/mL<br>**Detection** : 230 nm | [30] |
| 9 | **Telmisartan In Bulk And Tablet Dosage Form** | **UV Spectroscopy method** | **Solvent**: NaOH, Distilled water<br>**Linearity**: 2-10 µg/mL<br>**Detection** : 234 nm | [31] |
| 10 | **Telmisartan In Human Plasma** | **RP-HPLC Method** | **Column**:- Phenomenex LUNA C18, column (250 × 4.6 mm i.d, 5µm)<br>**Mobile phase**:- : Sodium dihydrogen phosphate buffer (pH:3.0): acetonitrile (42:58 v/v)<br>**Flow rate**:- 1.2 ml/min<br>**Detection**:- Ultraviolet (UV)-PDA detector at 297 nm | [32] |
| 11 | **Telmisartan In Tablet** | **RP-HPLC Method** | **Column**:- Column oven (Jasco), and a Reverse Phase C18 (phenyl) (25 cm × 4.6 mm i.d., 5 µm)<br>**Mobile phase**:- : Acetonitrile: buffer in the ratio of 90:10 v/v<br>**Flow rate**:- 0.8 ml/min<br>**Detection**:- UV detector at 296 nm | [33] |
| 12 | **Telmisartan In Pure And Pharmace-utical Dosage Form** | **RP-HPLC Method** | **Column**:- Reversed phase C18 column (4.6150 mm, 3.5 m, XTerra)<br>**Mobile phase**:- : Buffer and methanol (40:60 v/v, pH 3.0 with ortho phosphoric acid)<br>**Flow rate**:- 0.5 ml/min<br>**Detection**:- UV detector at 230 nm | [34] |

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| 13 | **Telmisartan In Tablet** | **RP-HPLC Method** | **Column**:- Waters symmetry column 250 × 4.6 mm, 5µ<br>**Mobile phase**:- : 10 mM potassium dihydrogen phosphate (pH 3.5): acetonitrile (64:40)<br>**Flow rate**:- 1.0 ml/min<br>**Detection**:- UV detector at 230 nm | [35] |
| 14 | **Telmisartan Intablet** | **RP-HPLC Method** | **Column**:- Column C18<br>**Mobile phase**:- Methanol-water (80:20 v/v) pH 4.0<br>**Flow rate**:- 1.0 ml/min<br>**Detection**:- UV detector at 225 nm | [36] |
| 15 | **Telmisartan In Tablet** | **RP-HPLC Method** | **Column**:- Chromosil C18 (250 mm × 4.6 mm, 5 µm) column<br>**Mobile phase**:- Methanol : 0.1 % orthophosphoric acid : acetonitrile (80:5:15 v/v/v)<br>**Flow rate**:- 1.5 ml/min<br>**Detection**:- Spectrophotometer UV detector at 256 nm | [37] |

**Indapamide**

**Table 5: Official Methods for Indapamide.**

| Sr. no. | Official in | Method | Description | Ref. |
|---|---|---|---|---|
| 1. | **IP** | **Chromato-graphy Method** | **Column** : stainless steel column 15 cm x 4.6 mm,<br>**Mobile phase** : : a mixture of 6 volumes of a solution containing 5 per cent w/v of sodium dodecyl sulphate and 3 per cent v/v of glacial acetic acid, 10 volumes of triethylamine, 20 volumes of butan-2-ol , 310 volumes of acetonitrile and 690 volumes of water, adjusted to pH 3.0 with orthophosphoric acid<br>**Flow rate** : 1.6 ml/min<br>**Detection Wavelength** : 240nm | [38] |
| 2 | **BP** | **Chromato-graphy Method** | **Column** : stainless steel column (15 cm × 4.6 mm)<br>**Mobile phase** : : 6 volumes of a solution containing 5% w/v of sodium dodecyl sulfate and 3% v/v of glacial acetic acid, 10 volumes of triethylamine, 20 volumes of butan-2-ol, 310 volumes of acetonitrile and 690 volumes of water, the mixture being adjusted<br>to pH 3.0 with orthophosphoric acid.<br>**Flow** rate : 1.6 ml/min | [39] |

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| | | | **Detection Wavelength** : 240nm | |
| 3 | **USP** | **Chromato-graphy Method** | **Column** : 4.5-mm × 10-cm column that contains a 3-µm packing L1.<br>**Mobile phase** : Dissolve 1.08 g of sodium 1-octanesulfonate in 700 mL of water, add 10 mL of glacial acetic acid, and mix. Add 300 mL of acetonitrile, mix, filter, and degas. Make adjustments if necessary (see System Suitability under Chromatography 〈621〉).<br>Internal standard solution—Prepare a solution of 2′-chloroacetophenone in acetonitrile having a concentration of about 0.25 mg per mL<br>Standard preparation—Dissolve an accurately weighed quantity of USP Indapamide RS in acetonitrile to obtain a solution having a known concentration of about 0.1 mg per mL. Transfer 5.0 mL of this solution and 3.0 mL of Internal standard solution to a 50-mL volumetric fask,dilute with a mixture of water and acetonitrile (50:10) to volume, and mix.<br>**Flow rate** : 1.0 ml/min<br>**Detection Wavelength** : 242 nm | [40] |

