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A REVIEW ON ANALYTICAL METHOD FOR THE ESTIMATION OF TELMISARTAN AND BISOPROLOL FUMARATE

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ABSTRACT

High blood pressure, sometimes known as hypertension, is a frequent disorder marked by unusually high blood vessel pressure. Many people get hypertension (HT), especially as they age. Although it is not a disease in and of itself, it is a substantial risk factor for cardiovascular mortality and morbidity. A more recent combination on the market, Telmisartan and Bisoprolol Fumarate, is effective in treating hypertension. This combination was developed to improve Stage II hypertension therapy. A beta 1-selective compound known as bisoprolol fumarate is also known as bis(1-[(propan-2-yl) amino] Cardio selective adrenoceptor blocker: 3-(4-[2-(propan-2-yloxy) ethoxy] methylphenoxy) propan-2-ol. Chemically, telmisartan is a 2-4-[[4-methyl-6-(1-methylbenzimidazol-2yl)-2-propylbenzimidazol-1yl] methyl] biphenyl and an AT1-receptor blocker. It contains details on the development of several analytical techniques such UV, HPTLC, HPLC are methods reported for bisoprolol fumarate and telmisartan as single medications and in drug combinations. All procedures presented have been shown to be straightforward, precise, cost-effective, and repeatable. According to our knowledge, there have been two techniques described for the combination of bisoprolol fumarate SS and telmisartan, which is the topic of this review.

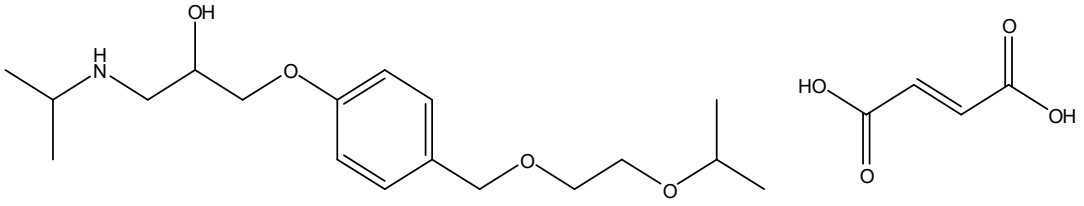
Keywords: Bisoprolol fumarate, Telmisartan, Analytical Method, HPLC, HPTLC, UV

INTRODUCTION:

Bisoprolol Fumarate:

The pharmacological class of synthetic beta1-adrenergic blockers, which includes bisoprolol, is used often in daily clinical practice to treat angina pectoris and hypertension. It is a beta adrenoreceptor blocker, bisoprolol fumarate. It is a crystalline white powder. Beta-blockers, which compete with beta-adrenergic receptor antagonists, are used to treat heart failure, angina pectoris, and hypertension. Bisoprolol fumarate is a synthetic beta 1-selective, cardio selective adrenoceptor blocker. It is available as a racemic mixture and contains an asymmetric carbon atom. The S (-) enantiomer performs the majority of the -blocking functions. Chemical formula $C_{40}H_{66}N_2O_{12}$ melting point: 100 °C, molecular weight: 766.97 g/mol. It appears as a white, crystalline powder that readily dissolves in several liquids, including water, methanol, ethanol, and chloroform. It is acknowledged by BP, USP, and IP **[1]**.

