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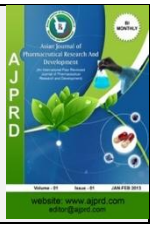

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Review Article

An Updated Review On Analytical Methods For Estimation Of Azelnidipine And Telmisartan

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A B S T R A C T

High blood pressure, also called hypertension, is a common condition that is characterized by having a higher amount of pressure in blood vessels than normal. Hypertension (HT) is a very common disorder, particularly past middle age. It is not a disease in itself, but is an important risk factor for cardiovascular mortality and morbidity. For improvement activity of hypertension, Azelnidipine and Telmisartan newer combination in market, which is effective in Hypertension. This combination was developed to improve medication for Stage II Hypertension. Azelnidipine is Ca^{2+} channel blocker and chemically 3-[1-(Benzyldrylazetidin-3-yl] 5-isopropyl- 2- amino 6 methyl-4-(3-nitrophenyl)-1,4- dihydropyridine-3, 5dicarboxylate.Telmisartan is AT1-receptor blocker and Chemically2-{4-[[4-methyl-6-(1-methylbenzimidazol-2yl)-2–propylbenzimidazol-1yl] methyl] biphenyl)-benzoic acid. It provides information about different analytical method development like UV spectrophotometry, HPTLC, HPLC, and LC-MS methods reported for Azelnidipine and Telmisartan for individual and other drug combination. All reported methods found to be simple, accurate, economic, precise and reproducible in nature. This Review focuses on recent development in analytical method development for Azelnidipine and Telmisartan, and there were two methods reported for this combination as per our knowledge.

Keywords: Azelnidipine, Analytical Method, HPLC, HPTLC, LC-MS, Hypertension, Telmisartan, UPLC, UV Spectrophotometry.

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INTRODUCTION

Azelnidipine is a dihydropyridine (DHP) type of calcium channel blocker (CCB) used for the treatment of hypertension and angina pectoris. Chemically Azelnidipine (Figure 1 A) is 3-[1-(Benzyldrylazetidin-3-yl]5-isopropyl-2-amino 6 methyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3, 5 dicarboxylate. The molecular formula and molecular weight of Azelnidipine is $C_{33}H_{34}N_4O_6$ and 583 or 582.646 g/mol. It is insoluble in water, slightly soluble in methanol, soluble in ethyl acetate, freely soluble in acetone and in acetic acid [1] and also soluble in ethanol. It acts by inhibiting trans membrane Ca^{2+} influx through the voltage dependent channels of smooth muscles in vascular walls. Ca^{2+} channels are classified into various categories, including L-type, T-type, N-type, P/Q-type and R-type Ca^{2+} channels. The L-type Ca^{2+} channels, normally, calcium induces smooth muscle contraction, contributing to hypertension, when calcium channels are blocked. The vascular smooth muscle does not contract, resulting in relaxation of vascular smooth muscle walls and decreased blood pressure [2-3]. Treatment of hypertension which lower the BP due to block calcium channel and decreases BP. Azelnidipine is official in Indian Pharmacopoeia [4]. A literature survey reported that analytical methods like Spectrophotometric methods, HPLC, HPTLC LC with tandem mass spectroscopy, LC-ESI-MS. Different trade names of marketed formulations and reported methods of Azelnidipine individually and combination with other drugs are presented in the Table 1, Table 4 and Table 5.

Telmisartan is a member of the class of benzimidazoles used in the treatment of hypertension. Telmisartan is an Angiotensin II AT_1 receptor blockers (ARB'S). It is a benzimidazole derivative and chemically (Figure 1 B) it is

2- {4- [[4-methyl-6-(1-methyl benzimidazole-2yl)-2-propyl benzimidazole-1-yl] methyl] biphenyl)-benzoic acid. The molecular formula and molecular weight of telmisartan is $C_{33}H_{30}N_4O_2$ and 514.6 g/mol. It is insoluble in water, sparingly soluble in dichloromethane, strong acid and organic solvents, soluble in strong base and methanol [4-5]. Telmisartan interferes with the binding of to the Angiotensin II AT_1-receptor by binding reversibly and selectively to the receptors in vascular smooth muscle and the adrenal gland. As Angiotensin II is a vasoconstrictor, which also stimulates the synthesis and release of an aldosterone blockage of its effects results in decreases in systemic vascular resistance. It is used for the treatment of hypertension, lowering high blood pressure helps prevent strokes, heart attacks, and kidney problems. Telmisartan is official in Indian pharmacopoeia and Japanese Pharmacopoeia. A literature survey revealed that analytical methods reported for the estimation of Telmisartan are RP-HPLC, HPLC UV-Spectrophotometric methods. Different trade names of marketed formulations and reported methods of Telmisartan individually and combination with other drugs are presented in the Table 2, Table 3 and Table 6.

