

AN IN-DEPTH REVIEW OF ANALYTICAL METHODS FOR BENIDIPINE  
HYDROCHLORIDE AND TELMISARTANNimitha M. H.<sup>\*1</sup>, Harsha K. Tripathy<sup>2</sup>, Chandanam Sreedhar<sup>3</sup>, T. Srinivasa Rao<sup>4</sup>, Manju S. V.<sup>5</sup> and Sahana K.<sup>6</sup><sup>1</sup>Student, <sup>2,4,5</sup>Professor, <sup>3</sup>Professor and HOD, <sup>6</sup>Student

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Article Received on 08/02/2025

Article Revised on 28/02/2025

Article Published on 18/03/2025

**ABSTRACT**

An age-associated, chronic illness called essential hypertension raises the risk of issues connected to the heart, brain, and kidneys. Two common medications used to treat hypertension are telmisartan, an angiotensin II receptor blocker, and Benidipine hydrochloride, a calcium channel blocker. This paper examines their pharmacological characteristics, modes of action, and estimate techniques. Their simultaneous estimate in bulk and tablet dose forms has been established and verified using a variety of techniques, such as RP-HPLC and UV spectroscopy, UV spectrophotometry, HPTLC and RP-UPLC. By guaranteeing precise medication analysis, stability, and quality control, these techniques help to better manage hypertension.

**KEYWORDS:** Benidipine HCl Telmisartan

RP-HPLC HPTLC

RP-UPLC

UV-Spectrophotometry

**INTRODUCTION**

Hypertension is defined as a rise in blood pressure without a known cause, which increases the likelihood of heart, brain, and kidney-related issues. In developed countries, more than 90% of individuals face a lifetime risk of developing hypertension (blood pressure >140/90 mm Hg). Common cardiovascular risk factors that often accompany essential hypertension include age, obesity, insulin resistance, diabetes, and high cholesterol levels.

Hypertension is a widespread, chronic condition that often comes with age. It can lead to serious cardiovascular and kidney issues. Blood pressure is usually assessed along with other cardiovascular risk factors. The use of automated blood pressure testing methods is becoming increasingly important for diagnosing hypertension. This condition affects not only the major arteries but also the microcirculation, the endocrine system, and the central nervous system. While hypertension is mainly a complex quantitative variable influenced by various hereditary and environmental factors, there are also monogenic forms of blood pressure dysregulation.<sup>[2]</sup>

Antihypertensive drugs are medications designed to manage high blood pressure, also known as hypertension. They function through various mechanisms

to reduce blood pressure levels. The five primary classes of antihypertensive medications include calcium channel blockers, beta-blockers, diuretics, angiotensin II receptor antagonists, and angiotensin-converting enzyme inhibitors. Effective management of hypertension typically involves the use of these antihypertensive medications, particularly calcium channel blockers (CCBs) and angiotensin II receptor blockers (ARBs).

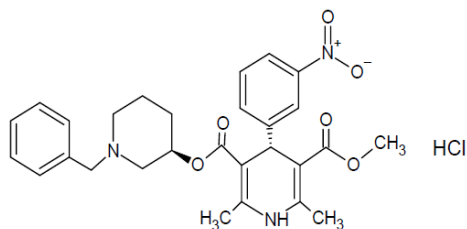
Benidipine Hydrochloride is a calcium channel blocker derived from dihydropyridine and shares several characteristics with nifedipine. It is expected to provide protective effects on vascular endothelial cells and demonstrates a relatively high vascular selectivity. This medication is taken orally to manage angina pectoris and hypertension.

Telmisartan is an angiotensin II receptor blocker (ARB) that specifically targets the angiotensin II type 1 (AT1) receptor, helping to prevent vasoconstriction and promote vasodilation. Its longer half-life provides enhanced cardiovascular protection and maintains blood pressure regulation over an extended period. The combination of Benidipine Hydrochloride and Telmisartan improves antihypertensive effectiveness by addressing various pathways involved in blood pressure control. Analytical techniques like UV spectroscopy and

RP-HPLC have been established for their simultaneous estimation in pharmaceutical formulations, ensuring precise dosage and quality assurance.