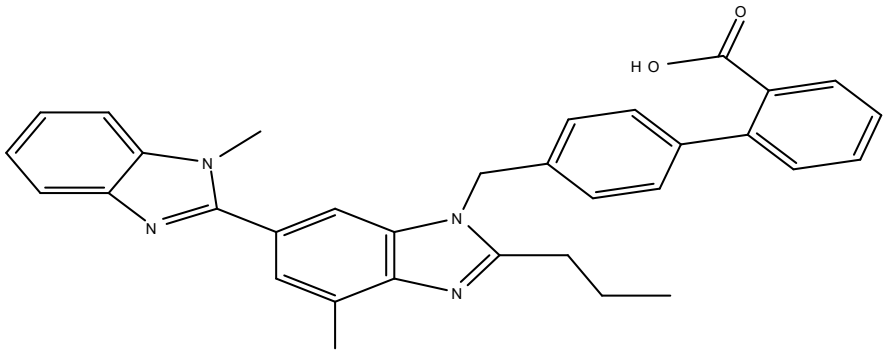
Chemical name: (2E)-but-2-enedioic acid; bis(1-[(propan-2-yl) amino]-3-(4-{[2-(propan-2-yloxy) ethoxy] methyl} phenoxy) propan-2-ol).



bisoprolol fumarate

Telmisartan:

Angiotensin II receptor antagonist (ARB) telmisartan is used to treat hypertension. Angiotensin II AT1 receptor blockers, or ARBs, include telmisartan. It is a derivative of the benzimidazole. Angiotensin II cannot attach to the AT1-receptor because telmisartan binds reversibly and selectively to receptors in the vascular smooth muscle and adrenal gland. A blockade of angiotensin II's effects reduces systemic vascular resistance since it is a vasoconstrictor and promotes the generation of aldosterone. Molecular weight $C_{33}H_{30}N_4O_2$, atomic mass 514.6 g/mol, essentially water insoluble Strong bases and acids may dissolve it without harming it, 261-263 °C, melting point Name of the chemical compound: 2-[4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl] methyl phenyl] benzoic acid. It is used to treat high blood pressure, which helps prevent strokes, heart attacks and renal problems.



telmisartan

LITERATURE REVIEW:

Telmisartan:

Telmisartan Official Method:

S. No.	Title	Description	Reference No.
1.	Telmisartan Indian pharmacopoeia (IP-2018) Volume III	Column: stainless steel column Column size: (12.5cm x 4.6 mm, bonded to porous silica and filled with octyl silane 5µm – particle size) Solvent: methanol: acetonitrile (20:80 v/v) Flow rate: 1 ml min^{-1} Injection volume: 20 microlitre	[2]
2.	Telmisartan United state pharmacopoeia (USP-2015) Volume III	Column: stainless steel column Column size: 4.0 mm x 12.5cm x 5µm packaging Solvent: acetonitrile: methanol (4:1v/v) Flow rate: 1 ml min^{-1} Injection volume: 2 microlitre	[3]
3.	Telmisartan British pharmacopoeia (BP- 2009) Volume II	Column: octadecyl (C_{18}) silica gel for chromatography Column size: 0.125m x 4 mm (ID) x 5µm packaging Solvent: methanol: acetonitrile (20:80 v/v) Flow rate: 1 ml/min^{-1} Injection volume: 10 microlitre	[4]

Telmisartan Reported Methods:

S. No.	Title	Method	Description	Reference No.
1.	Azelnidipine and Telmisartan	Stability Indicating RP HPLC	Column: C_{18} Column (150mm x 4.6mm, 5µm) Mobile Phase: 0.1.% OPA: Acetonitrile (60:40, v/v) Flow Rate: 1.0 ml min^{-1} λ_{max}: 242 nm Range TEL: 10-60 µg ml^{-1}, AZL: 2- 12 µg ml^{-1} Retention Time: 2116-3.188 min	[5]
2.	Impurity profiling of Azelnidipine and Telmisartan	RP HPLC	Column: C_{18} Column (150mm x 4.6mm, 5µm) Mobile Phase: Buffer and Acetonitrile (25:75, v/v) Flow Rate: 1.5 ml min^{-1} λ_{max}: 254 nm Range: AZL: 22.50-67.49 µg ml^{-1}, TEL: 238.71-716.12 µg ml^{-1} Retention Time: 40 min	[6]