Both combination of Azelnidipine and Telmisartan drugs are used for the treatment of hypertension. Literature survey, reported methods like stability indicating RP-HPLC methods development and validation for simultaneous estimation of Azelnidipine and Telmisartan in bulk and pharmaceutical dosage form, and Impurity profiling of Azelnidipine and Telmisartan in fixed dose combination. The aim of the present review depicts the information about the various methods reported for the determination of Azelnidipine and Telmisartan including official pharmacopeial methods.

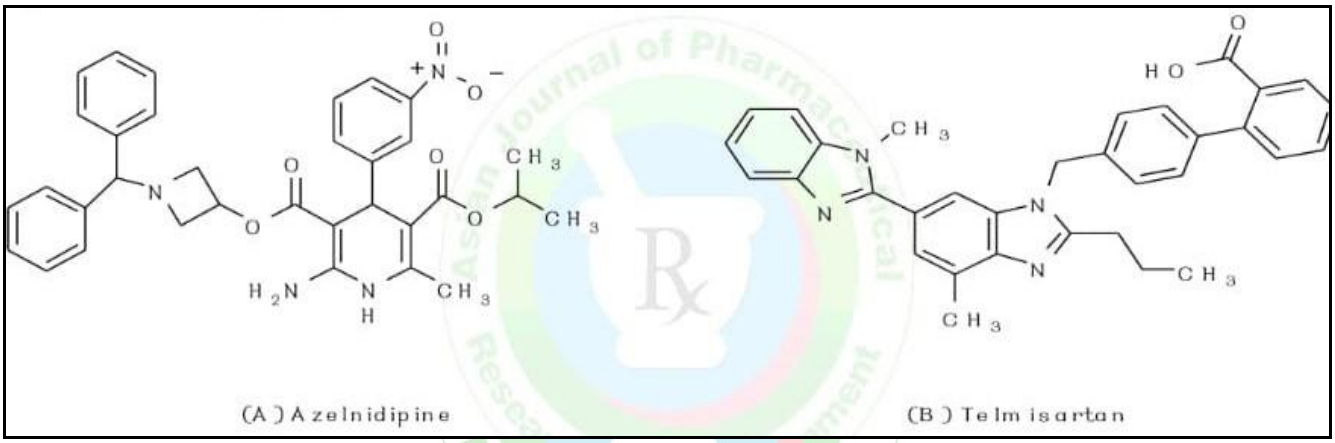

Figure 1: Chemical Structures of (A) Azelnidipine and (B) Telmisartan

Table 1: List of trade names of Azelnidipine [6]

S. No.	Brand Name	Name of the drug and Strength	Manufactured Company
1	Azovas®16	Azelnidipine -16 mg	J.B. Chemicals and Pharmaceuticals Ltd –India
2	Azusa	Azelnidipine -16 mg Azelnidipine – 8 mg	Ajanta Pharma Ltd – India
3	Azelikem 16 Azelikem 8	Azelnidipine -16 mg Azelnidipine -8 mg	Steris Healthcare Pvt. Ltd – India
4	Zeblong®16	Azelnidipine -16 mg	IPCA Laboratories Ltd – India
5	Uniaz®16	Azelnidipine -16 mg	Torrent pharmaceuticals Ltd – India
6	Azeldip™16	Azelnidipine -16 mg	Glenmark Pharmaceuticals Ltd –India

Table 2: List of trade names of Telmisartan [7]

S. No.	Brand Name	Name of the drug and Strength	Manufactured Company
1	Sandoz -20	Telmisartan -20mg	Sandoz Novartis Division or Company – Europe
2	Telista -20 Telista -40	Telmisartan-20 mg Telmisartan 40 mg	Lupin Ltd – India
3	Telsartan™-40	Telmisartan 40 mg	Dr. Reddy 'S Laboratories Ltd –India
4	Telstan -40	Telmisartan-40 mg	Alembic Pharmaceuticals' – India
5	Venpres -40	Telmisartan-40 mg	Lee ford Healthcare Ltd (Generics) – India
6	Watson -40	Telmisartan 40mg	California pet Pharmacy.Com – USA
7	Telin -40	Telmisartan-40 mg	Pharma Drugs and Chemicals – India
8	Uzitel -40	Telmisartan -40 mg	Dr. Kumar's Pharmaceuticals – India
9	Tesian -80	Telmisartan -80 mg	Next well Pharmaceutical Pvt.Ltd – India

Table 3: Combination of Azeldipine and Telmisartan [7]

S. No.	Brand Name	Name of the drug and Strength	Manufactured Company
1	Azelikem –T 40	Azelnidipine -8 mg Telmisartan -40 mg	Steris Healthcare Pvt. Ltd – India
2	Telmiwal™-AP	Azelnidipine -8 mg Telmisartan -40 mg	Intra life India.Com – India
3	Uniaz -40	Azelnidipine -8mg Telmisartan -40mg	Torrent Pharmaceuticals Ltd – India
4	Azovas®T -40	Azelnidipine -8 mg Telmisartan -40 mg	J.B. Chemicals and Pharmaceuticals Ltd – India
5	Azusa T-40	Azelnidipine -8 mg Telmisartan -40 mg	Ajanta Pharma Ltd – India
6	Telma®-AZ	Azelnidipine -8 mg Telmisartan -40 mg	Synokem Pharmaceuticals. Ltd – India
7	Cortel -AZ	Azelnidipine -8 mg Telmisartan -40 mg	Corona Remedies Pvt.Ltd – India