**Table 6: Reported methods for indapamide.**

| Sr no. | Matrix | Method | Description | Ref. |
|---|---|---|---|---|
| 1 | **Amlodipine Besylate And Indapamide In Tablet** | **RP-HPLC** | **Detection wavelength**: 238nm<br>Column: C-18,ODS bonded column<br>**Mobile phase**: Methanol: water (95:5)v/v<br>**Flow rate** : 1.0ml/min<br>**Linearity range**: Indapamide: 1-7 µg/ml Amlodipine : 2-16µg/ml<br>Retention time:<br>**Indapamide**: 2.850min<br>**Amlodipine** : 8.780min | [41] |
| 2 | **Perindopril And Indapamide In Pharmaceuti-cal Formulations** | **RP-HPLC** | **Detection wavelength**: 215nm<br>**Column**: Reverse phase RP-YMC pack ODS A-132 C18 column<br>**Mobile phase**: Phosphate buffer pH 2.4 : Acetonitrile (70:30)v/v<br>**Flow rate**: 1ml/min<br>**Linearity range**:<br>**Indapamide**: 10-30µg/ml | [42] |

| | | | | |
|---|---|---|---|---|
| | | | **Perindopril**: 10-50µg/ml<br>**Retention time**:<br>**Indapamide**: 5.80min<br>**Perindopril**: 3.20min | |
| 3 | **Amlodipine Besylate And Indapamide In Bulk Drug And Tablet Dosage Form** | **RP-HPLC Method** | **Detection wavelength**: 238nm<br>Column: C-18<br>**Mobile phase**: Acetonitrile: Water 70:300v/v<br>**Flow rate**: 8ml/min<br>**Retention time**:<br>**Indapamide**:3.27mins<br>**Amlodipine**:4.7min | [43] |
| 4 | **Indapamide In Pharmaceuti-cal Dosage Form** | **RP-HPLC Method** | **Detection wavelength**: 240nm<br>**Column**: RP C-8<br>**Mobile phase**: 0.15% Triethylamine (pH3.5): Acetonitrile 63:37 v/v<br>**Linearity range**: 10-100ng/ml<br>LOQ:10 | [44] |
| 5 | **Indapamide In Bulk And Tablet Dosage Form** | **RP-HPLC Method** | **Detection wavelength**: 242nm<br>**Column**: C-18<br>**Mobile phase**:<br>Acetonitrile:Methanol:Water 40:50:10 v/v/v<br>**Flow rate**: 1ml/min<br>**Linearity range**: 10-60µg/ml<br>**Retention time**: 3.233min | [45] |
| 6 | **Atenolol And Indapamide In Pharmaceuti-cal Formulations** | **RP-HPLC Method** | **Detection wavelength**: 230nm<br>**Column**: Waters C-18<br>**Mobile phase**: Methanol:Water 80:20 v/v<br>**Flow rate**: 1ml/min<br>**Linearity range**:<br>**Indapamide**: 0.625-7.5 µg/ml<br>**Atenolol**: 12.5-150µg/ml **Retention time**:<br>**Indapamide**: 3.405min<br>**Atenolol**: 1.766 min | [46] |
| 7 | **Amlodipine Besylate And Indapamide In Pharmaceuti-cal Formulations** | **RP-HPLC Method** | **Detection wavelength**: 242nm<br>Column: Brownlee C-18<br>**Mobile phase**: 0.02M Potassium dihydrogen phosphate(pH 3):methanol 30:70 v/v<br>**Retention time**:<br>**Indapamide**: 3.6min<br>**Amlodipine Besylate**: 5.9 min | [47] |
| 8 | **Indapamide And Amlodipine Besylate Tablet Dosage Form** | **RP-HPLC Method** | **Column**: Nucleosil C-18<br>**Mobile phase**: 0.01M Potassium dihydrogenphosphate(Ph-3), Methanol 30:70 v/v<br>**Detection wavelength**: 241nm | [48] |