3.	**Efonidipine Hydrochloride Ehanolate and Telmisartan**	**RP HPLC**	**Column: C_{18} column (250 mm x 4.6 mm, 5µm)** **Mobile Phase: Acetonitrile: Phosphate Buffer (45:55, v/v)** **Flow rate: 1.0 ml min^{-1}** **λ_{max}: 274 nm** **Range** **EHE: 5-30µg ml^{-1}, TEL: 10-60µg ml^{-1}** **Retention time** **EHE: 7.77 min, TEL: 4.10 min**	**[7]**
4.	**Telmisartan and Hydrochlorothiazide/ QBD based HPLC**	**HPLC**	**Column: Kromasil C_{18}(125mm x 4.0mm, 5µm), Inertsil ODS 3 V (150 mm x 4.6 mm, 3.5µm)** **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 ml min^{-1}** **λ_{max}: 230 nm** **Range:** **TEL: 1.5µg ml^{-1}, HCZ: 0.6µg ml^{-1}** **Retention time:** **TEL: 8-15 min, HCZ: 40-50 min**	**[8]**
5.	**Simvastatin, Atorvastatin, Telmisartan and Irbesartan**	**RP HPLC**	**Column: C_{18}(75 mm x 4.6 mm, 3.5µm)** **Mobile Phase:** **Acetonitrile: Ammonium acetate buffer (60:40, v/v)** **Flow rate: 1ml min^{-1}** **λ_{max}: 220 nm** **Range: 1-16µg ml^{-1}** **Retention Time:** **IRB: 1.20 min, ATV: 1.82 min.** **TLM: 2.40 min, SMV: 6.03 min**	**[9]**
6.	**Telmisartan and Atorvastatin**	**RP HPLC**	**Column: Inertsil-ODS C_{18} (250 mm x 4.6 mm, 5µm)** **Mobile Phase: Methanol: water (50:50, v/v)** **Flow rate:1 ml min^{-1}** **λ_{max}: 250 nm** **Range: 20-80 µg ml^{-1}** **Retention Time:** **TEL: 2.4 min, ATC: 3 min**	**[10]**
7.	**Amlodipine besylate, Telmisartan**	**RP HPLC**	**Column: Hypersil BDS (100mm × 4.6 mm, 5µm)** **Mobile phase: Phosphate buffer: Acetonitrile (57:43, v/v)** **λ_{max}: 237 nm** **Range: Telmisartan: 10-60 µg ml^{-1}** **Amlodipine: 12.5-75 µg ml^{-1}** **Flow rate: 1.0 ml min^{-1}** **Retention time:** **TEL: 2.560 min, AML: 3.148 min**	**[11]**
8.	**Telmisartan and Atorvastatin**	**RP HPLC**	**Column: Boston ODS C_{18} (250mm ×4.6 mm, 5 µm)** **Mobile Phase: Buffer: methanol: acetonitrile (40:35:25, v/v)** **Flow rate: 1.0 ml min^{-1}** **λ_{max}: 235 nm** **Range: 60-140 µg ml^{-1}** **Retention Time:** **TEL: 3.5 min, ATC :2.3 min**	**[12]**