## DRUG PROFILE

### (A) BENIDIPINE HCL



**IUPAC NAME:** 3-(3R)-1-benzylpiperidin-3-yl 5-methyl (4R)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate hydrochloride

**Molecular formula:** C<sub>28</sub>H<sub>32</sub>ClN<sub>3</sub>O<sub>6</sub>

**Molecular weight:** 542.02 g/mol

**Melting point:** 200°C

**Colour:** Yellow powder

**Pka value:** 7.89

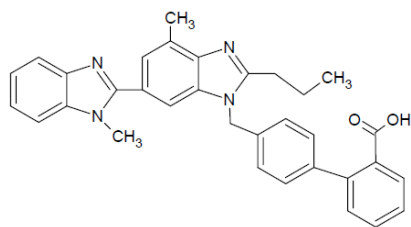
**Solubility:** Benidipine HCl is soluble in organic solvents like ethanol, DMSO, and DMF.

**Storage:** Store for 3 years from the date of receipt at -20°C.

**Category:** Benidipine HCl is a calcium channel blocker used for treating hypertension.

**Mechanism of action:** Benidipine acts as a tri-type calcium channel inhibitor by blocking L, N, and T type calcium channels. Its long-lasting effects are attributed to its strong affinity for cell membranes at the DHP binding site, which indicates prolonged pharmacological activity. Additionally, benidipine exhibits vascular selectivity towards peripheral blood vessels.

### (B) TELMISARTAN



**IUPAC NAME:** 2-(4-([4-Methyl-6-(1-methyl-1H-1,3-benzodiazol-2-propyl)-1H-1,3-benzodiazol-1-yl]methyl)phenyl)benzoic acid

**Molecular formula:** C<sub>33</sub>H<sub>30</sub>N<sub>4</sub>O<sub>2</sub>

**Molecular weight:** 514.629 g/mol

**Melting point:** 261-263°C

**Color:** white to slightly yellowish solid

**Pka value:** 3.5, 4.1, and 6.0

**Solubility:** Extremely low water solubility but freely soluble in highly alkalized solutions. Soluble in organic solvents like DMSO (dimethyl sulfoxide) and DMF (dimethyl formamide)

**Storage:** below 30°C.

**Category:** Telmisartan is utilized in treating hypertension and functions as an angiotensin II receptor blocker.

**Mechanism of action:** It operates by inhibiting a substance in the body that causes blood vessels to constrict. Consequently, Telmisartan relaxes the blood vessels, which lowers blood pressure and enhances the flow of blood and oxygen to the heart. It blocks the effects of certain natural substances that narrow the blood vessels, allowing blood to circulate more freely and enabling the heart to pump more effectively.

## ANALYTICAL METHODS

UV spectroscopy and HPLC are the techniques used to estimate Benidipine HCl and Telmisartan at the same time.

**Ultraviolet (UV) spectroscopy** is a method that helps determine the concentration and structural features of compounds by measuring how much ultraviolet light they absorb in the 200–400 nm wavelength range. This technique is commonly used in pharmaceutical, chemical, and biological research for both qualitative and quantitative analysis.

## HPLC

High-performance liquid chromatography is a technique in analytical chemistry that identifies, quantifies, and separates specific components within mixtures.

## RP-HPLC

This type of liquid chromatography employs polar mobile phases and a non-polar stationary phase to effectively separate organic molecules.