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| | | | **Retention time**:<br>**Indapamide**: 3.84min<br>**Amlodipine Besylate**: 5.96 min | |
| 9 | **Indapamide And Nebivolol Hydrochloride In Tablet Dosage Form** | **RP-HPLC Method** | **Column**: Kromosil C-18<br>**Mobile phase**: Ammonium acetate (pH 4.5):Methanol 45:65 v/v<br>**Detection wavelength**: 266nm<br>**Flow rate**: 1ml/min<br>**Linearity range**:<br>**Indapamide**: 9-21 µg/ml<br>**Nebivolol hydrochloride**: 30-70µg/ml<br>**Retention time**:<br>**Indapamide**: 2.35min<br>**Nebivolol hydrochloride**: 3.49min | [49] |
| 10 | **Atenolol And Indapamide In Tablet Dosage Form** | **RP-HPLC Method** | **Column**: L1 column Hypersil gold Column temperature: 300C **Mobile phase**: 0.1% Triethylamine (pH 3):Methanol 30:770 v/v<br>**Detection wavelength**: 240nm<br>**Flowrate**:1ml/min<br>**Retention time**:<br>**Indapamide**: 3.93min<br>**Atenolol**: 3.05 min | [50] |
| 11 | **Atenolol And Indapamide In Tablet Dosage Form** | **RP-HPLC Method** | **Column**: C-18<br>**Mobile phase**: Methanol:Water 60:40 v/v<br>**Detection wavelength**: 260nm<br>**Flowrate**:1ml/min<br>**Linearity range**:<br>**Indapamide**: 0.225-25 µg/ml<br>**Atenolol**: 4.5-500µg/ml<br>**Retention time**:<br>**Indapamide**: 8.9min | [51] |
| 12 | **Atenolol And Indapamide In Tablet Formulation** | **HPTLC Method** | **Column**: Aluminium foil plates with silica gel 60F254<br>**Mobile phase**: Toulene:Ethyl acetate:Methanol:Ammonia 5:3:3:0.1 v/v/v/v<br>**Detection of spot**: 229nm<br>**Linearity range**:<br>**Indapamide** : 100-600ng/spot<br>**Atenolol**: 200-1200ng/spot<br>**Retardation Factor**:<br>**Indapamide** : 0.71<br>**Atenolol**: 0.27 | [52] |
| 13 | **Olmesartan And Indapamide In Tablet Formulation** | **HPTLC Method** | **Column**: Aluminium plates with silica gel 60F254<br>**Mobile phase**: Toulene:Chloroform:Methanol 4:1:1 | [53] |

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| | | | v/v/v<br>**Linearity range**:<br>**Indapamide**: 100-600 µg/ml<br>**Olmesartan medosomil**: 100-700µg/ml<br>**Retardation Factor**:<br>**Indapamide**: 0.47<br>**Olmesartan medosomil**: 0.15 | |
| 14 | **Amlodipine Besylate And Indapamide In Tablet Formulation** | **HPTLC Method** | **Column**: 60F254 Silica gel on Aluminium sheet<br>**Mobile phase**: Dichloromethane:Ethanol:Ammonia 8.5:1.5:0.1 v/v/v<br>**Detection of spot**: 241nm<br>**Correlation coefficient**:<br>**Indapamide**: 0.9977<br>**Amlodipine Besylate**: 0.9995<br>%Recovery:<br>**Indapamide** : 99.2-102.09<br>**Amlodipine Besylate**: 98.49-102.05 | [54] |
| 15 | **Telmisartan And Indapamide In Pharmaceuti-cal Solid Dosage Form** | **HPTLC Method** | **Column**: Precoated Silica gel GF 254<br>**Mobile phase**: Hexane: Ethyl acetate: Methanol: Glacial acetic acid 14:6:2:1<br>**Linearity range**: Telmisartan: 2000-7000ng/spot Indapamide: 75-262.5 ng/spot<br>**Retardation factor**:<br>**Telmisartan**: 0.21<br>**Indapamide**: 0.36 | [55] |
| 16 | **Indapamide In Human plasma** | **LCMS** | **Column**: Stainless C-18 shim pack Ionizer: Electron spray ionizer<br>**Flow rate**: 0.2ml/min<br>**Analyzer**: Single quadrupole mass spectrophotometer<br>**Concentration Range**: 0.5-100ng/ml<br>**Coefficient of determination**:0.9998 | [56] |
| 17 | **Indapamide In Human plasma** | **LCMS** | **Column**: C-18 Ionizer: Electron spray ionizer<br>**Mobile phase**: 10mM Ammonium acetate:Methanol 22:78 v/v<br>**Analyzer**: Single quadrupole mass spectrophotometer<br>**Concentration Range**: 0.1-100ng/ml | [57] |
| 18 | **Perindopril Arginine And Indapamide Hemihydrate In Combined Dosage Form** | **UHPLC- UV** | **Detector**: UHPLC-Quadrupole-TOFMS Column: BEH C-18 **Mobile phase**: 0.01% Formic acid (pH 4):Acetonitrile 40:60 v/v **%RSD**:<br>**Indapamide**:0.63%<br>**Perindopril Arginine**:0.84% | [58] |

## CONCLUSION

This review gathers and critically examines the reported spectroscopic and chromatographic techniques for estimating the chosen drugs both individually and in various combinations. The literature clearly shows that a number of validated analytical methods, especially RP-HPLC and UV spectroscopic techniques, have been successfully developed, showing good accuracy, precision, sensitivity, and reproducibility. A common trend across chromatographic methods is the frequent use of mobile phases made up of acetonitrile, water, and phosphate buffer systems. To get good resolution, the flow rates are usually set between 1.0 and 1.5 mL/min. Methanol is a popular solvent in spectroscopic methods because it dissolves well and works well for analysis. According to the literature, these medications are most frequently examined in conjunction with other agents, and these techniques are tried-and-true. However, since there is currently no documented analytical technique for the simultaneous estimation of the chosen three medications in a single combined dosage form.

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