9.	**Nebivolol and Telmisartan**	**HPLC**	**Column: Agilent C_{18} (250mm x 4.6 mm, 3µm) Mobile Phase: Acetonitrile: Disodium Hydrogen (Na_2HPO_4) Buffer (40:60, v/v) Flow Rate: 1 ml min^{-1} λ_{max}: 235 nm Range: NBV: 25-75 µg ml^{-1}, TEL: 100-300 µg ml^{-1} Retention Time: NBV: 2.920 min, TEL: 8.093 min**	**13**
10.	**Telmisartan**	**UV**	**Model: UV visible double beam spectrophotometers SL 210 Elico Solvent: Methanol, Acetic Acid λ_{max}: 296.5 nm Range: 5 -25 µg ml^{-1}**	**[14]**
11.	**Amlodipine Besylate and Telmisartan**	**RP HPLC**	**Column: Phenomenix C_{18}(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^{-1} λ_{max}:254 nm Range: TEL: 0.8 -160 µg ml^{-1}, AMLB: 0.1-2 µg ml^{-1} Retention Time: TEL: 2.65 min, AMLB: 4.996 min**	**[15]**
12.	**Cilnidipine and Telmisartan**	**UV**	**Model: Shimadzu UV Visible double beam spectrophotometer Solvent: Acetonitrile λ_{max}: TEL: 241 nm, CIL: 203 nm Range: TEL: 0.5-2.5 µg ml^{-1}, CIL: 2-10 µg ml^{-1}**	**[16]**
13.	**Telmisartan and Hydrochlorothiazide**	**RP HPLC**	**Column: Agilent C_{18} (4.6 mm×150 mm,5µm) Mobile Phase: Methanol: Acetonitrile (70: 30, v/v) Flow rate: 1 ml min^{-1} λ_{max}: 240 nm Range: TEL: 15- 55 µg ml^{-1}, HCTZ: 50 -250 µg ml^{-1} Retention Time: TEL: 1.8 min, HCTZ: 2.4 min**	**[17]**
14.	**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^{-1} λ_{max}: AML: 237.5nm, HCTZ: 270 nm, TLM :297nm Range: AML: 200-1000 ng/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**	**[18]**
15.	**Telmisartan and Nifedipine In Synthetic Mixture**	**RP HPLC**	**Column: Phenomenex Luna C_{18}(250 mm ×4.6 mm, 5µm) Mobile Phase: CAN: Water: Methanol (10:20:70, v/v/v) λ_{max}: 234 nm**	**[19]**

			Flow rate: 1 ml min^{-1} Range: TEL: 4-20 µg ml^{-1}, NIF: 2-10 µg ml^{-1} Retention Time: TEL: 2.563 min, NIF: 4.403 min	
16.	**Metformin And Telmisartan**	**RP HPLC**	**Column: BDS (250mm x 4.6 mm, 5 µm) Mobile Phase: Acetonitrile: buffer: Methanol (55:35:10, v/v/v) Flow rate: 1ml min^{-1} λ_{max}: 237 nm Range: MET: 5-30 µg ml^{-1}, TEL: 62.5-375µg ml^{-1} Retention Time: MET: 2.4 min, TEL: 3.2 min**	**[20]**
17.	**Telmisartan and Chlorthalidone**	**RP HPLC**	**Column: CAPCELL C_{18} (250 mm x 4.6 mm, 5µm) Mobile Phase: Potassium dihydrogen ortho phosphate buffer: Acetonitrile: Methanol (35:45:20, v/v/v) Flow Rate: 0.8 ml min^{-1} λ_{max}: 296 nm Range: TEL :20- 100µg ml^{-1}, CHLT: 6.25-31.25µg ml^{-1} Retention Time: TEL: 4.97 min, CHLT: 3.46 min**	**[21]**
18.	**Telmisartan And Amlodipine**	**RP HPLC**	**Column: Hypersil BDS C_{18} Column (100 mm x 4.6 mm, 5µm) Mobile Phase: Phosphate Buffer: Acetonitrile (60:40, v/v) Flow rate: 1 ml min^{-1} λ_{max}: 234 nm Range: TEL: 10–150 µg ml^{-1}, AMLB: 1–20 µg ml^{-1} Retention Time: TEL: 4.1 min, AMLB: 2.6 min**	**[22]**
19.	**Telmisartan, cilnidipine**	**HPLC**	**Column: inertsil ods C_{18}(250mm x 4.6 mm, 5µm) Mobile phase: Methanol: Phosphate buffer: acetonitrile (40:30:30, v/v/v) λ_{max}: 232 nm Range: TEL: 48-112 µg ml^{-1}, CIL: 12-28 µg ml^{-1} Flow rate: 1.0 ml min^{-1} Retention time: TEL: 2.735 min, CIL: 4.958 min**	**[23]**
20.	**Telmisartan and Cilnidipine**	**RP HPLC**	**Stationary Phase (Column): C_{18} column (250 x 4.6mm, 5 µm) Mobile Phase: Acetonitrile: Buffer with Orthophosphoric Acid (68:32v/v) Flow rate: 1.0 ml min^{-1} λ_{max}: Telmisartan: 245 nm Range: 40-160 µg ml^{-1} Retention Time: Cilnidipine: 2 min, Telmisartan: 2.8 min Range: 10-40 µg ml^{-1} Retention Time: CLN: 4 min, TEL: 2.6 min**	**[24]**
21.	**Telmisartan and Atorvastatin/ HPTLC, HPLC**	**HPLC HPTLC**	**HPTLC: Stationary phase: Separation (Silica Gel 60F254) Mobile Phase:**	**[25]**