Table 4: Official Methods for Azelnidipine and Telmisartan

S. No.	Drug and Official in	Method	Description	Ref.No.
1	Azelnidipine Indian Pharmacopoeia (2018)	Liquid Chromatography	**Column**: Octadecylsilane Silica (25cm x 4.6 mm,5µm) **Mobile Phase**:0.03 M potassium dihydrogen orthophosphate in water: Acetonitrile (50:50) v/v **Wavelength:** 256 nm **Flow rate**: 1.0 ml/min **Injection volume** :20 µL	4

2	Telmisartan Indian Pharmacopoeia (2018)	Liquid Chromatography	**Stationary Phase (Column):** A Stainless-steel Column 12.5cm ×4mm, packed with octadecylsilane bonded to porous silica (5 µm) **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 1000 ml with water. B) A Mixture of 20 Volume of Methanol and 80 Volume of Acetonitrile (20:80 v/v) **Flow Rate:** 1ml/min. **Wavelength:** 230 nm **Injection Volume:** 10 ml	4
3	Telmisartan Japanese Pharmacopoeia (2018)	Liquid Chromatography	**Stationary Phase (Column):** A Stainless-Steel Column (12.5 cm× 4 mm × 5 µm) **Mobile phase:** A) Dissolve 2 g of potassium dihydrogen phosphate and 3.4 g of sodium1-pentanesulphonate in 1000mL of water, adjusted to pH 3 with dilute orthophosphoric acid. B) A Mixture of Acetonitrile and Methanol (4:1 v/v) **Flow Rate:** 1.0 ml/min **Wavelength:** 230 nm	5

Table 5: Reported Methods for Assessment of Azelnidipine

S. No.	Drugs /Method	Method Description	Ref.No.
1	Azelnidipine/UV Spectrophotometric	**Model:** Shimadzu 1800 UV Visible spectrophotometer **Solvent:** Methanol **Wavelength:** 255 nm **Linearity:** 2 - 14 µg/ ml	8
2	Azelnidipine and Olmesartan Medoxomil/ First Derivative Spectrophotometric	**Model:** Shimadzu – 1800 UV Visible Spectrophotometer **Solvent:** Methanol **Method:** 1.First Derivative Spectrophotometric method **Wavelength (nm):** AZL: 217nm, OLM: 239.4 nm **Linearity:** 4 - 32 µg/ ml	9
3	Azelnidipine/ Spectrophotometric	**Model**: Shimadzu 1800 UV Visible Spectrophotometer **Solvent**: Methanol	10

	.	Method: 1. Second Derivative Spectrophotometric method **Wavelength:** 233.8 nm **Linearity**: 1 - 20 µg / ml	
4	Azelnidipine/ RP-HPLC	**Column:** C18 column (250 mm x 4.5 mm, 5µm) **Mobile Phase:** Methanol: Water (75:25 v/v),0.1% glacial acetic acid. **Flow rate**: 1 mL/min **Wavelength**: 254nm **Linearity:** 10 - 50 µg/ml **Retention Time**: 6.13 min.	11
5	Azelnidipine/ RP-HPLC	**Column:** C18 column (250 mm x 4.5 mm, 5µm) **Mobile Phase**: Methanol: Water (80:20) v/v, Orthophosphoric acid (pH-3) **Flow rate**:1 mL/min. **Wavelength:**257 nm **Linearity:**20-100 µg/ml **Retention Time**: 6.5 min.	12
6	Azelnidipine and two metabolites in Human Plasma/ LC-MS	**Column:** Intersil ODS-3 C18 (2.1 mm ×150 mm,5 µm) **Mobile Phase:** Methanol: Water: Acetic Acid (800:200:0.2 v/v) **Flow rate**: 0.2 ml/min. **Wavelength**: 256 nm **Linearity:** 0.5-40 mg/ml **Retention Time:** AZL –3.6min. M-1 (Aromatized form) -10.2 min. M-2 (Hydroxylated Form)-6.8 min.	13
7	Azelnidipine and Olmesartan Medoxomil/UFLC	**Column:** ODS (250 mm x 4.6 mm, 5 µm) **Mobile Phase:** Methanol: Water (85:15) v/v **Flow Rate**: 1.5 ml/min. **Wavelength:** 255 nm **Linearity:** 2-16 mg/ml **Retention Time**: AZL - 6.80 min, OLM -1.72 min.	14
8	Azelnidipine/ UV and HPLC	**UV Spectrophotometric method:** **Solvent:** Methanol: Water (80:20) v/v **Methods:** **Method 1:** Zero order Spectrophotometric method **Method 2:** First order Derivative Spectrophotometric method **Wavelength**:	15