			Toluene: Methanol: Ethyl Acetate: Acetic Acid (5:1:1:0.3, v/v/v/v) **Compact Bands:** **Telmisartan: R_f 0.37 ± 0.02** **Atorvastatin R_f 0.63 ± 0.01** **λ_{max}: 279 nm** **Range:** **Telmisartan: 40-240 ng/band** **Atorvastatin: 10-60 ng/band** **RP-HPLC:** **Column: C_{18}** **Mobile phase:** **Acetonitrile: 0.025 M Ammonium Acetate (38:52, v/v)** **Flow rate: 1.0 ml min^{-1}** **λ_{max}: UV Detection at 281 nm** **Range Range:** **TEL: 12-72 µg ml^{-1}, ATS: 3-18 µg ml^{-1}** **Retention time: TEL: 3.490 min, ATS: 2.350 min**	
22.	**Telmisartan**	**RP HPLC**	**Column: Zorbax-SB-18; (ODS), (150mm x 4.6 mm; 3.5 µm)** **Mobile Phase:** **Methanol: buffer (60:40, v/v)** **Flow rate: 1.2 ml min^{-1}** **λ_{max}: 230 nm** **Concentration range: 4-20 µg ml^{-1}** **Retention Time: 3-4 min**	**[26]**
23.	**Metoprolol Succinate and Telmisartan**	**RP HPLC**	**Column: Prontosil C_{18} (5 µm, 250 mm x 4.60 mm)** **Mobile Phase:** **Acetonitrile: Methanol: Phosphate Buffer (35:35:30, v/v/v)** **Flow Rate: 1.0 ml min^{-1}** **λ_{max}: 225 nm** **Range:** **TEL: 0.16-0.24 µg ml^{-1}, MET: 0.2-0.3 µg ml^{-1}** **Retention Time:** **MET: 5-25 µg ml^{-1}, TEL: 8-40 µg ml^{-1}**	**[27]**
24.	**Telmisartan; Amlodipine besylate**	**HPTLC**	**Stationary phase: silica gel plate 60 F254** **Mobile phase: Tetrahydrofuran: dichloroethane: methanol: ammonia solution (3:1:0.5:0.2, v/v/v/v)** **λ_{max}: 326 nm** **Range:** **TEL: 1200-7200 ng $spot^{-1}$** **AML: 400-1400 ng $spot^{-1}$** **R_f value:** **TEL: 0.22 ± 0.02** **AMB: 0.45 ± 0.02**	**[28]**
25.	**Telmisartan, Hydrochlorothiazide**	**HPTLC**	**Stationary phase: silica gel plate 60 F254** **Mobile phase: acetate: chloroform: methanol (10:3:1, v/v/v)** **λ_{max}: 270 nm** **Range:** **Hydrochlorothiazide: 500-750 µg ml^{-1}** **Telmisartan: 1600-2400 µg ml^{-1}** **R_f values: TEL: 0.9998, HCZ:0.9999**	**[29]**

Bisoprolol Fumarate:

Bisoprolol Fumarate Official Methods:

No.	Title	Description	Reference No.
1.	**Bisoprolol fumarate (IP-2018)**	**Column: stainless steel column Column size: (12.5cm x 4.6 mm, packed with octyl silane bonded to porous silica 5µm – particle size) λ_{max}: 273 nm Solvent: water: acetonitrile (65:35v/v) Flow rate: 1 ml min^{-1} Injection volume: 10µl**	**[30]**
2.	**Bisoprolol fumarate (USP-2015)**	**Column: LiChrospher 7 column (octasilane C_8 column) Column size: (12.5cm × 4.6 mm, 5µm – particle size) λ_{max}: 273 nm Solvent: water: acetonitrile (65:35v/v) Flow rate: 1 ml min^{-1} Injection volume: 10 µl**	**[31]**
3.	**Bisoprolol fumarate (BP-2009)**	**Column: C_{18} column Column size: (0.25m × 4.6mm, packed with octyl silane 5µm – particle size) λ_{max}: 225 nm Solvent: acetonitrile: water (20:80v/v) Flow rate: 1 ml min^{-1} Injection volume: 10 µl**	**[32]**

Bisoprolol Fumarate Reported Methods:

No.	Title	Method	Description	Reference No.
1.	**Bisoprolol, Amlodipine,**	**Stability indicating RP-HPLC**	**Column: Oyster ODS3 (150mm x 4.6 mm, 5 µm) Mobile phase: Orthophosphoric acid: methanol: acetonitrile (42:29:29, v/v/v) λ_{max}: 230 nm Flow rate: 1.0 ml min^{-1} Range: BIS: 60.08– 140.19 µg ml^{-1} AML: 59.73–139.37 µg ml^{-1} Retention time: BIS: 4.4 min, AML: 6.4 min**	**[33]**
2.	**Bisoprolol, Enalapril**	**HPLC**	**Column: Zorbax Rx C_8 (250mm×4.6mm, 5µm) Mobile phase: Methanol: perchloric acid (55:45v/v) Flow rate: 1ml min^{-1} λ_{max}: 214nm Range: Bisoprolol: 20–200 ug ml^{-1} Enalapril: 20–200 ug ml^{-1} Retention time: BIS: 4.6 min, ENL: 5.18 min**	**[34]**
3.	**Bisoprolol Fumarate, Cilnidipine**	**RP-HPLC**	**Column: (C_{18}) Inertsil ODS 3V column (150 x 4.6mm,5µm) Mobile phase: buffer: methanol: (20:80 v/v) Flow rate: 1.0ml min^{-1} λ_{max}: 231nm Range: Bisoprolol Fumarate: 5-25µg ml^{-1} Cilnidipine: 10-50µg ml^{-1} Retention time: BIS: 2.84 min, CIL: 1.51 min**	**[35]**
4.	**Amlodipine, Bisoprolol Fumarate**	**RP-HPLC**	**Column: Column C_{18} (250 mm× 4.6 mm) Mobile phase:**	**[36]**