		Method 1: 257 nm **Method 2**: 242.6 nm **Linearity:** 2-10 µg/ml **Method 3:** RP HPLC Method Column: ODS C18 (250 mm × 4.6 mm.,5 µm) **Mobile Phase:** Sodium diabasic Phosphate Buffer: Acetonitrile: Methanol (10:50:40 v/v/v), orthophosphoric acid (pH - 4.5) **Flow rate:** 1 mL/min **Wavelength**: Method 3 -256 nm **Linearity:** 2-12 µg/ml **Retention Time:** 6.1 min.	
9	Azelnidipine and Olmesartan/ RP-HPLC	**Column:** Hypersil GOLD C18 (150 mm × 4.6 mm, 5 µm) **Mobile Phase**: Methanol: Acetonitrile: Water (40:40:20 v/v/v) **Flow rate**: 0.5 mL/min **Wavelength:** 260 nm **Linearity:** AZL :2-48 µg/ml, OLM :2.5-60 µg/ml **Retention Time:** AZL: 8.56 min, OLM: 3.04 min	16
10	Azelnidipine/ HPTLC	**Stationary Phase**: Silica gel 60 F254 (20cm × 10 cm, 0.2mm) **Mobile Phase:** Chloroform: Ethyl acetate: methanol 6.5:3.5:0.1 (v/v/v) **Wavelength:** 255 nm **Linearity**:300-800 ng/band **Rf Value** :0.59,0.60	17
11	Azelnidipine/ Related Derivative in Human Plasma UPLC-MS	**Column:** C18 (50 mm × 2.1 mm.,1.7 µm) **Mobile Phase**: A (20 mM Ammonium acetate aqueous solution) B (0.1 % formic acid in Acetonitrile) **Flow Rate:** 0.5 mL/min **Linearity:** 0.01-10 mg/ml **Retention Time:** AZL: 1.38 min, IS :1.26	18
12	Azelnidipine in human plasma /liquid chromatography-tandem mass spectrometry	**Mobile Phase:** Isocratic mobile phase conditions **Linearity range:** r^2 >0.997 **Chromatographic run time:** 5.0 min/injection	19
13	Azelnidipine in human plasma/ liquid chromatography-electrospray ionization-mass spectrometry	**Column:** C18 column **Mobile phase:** Methanol-5mM Ammonium acetate solution (90;10, v/v)	20

Table 5: Reported Methods for Assessment of Telmisartan

S. No.	Drugs /Method	Method Description	Ref. No.
1	Telmisartan/HPTLC	**Model:** TLC Plates **Mobile Phase:** Chloroform: Methanol (8.6:1.4 v/v) **Wavelength**:297 nm **Linearity**: 20-160 µg/ml	21
2	Telmisartan and Cilnidipine/ RP-HPLC	**Stationary Phase (Column):** C18 column (250 x 4.6mm, 5 µm) **Mobile Phase:** Acetonitrile (ACN): Buffer PH 3.0 With Orthophosphoric Acid (68:32) **Flow rate**: 1.0 mL/min **Wavelength**: 245 nm **Telmisartan**: **Linearity**: 40-160 µg/ml **Correlation Coefficient:** 0.9990 **Retention Time**: 2min **Cilnidipine**: **Linearity:** 10-40 µg/ml **Correlation Coefficient**: 0.9989 **Retention Time:** 4 min	22
3	Telmisartan and Atorvastatin/ HPTLC HPLC	**HPTLC:** Separation (Silica Gel 60F254) **Mobile Phase**: Toluene: Methanol: Ethyl Acetate: Acetic Acid (5:1:1:0.3 v/v) **Compact Bands:** Telmisartan**:** Rf 0.37 ± 0.02 Atorvastatin 0.63 ± 0.01 **Wavelength**: 279 nm **Linearity**: Telmisartan:40-240 ng/band Atorvastatin**:** 10-60 ng/band **RP-HPLC:** **Column:** C18 **Mobile phase:** Acetonitrile: 0.025 M Ammonium Acetate (38:52% v/v) **Flow rate**: 1.0 mL/min **Wavelength**: UV Detection at 281 nm **Linearity Range**: Telmisartan: 12-72 µg/ml, Atorvastatin: 3-18 µg/ml	23