			Methanol: Water (65:35 v/v) **λ_{max}: 230 nm** **Range: 5-25 µg ml^{-1}** **Flow rate: 0.1 ml min^{-1}** **Retention time:** **AML: 3.49 min, BIS: 6.52 min**	
5.	**Bisoprolol Fumarate, Cilnidipine**	**UV**	**Model: shimadzu1800uv/VIS** **Solvent:** **methanol: water (80:20v/v)** **λ_{max}: 200-400 nm** **Range:** **BIS: 5- 15µg ml^{-1}** **CIL:10-30µg ml^{-1}**	**[37]**
6.	**Bisoprolol fumarate**	**HPLC**	**HPLC: in human plasma** **Column: C_{18} reverse-phase column (Inertsil, 4 mm, 150 × 4.6 mm)** **Mobile phase:** **methanol-water (70: 30v/v)** **Flow rate: 1.2 ml min^{-1}** **Range: 10–2000 mg ml^{-1}** **Retention time: 4.79 min**	**[38]**
7.	**Bisoprolol fumarate**	**UV**	**Model: shimadzu1800 uv/VIS** **Solvent: water** **λ_{max}: 200-400 nm** **Range:** **BIS: 5-25µg ml^{-1}**	**[39]**
8.	**Cilnidipine, Bisoprolol Fumarate**	**RP-HPLC**	**Column: Shiseido – C_{18} (250mm×4.6mm, 5 µm)** **Mobile phase: Phosphate buffer (pH-3.5): Methanol (60:40v/v)** **Flow rate: 1.0ml min^{-1}** **λ_{max}: 225 nm** **Range:** **CIL: 10-30 µg ml^{-1}** **BIS: 5-15 µg ml^{-1}** **Retention time:** **CIL: 4.053 min, BIS :5.730 min**	**[40]**
9.	**Bisoprolol**	**HPLC**	**Column: C_{18} (5µm, 4.6mm×250 mm)** **Mobile phase:** **methanol: phosphate buffer solution (65:35 v/v)** **Flow rate: 1.0 ml min^{-1}** **λ_{max}: 225 nm** **Range: BIS: 5-25µg ml^{-1}** **Retention time: 2.8 min**	**[41]**
10.	**Bisoprolol**	**UV**	**Model: SL 210 Elico** **λ_{max}: 223.5 nm** **R^2: 0.999** **Range: 5-25 µg ml^{-1}**	**[42]**
11.	**Bisoprolol fumarate; Hydrochlorothiazide**	**HPLC**	**Column: Shim-pack RP_{18} column (5µm** **Mobile phase: acetonitrile: KH_2PO_4 (40:60, v/v)** **λ_{max}: 232nm** **Flow rate: 1ml min-1** **Range: BIS:1-7 µg ml^{-1}** **HCZ: 2.5-17.5 µg ml^{-1}** **Retention time:** **BIS: 5.058 min, HCZ: 2.783 min**	**[43]**
12.	**Bisoprolol fumarate, Hydrochlorothiazide**	**UV**	**Model: UV2401 PC** **Solvent: 0.1 N NAOH** **λ_{max}:** **BIS: 238.4 nm, HCZ: 274 nm** **Range:** **BIS: 8 - 96µg ml^{-1}** **HCZ: 4 - 48µg ml^{-1}**	**[44]**

13.	**Bisoprolol fumarate**	**UV**	**Model: Jenway 7315 single beam Solvent: water λ_{max}: 271nm Range: 5-25 µg ml^{-1}**	**[45]**
14.	**Bisoprolol fumarate and Hydrochlorothiazide**	**RP-HPLC**	**Column: BDS Hypersil C_8 column (250 × 4.6 mm, 5 µm) Mobile phase: acetonitrile: ammonium dihydrogen phosphate/orthophosphoric acid buffer solution (80:20, v/v)] Flow rate: 1.5 ml min^{-1} λ_{max}: 220 nm Range: BIS :1.5–46.2 µg ml^{-1} HCZ: 3.8– 114.0 µg ml^{-1} Retention time: BIS: 5.55 min, HCZ: 2.85 min**	**[46]**
15.	**Bisoprolol fumarate**	**HPLC**	**Column: Eclipse XDB C_{18}column (150 mm x 4.6 mm, 5 µm) Mobile phase: water: methanol: acetonitrile in a ratio of 50:30:20 (v/ v/v). Flow rate: 1 ml min^{-1} λ_{max}: 225 nm Range: 8-80 g ml^{-1} Retention time: 4.65 min**	**[47]**
16.	**Bisoprolol fumarate**	**UV**	**Model: Hewlett Packard 8453 double beam Solvent: water λ_{max}: 412 nm Range: 5-30 µg ml^{-1}**	**[48]**
17.	**Bisoprolol fumarate, Hydrochlorothiazide**	**HPTLC**	**Stationary phase: silica gel 60F254 (Merck) Mobile phase: Ethyl acetate: Methanol: Ammonia 10:0.5:0.5 (v/v) λ_{max}: 225 nm Range: BIS: 150-900 ng $spot^{-1}$ HCZ: 100-600 ng $spot^{-1}$ R_f: BIS: 0.3, HCZ:0.6**	**[49]**
18.	**Bisoprolol fumarate, Amlodipine besylate**	**RP-HPLC**	**Column: C_{18} column (5, 250×4.6 mm) Mobile phase: Acetonitrile: Sodium dihydrogen orthophosphate (50:50v/v) λ_{max}: 230 nm Flow rate:1.0 ml min^{-1} Range: 1.3 µg ml^{-1} to 10.8 µg ml^{-1} R^2: BIS: 0.999 AML: 0.998 Retention time: BIS :4.4 min AML: 6.4 min**	**[50]**
19.	**Bisoprolol fumarate, Hydrochlorothiazide**	**UV RP-HPLC**	**UV: Model: Shimadzu (Columbia, MD) 1601 Solvent: methanol λ_{max}: BIS: 246 nm, HCZ: 257 nm RP-HPLC: Column: Zorbax Eclipse XDB-C_{18}column (150 x 4.6 mm, 5 µm) Mobile phase: Water: Acetonitrile (75:25, v/v) Flow rate: 1.0 ml min^{-1} λ_{max}:**	**[51]**

			BIS: 246 nm HCZ: 257 nm Range: BIS: 0.5–12 µg ml^{-1} HCZ: 0.2–8.0 µg ml^{-1} Retention time: BIS: 5.55 min HCZ: 2.85 min	
20.	**Bisoprolol fumarate, Amlodipine besylate**	**RP-HPLC**	**Column: C_{18}Intersil (4.6µm × 150 mm) Mobile phase: Methanol: Acetonitrile: 50mm Potassium dihydrogen phosphate buffer KH_2PO_4 (25:30:45 v/v) Flow rate: 1 ml min^{-1} λ_{max}: 267 nm. Range: 20µg ml^{-1} Retention time: BIS:2.3 min, AML:5.2 min**	**[52]**

Reported Methods for Bisoprolol Fumarate and Telmisartan:

No.	Title	Method	Description	Reference No.
1.	**Bisoprolol fumarate and Telmisartan**	**HPLC**	**Stationary phase: C_{18} (4.6mm x 250 mm) Mobile phase: Methanol and water (75:25 v/v) Flow rate: 1ml/min Wavelength: 231nm Range: BIS:5-25 µg/ml TEL: 40-200 µg/ml Retention time: BIS: 5.7 min TEL: 7.6 min**	**[53]**
2.	**Bisoprolol fumarate and Telmisartan**	**UV (AUC)**	**Model: shimadzu1800 Solvent: Methanol Range: BIS:5µg/ml, TEL: 8-40µg/ml Wavelength: BIS: 219-229 nm TEL: 287-304 nm Correlation coefficient: BIS: 0.999 TEL: 0.998**	**[54]**
3.	**Bisoprolol fumarate and Telmisartan**	**HPLC**	**Stationary phase: C18 Column (4.6 x 150mm, 5µm) Mobile phase: 0.1% of Tri Fluro acetic acid in Water: Acetonitrile (80:20v/v) Flow rate: 1ml/min Wavelength: 227 nm Range: BIS: 5-25µg/ml TEL: 40-200µg/ml Retention time: BIS: 2.79 min TEL: 3.52 min**	**[55]**

CONCLUSION:

So, from all above information it should be concluded that various spectroscopic methods, chromatographic methods and other methods developed and validated for estimation of Bisoprolol fumarate and Telmisartan. According to this review it was concluded that different spectroscopic and chromatographic methods for Bisoprolol fumarate in alone or in combination and for

Telmisartan in alone. It was observed that, chromatographic method flow rate is 1 ml/min to get good resolution time. It also observed that the spectroscopic methods common solvent is methanol. Most of methods were of RP-HPLC and UV because these methods provided with best available reliability, analysis time, repeatability, and sensitivity.

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