4	Telmisartan/ RP-HPLC	**Column:** Zorbax-SB-18; (ODS), (150 x 4.6 mm; 3.5 µm) **Mobile Phase**: Buffer: Methanol (40:60 v/v) **Flow rate**: 1.2 mL/min **Wavelength**: 230 nm **Concentration range**: 4-20 µg/ml **Correlation Coefficient:** 0.9999 **Retention Time**: 3-4 min	24
5	Hydrochlorothiazide, Amlodipine Besylate and Telmisartan/ RP-HPLC	**Column:** RP-C18 **Mobile Phase**: Acetonitrile: Acetate Buffer (Adjusted to PH5 with Orthophosphoric Acid) (60:40 % V/V) **Flow Rate**: 1.0 mL/min **Wavelength**: 333 nm **Concentration Range**: 20-100 µg/ml **Retention Time**: Hydrochlorothiazide**:** 2.9 min Amlodipine Besylate**:** 5.1 min Telmisartan**:** 8.2 min	25
6	Benidipine Hydrochloride, Telmisartan and Chlorthalidone/ RP-HPLC	**Column:** C18 (25cmx0.46cm) Hypersil BDS **Mobile Phase**: Buffer (PH3.0): Methanol (50:50 v/v) **Flow Rate**: 1ml/min **Wavelength**: 230 nm **Retention Time**: Benidipine Hydrochloride**:** 6.690 min Telmisartan**:** 8.813 min Chlorthalidone: 4.887 min **Linearity Range**: Benidipine Hydrochloride**:** 2-6µg/ml Telmisartan**:** 20-60 µg/ml Chlorthalidone: 6.25-18.75 µg/ml	26
7	Metoprolol Succinate and Telmisartan/ RP-HPLC	**Column:** Prontosil C 18 (5 µm,250 mmx 4.60 mm) **Mobile Phase**: Acetonitrile: Methanol: Phosphate Buffer PH5 (35:35:30% v/v/v) **Flow Rate**: 1.0 mL/min **Wavelength**: UV PDA Detector-225 nm **Retention Time**: Metoprolol Succinate: (5-25 µg/ml) Telmisartan: (8-40 µg/ml) **Correlation Coefficient**: 1	27

8	Nebivolol and Telmisartan/HPLC	**Column:** Agilent C18 (250 x 4.6 mm; 3µm) **Mobile Phase**: Acetonitrile:0.05M (PH 6.5) Disodium Hydrogen (Na_2HPO_4) Buffer **Retention Time**: Nebivolol: 2.920 min Telmisartan: 8.093 min **Flow Rate**: 1mL/min **Wavelength**:235 nm **Concentration Range:** Nebivolol: 25-75 µg/ml Telmisartan: 100-300 µg/ml **Linearity Regression**: 0.999	28
9	Cilostazol and Telmisartan/ UV-Visible	**Method:** UV-Visible **Method-1:** **Wavelength:** Cilostazol: 258 nm Telmisartan**:** 296 nm **Method-2:** Cilostazol: 237.5nm (Iso Absorptive Point) Telmisartan**:** 258nm (λ max of Cilostazol) **Method-3:** **Beer's Lambert's Law:** **Concentration Range:** Cilostazol: 1-40 µg/ml Telmisartan: 1-25 µg/ml	29
10	Telmisartan/ UV	**Model:** Shimadzu UV1800 UV-Visible double beam spectrophotometer **Solvents:** Ethanol (95%), 0.1 N $NaHCO_3$ **Wavelength:** 240 nm **Linearity:** 2-14 µg/ml	30
11	Telmisartan and Metoprolol Succinate/UV	**Model:** UV-Visible double beam spectrophotometer Shimadzu UV1800 **Solvent:** Methanol **Method 1:** Absorbance correction method **Wavelength:** **Telmisartan:** 296 nm **Metoprolol:** 223 nm **Linearity: Metoprolol:** 2-16 µg/ml; **Metoprolol:** 3 -24 µg/ml	31
12	Amlodipine Besylate And Telmisartan/ UV	**Model:** UVA 1002 E **Solvent:** 0.1 N HCL **Method:**	32

		1. Absorbance correction method, 2. Absorbance ratio Method **Wavelength:** Telmisartan:292 nm, Amlodipine: 326 nm **Linearity:** **Method 1:** **Absorbance correction method** Telmisartan 3-24 µg/ml, Amlodipine:0.5-20 µg/ml **Method 2:** **Absorbance ratio Method** Telmisartan:3-24 µg/ml, Amlodipine: :0.5-15.5 µg/ml	
13	Metoprolol Succinate and Telmisartan/ UV	**Model:** Spectrophotometer Shimadzu UV-1700 Double Beam **Solvent:** Methanol **Method:** **Method A:** First derivative simultaneous equation method (Vierodt's method) **Method B:** First derivative Q-Absorbance equation method. **Method C:** Absorbance correction method **Method D:** First derivative dual wavelength. **Wavelength:** **Methods of Telmisartan**: 1.First derivative simultaneous equation method (Vierodt's method)**:** 237nm 2. First derivative Q-Absorbance equation method**:** 237 nm 3. Absorbance correction method: 296.6 nm 4. First derivative dual wavelength Method: 330 nm **Methods of Metoprolol Succinate:** 1.First derivative simultaneous equation method (Vierodt's method)**:** 230.2 nm 2. First derivative Q-Absorbance equation method**:** 231.8 nm 3. Absorbance correction method: 223 nm 4. First derivative dual wavelength Method: 282.4 nm,284.6 nm **Linearity:** **Methods of Telmisartan:** 1. First derivative simultaneous equation method: 4-16 µg/ml 2. First derivative Q-Absorbance equation method: 4-16 µg/ml 3.Absorbance correction method: 4-16 µg/ml 4. First derivative dual wavelength Method: 4-16 µg/ml **Methods of Metoprolol Succinate:** 1. First derivative simultaneous equation method: 3-20 µg/ml 2. First derivative Q-Absorbance equation method: 3-20 µg/ml 3.Absorbance correction method: 3-20 µg/ml	33

		4. First derivative dual wavelength Method: 3-20 µg/ml	
14	Telmisartan/ UV	**Model:** Shimadzu UV- 1700 **Solvent:** 0.1 N NaOH, Distilled water **Wavelength:** 234 nm **Linearity:** 2-10 µg/ml	34
15	Telmisartan/UV	**Model:** Double beam UV Visible Spectrophotometer Shimadzu UV 1800 **Diluent:** Methanol **Wavelength:**296 nm **Linearity:** 2-12 µg/ml	35
16	Cilnidipine and Telmisartan/ UV Visible	**Model:** Shimadzu UV/Visible double beam spectrophotometer (Model 1700) **Solvent:** Acetonitrile **Wavelength:** **Telmisartan** :241nm Cilnidipine: 203 nm **Linearity:** **Telmisartan:** 0.5-2.5 µg/ml **Cilnidipine:** 2-10 µg/ml	36
17	Telmisartan/ UV	**Model:** UV visible double beam spectrophotometers SL 210 Elico **Solvent:** Methanol, Acetic Acid **Wavelength:** 296.5 nm **Linearity:** 5 -25 µg/ml	37
18	Cilostazol And Telmisartan/ UV Visible	**Model:** Shimadzu model 1700 double beam UV-Visible spectrophotometer **Solvent:** Methanol **Methods:** 1. Simultaneous Equation method 2. Absorbance Ratio method **Wavelength:** TEL :258 nm, 237.5 nm CLZ: 258 nm, 237.5 nm **Linearity:** TEL :1 -5 µg/ml, CLZ: 4-20 µg/ml	38
19	Telmisartan/ RP-HPLC.	**Column:** C18 sun fire column (250 mm x 4.6 mm,5 µm) **Mobile Phase:** Potassium di-hydrogen Phosphate: Acetonitrile (60:40) v/v **Flow Rate:** 1 mL/min	39

		Wavelength: 243nm **Linearity:** 50 -150 µg/ml **Retention Time:** 3.4 min.	
20	Telmisartan/ RP-HPLC	**Column:** Hibar C18 (250 mm x 4.6 mm ,5 µm) **Mobile Phase:** Ammonium format solution (pH 4.0) : Methanol (70:30), v/v **Flow Rate:** 1 mL/min **Wavelength:** 275 nm **Linearity:** 0.1-1.5 (µg/ml) **Retention Time:** 3.7 min.	40
21	Telmisartan and Hydrochlorothiazide/ RP HPLC	**Column:** Agilent C18 (4.6 mm×150 mm,5µ) **Mobile Phase:** Methanol: Acetonitrile (70: 30) v/v **Flow rate:** 1mL/min **Wavelength:** 240nm **Linearity:** TEL: 15- 55 µg/ml, HCTZ :50 -250 µg/ml **Retention Time:** TEL: 1.8 min, HCTZ: 2.4 min	41
22	Telmisartan and Hydrochlorothiazide/ QbD based HPLC	**Column:** Kromasil C18(125mm× 4.0 mm, 5 µm), Inertsil ODS 3 V (150 mm 4.6 mm, 3.5 µm) **Mobile Phase:** **Solvent A:** Potassium dihydrogen phosphate buffer, (pH 3.5) 1%Ortho phosphoric acid solution **Solvent B:** Purified water and acetonitrile (100:900) v/v **Flow rate:** 1.0 mL/min. **Wavelength:** 230 nm **Linearity:** TEL :1.5 µg/mL, HCZ: 0.6 µg/mL **Retention Time:** 3.2 min.	42
23	Simvastatin, Atorvastatin, Telmisartan and Irbesartan/ RP- HPLC	**Column:** C18 (75 mm × 4.6 mm ,3.5 µ) **Mobile Phase:** Ammonium acetate buffer (10 mM (pH 4.0): Acetonitrile (40:60) v/v **Flow rate:** 1 mL/min **Linearity:** 1–16 µg/mL **Wavelength:**220 nm **Retention Time:** IRB: 1.20 min, ATV: 1.82 min. TLM: 2.40 min, SMV: 6.03 min.	43
24	Telmisartan and Metformin Hydrochloride/ Spectrophotometric	**Model:** Shimadzu model 1700 **Diluents:** Methanol: Water (50: 50) v/v	44

		Method: First Order Derivative **Linearity:** TEL :6-16 µg/m, MET: 6–16 µg/mL **Wavelength:** TEL: 251 nm, MET: 217 nm	
25	Telmisartan and Atorvastatin/ RP- HPLC	**Column:** Boston ODS C18 (250mm x 4.6 mm, 5 µ) **Mobile Phase:** Methanol: Acetonitrile: buffer (35:25:40) v/v **Flow rate:** 1.0 mL/min. **Wavelength:** 235 nm **Linearity:** 60-140 µg/ml **Retention Time:** TEL: 3.5 min, ATC :2.3 min**.**	45
26	Amlodipine Besylate, Hydrochlorothiazide and Telmisartan/ HPTLC	**Stationary phase:** pre-coated with silica gel 60F254(10×10 cm) **Mobile Phase:** Chloroform: Butanol: Ammonia (6: 4: 0.1) v/v/v **Flow Rate:** 1 mL /min. **Wavelength:** AML :237.5nm, HCTZ: 270 nm, TLM :297nm **Linearity:** AML: 200-1000ng/band, HCTZ: 500-2500 ng/band, TLM :1600-8000 ng/band **Retention Time:** AML: 3.2 min, HCTZ: 3.1 min, TEL :3.5 min**.**	46
27	Telmisartan/ RP-HPLC	**Column:** RP18 (250mm×4.6mm,5µ**)** **Mobile Phase:** 0.025M potassium dihydrogen phosphate: Acetonitrile: Methanol (45:50:5) v/v/v **Flow rate:** 1 ml/min. **Wavelength:** 216 nm **Linearity:** 100 - 500 µg/ml **Retention Time:** 3.6 min.	47
28	Telmisartan and Atorvastatin / RP-HPLC	**Column:** Inertsil-ODS C18 (250mm×4.6mm,5µ) **Mobile Phase:** Methanol: water (50:50) v/v **Wavelength:** 250 nm **Flow rate:**1 mL/min **Linearity:** 20 to 80 µg/ml **Retention Time:** TEL: 2.4 min, ATC: 3 min	48

29	Telmisartan In Rat Plasma /HPLC	**Column:** Phenomenex Luna® C8 (300mm× 4.6 mm,5µ) **Mobile Phase:** Methanol: Acetonitrile (70:30 (v/v) **Flow rate:** 1 ml/min **Wavelength:** 190-800 nm **Linearity:** 10 - 1000 µg/ml **Retention Time:** 2.3 min.	49
30	Metformin And Telmisartan/ RP-HPLC	**Column:** BDS (250mm x 4.6 mm, 5 µm) **Mobile Phase:** Buffer: Acetonitrile: Methanol (35:55:10) v/v/v **Flow rate:** 1mL/min **Wavelength:** 237nm **Linearity:** MET: 5-30 µg/ml, TEL: 62.5-375µg/ml **Retention Time:** MET: 2.4 min, TEL: 3.2 min.	50
31	Amlodipine Besylate and Telmisartan/ RP-HPLC	**Column:** Phenomenix C18 (250 mm × 4.6 mm, 5 µm) **Mobile Phase:** 0.02M Ammonium Phosphate buffer: Acetonitrile: Methanol (40:35:25) v/v/v **Flow rate:** 1.0 mL/min **Wavelength:**254 nm **Linearity:** TEL: 0.8 -160 µg/ml, AMLB: 0.1-2 µg/ml **Retention Time:** TEL: 2.65 min, AMLB: 4.996 min.	51
32	Telmisartan/ RP-HPLC	**Column:** C18 column (4.6 mm×250 mm, 5 µm) **Mobile Phase:** Methanol:0.01 M sodium dihydrogen orthophosphate (41:10:49) v/v/v (pH 3.0) Orthophosphoric acid **Wavelength:** 291 nm **Flow rate:** 0.8mL/min **Linearity:** 0.1-10µg/ml **Retention Time:** 2.4 min.	52
33	Telmisartan and Nifedipine In Synthetic Mixture/ RP-HPLC	**Column:** Phenomenex Luna C18(250 mm×4.6 mm,5µ) **Mobile Phase:** ACN: Water: Methanol (10:20:70 v/v/v) pH 3.8 **Wavelength:** 234 nm **Flow rate:** 1 ml/min **Linearity:** TEL: 4-20 µg/ml, NIF: 2-10 µg/ml	53

		Retention Time: TEL: 2.563 min NIF: 4.403 min	
34	Telmisartan and Chlorthalidone/ RP-HPLC	**Column:** CAPCELL C18 (250 mm×4.6 mm, 5 µm) **Mobile Phase:** Potassium di hydrogen ortho phosphate buffer: Acetonitrile: Methanol (35:45:20) v/v/v (pH 3.5) Ortho phosphoric acid **Flow Rate:** 0.8 mL/min. **Wavelength:**296nm **Linearity:** TEL :20- 100µg/mL, CHLT: 6.25-31.25 µg/mL **Retention Time:** TEL: 4.97 min, CHLT: 3.46 min.	54
35	Telmisartan and Cilostazol in the Synthetic mixture/ RP-HPLC	**Column:** C18G (250 mm × 4.6 mm, 5 µm) **Mobile Phase:** Potassium di hydrogen phosphate buffer (10mM): Methanol: Acetonitrile (30:10:60) v/v/v (pH 5.8) **Flow rate:** 1.0 mL/min. **Wavelength:** 257 nm **Linearity:** TEL :2-10 µg/ml, CIL :4-20 µg/ml **Retention Time:** TEL: 9.6 min, CIL: 5.49 min.	55
36	Bisoprolol Fumarate and Telmisartan/ RP HPLC	**Column:** Waters X Bridge RP C18(250mm x 4.6 mm,5µm) **Mobile Phase:** Methanol and water (75:25 v/v) **Flow Rate:** 1ml/min. **Wavelength:** 231nm **Linearity:** BIS: 5-25 µg/ml TEL: 40-200 µg/ml **Retention Time:** BIS: 5.7 min, TEL: 7.6 min.	56
37	Telmisartan/ RP-UHPLC	**Column:** Poroshell 120EC-C18 column (4.6 x 50mm, 2.7 µm) **Mobile Phase:** Acetonitrile: 50 mM ammonium acetate buffer (45: 55) v/v, (pH 4.5) acetic acid. **Flow rate:** 1mL/min. **Wavelength:** 290 nm **Linearity:**100-300 µg/ml	57

38	Telmisartan And Amlodipine/ RP-HPLC	**Column:** Hypersil BDS C18 Column (100 mm x 4.6 mm, 5µ.) **Mobile Phase:** Phosphate Buffer (pH 3.6): Acetonitrile (60:40 v/v) **Flow rate:** 1 mL/min. **Wavelength:** 234 nm **Linearity:** TEL :10–150 µg/ml AMLB :1–20 µg/ml **Retention Time:** TEL: 4.1 min, AMLB: 2.6 min	58
39	Telmisartan/ Stability Indicating RP-HPLC	**Column:** C18 Column (4.6x150mm,3.5µm Make: X Terra) **Mobile Phase:** Buffer: Methanol (40:60 v/v) **Flow Rate:** 0.5mL/min **Wavelength:**230 nm **Linearity:** 20-100 µg/ml **Retention Time:** 2.6 min	59
40	Telmisartan/RP-HPLC	**Column:** C18 Column (250 x 4.6mm,5 µm) **Mobile Phase:** 10mM Potassium Dihydrogen Phosphate: Acetonitrile (64:40) **Flow Rate:** 1.0mL/min **Wavelength:**230 nm **Linearity:** 10-50 µg/ml **Retention Time:** 12 min	60
41	Telmisartan/ stability indicating HPLC	**Column :X-Bridge** C18 Column (150x4.6mm,3.5µm) **Mobile Phase: 25** mM Potassium Dihydrogen Phosphate: Acetonitrile and 10mM of 1- Hexane sulphonic Acid **Linearity:** 0.08-500 µg/ml	61
42	Azelnidipine and Telmisartan/ Stability Indicating RP-HPLC	**Column:** C18 Column (150x4.6mm,5µm) **Mobile Phase:** 0.1%. OPA: Acetonitrile (60:40 v/v) **Flow Rate:** 1.0mL/min **Wavelength:** 242.0 nm **Retention Time:** 2116-3.188 min	62
43	Impurity profiling of Azelnidipine and Telmisartan/Gradient RP-HPLC	**Column:** C18 Column (150x4.6mm,5µm) **Mobile Phase:** Acetonitrile and Buffer **Flow Rate:** 1.5mL/min **Wavelength:**254 nm **Retention Time:** 40.0 min	63
44	Olmesartan and Azelnidipine/ Stability Indicating Liquid Chromatographic Method	**Column:** Hypersil Gold C18 Column (150x4.6mm,5µm) **Mobile Phase:** Methanol: Acetonitrile: Water (40:40:20v/v) **Flow Rate:** 0.5mL/min **Wavelength:**260 nm	64

		Retention Time: **Azelnidipine:**8.56min **Olmesartan:**3.04min **Linearity Range:** 2-48 µg/ml	

CONCLUSION

This review article presents with Physico-chemical properties, Pharmacological actions, and trade names of some marketed formulations of Azelnidipine and Telmisartan. The presented review depicts the information about the various methods available in the literature for the determination of Azelnidipine and Telmisartan including official pharmacopeial assay methods. According to this review it was concluded that the different analytical methods are reported for estimation Azelnidipine and Telmisartan individual and other combination like UV Spectroscopy, HPTLC, HPLC, LC-MS. Hence all methods found to be simple, accurate, economic, precise and reproducible in nature. Most of Methods were of RP-HPLC (21 methods) and UV Spectrophotometric methods (11 methods) because these methods provided with best available reliability, repeatability, analysis time and sensitivity. The given Literature review focus that there is two HPLC methods are reported for Azelnidipine and Telmisartan in fixed dose combination. This review will help in future to develop the analytical methods for this new combination and also gives the knowledge about its characteristics of both drugs.

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