**Table 1: RP-HPLC methods for simultaneous estimation of Benidipine HCl and Telmisartan.**

Sl. No	Title	Method	Column	Mobile phase [M.P], Flow rate [F.R] & Injection Volume [I.V]	Retention time & Wavelength	Ref. No
1.	Sapkal A <a href="#">et al.</a> , (2020)	RP-HPLC	Chemsil ODS C18 (250mm x 4.6ID, Particle size: 5 micron)	<b>MP:</b> Methanol: Ammonium acetate buffer (85:15) pH 3 <b>FR:</b> 1.2 ml/min, <b>IV:</b> 10 µL	<b>RT:</b> 3.47min <b>W:</b> 237 nm	[5]
2.	Prajapati P <a href="#">et al.</a> , (2022)	RP-HPLC	Shimpack ODS C18 column	<b>MP:</b> acetonitrile: 0.1% v/v triethylamine (45:55, % v/v) <b>FR:</b> 1.0 mL/min	<b>RT:</b> 3.44 ± 0.02min <b>W:</b> 220 nm	[6]
3.	Sujana K <a href="#">et al.</a> , (2011)	RP-HPLC	C8 column (4.6 x 150mm, 3.5µ m, Make: Terra)	<b>MP:</b> Methanol: Potassium dihydrogen phosph ate solution (60:40 v/v) <b>FR:</b> 0.5 ml/min	<b>RT:</b> 2.6 min <b>W:</b> 230 nm	[7]
4.	Londhe SV <a href="#">et al.</a> , (2010)	RP-HPLC	(250 mm × 4.6 mm, 5-µm particle, FinepakC18 and ODS HypersilC18)	<b>MP:</b> methanol-to- water ratio of 80:20 (v/v) at pH 4.0 <b>FR:</b> 1.0 mL/ min	<b>RT:</b> 4.85 min <b>W:</b> 225 nm	[8]
5.	Rao MB <a href="#">et al.</a> , (2012)	RP-HPLC	ChromosilC18 column (250 mm × 4.6 mm, 5 µm)	<b>MP:</b> methanol: 0.1% orthophosphoric acid: acetonitrile in the ratio of 40:50:10 v/v <b>FR:</b> 1.5 ml/min <b>IV:</b> 20µL	<b>RT:</b> 2.7 min <b>W:</b> 256 nm	[9]
6.	Patel B <a href="#">et al.</a> , (2019)	RP-HPLC	Zorbax-SB-18, 150 mm x 4.6 mm; 3.5µm	<b>MP:</b> Pentane sulphonic acid sodium salt mono hydrate buffer and methanol in the ratio of 40:60 v/v <b>FR:</b> 1.2 ml/min <b>IV:</b> 10 µl	<b>RT:</b> 6.269 min <b>W:</b> 230nm	[10]
8.	Divya Shikha <a href="#">et al.</a> , (2023)	RP-HPLC	XbridgeC18 (250x 4.6 i.d; 5µm) column	<b>MP:</b> methanol: acetonitrile (80:20v/v/ with 0.1% v/v TEA) <b>FR:</b> 1mL/min	<b>RT:</b> 6.891(BEN) and 8.997(TEL) minutes <b>W:</b> 237(BEN) and 297(TEL)nm	[11]
9.	Payal G. Jain <a href="#">et al.</a> , (2018)	RP-HPLC	Inertsil ODS C18 column (150 x 4.6 mm, 5 µm)	<b>MP:</b> 0.05M Potassium Dihydrogen Phosphate Buffer (pH - 4.5 adjusted with 1% OPA) and Acetonitrile (40: 60% v/v) <b>FR:</b> 1 mL/min <b>IV:</b> 20 µl	<b>RT:</b> 2.977(BEN)min and 5.167(TEL)min <b>W:</b> 267 nm	[12]
10.	Varsha Chandgude <a href="#">et al.</a> , (2018)	RP-HPLC	PhenomenaxC1 8 Column (250×4.6 mm, 5µm particle size) w	<b>MP:</b> Methanol: Acetonitrile: water in the ratio of 70:20:10 v/v <b>FR:</b> 0.8ml/min <b>IV:</b> 20 µl	<b>RT:</b> 2.51 min (BPH) and 3.227 min (TEL) <b>W:</b> 237 nm	[13]

### Novel methods for simultaneous estimation of Benidipine HCl and Telmisartan UV-Vis spectrophotometer

It is an analytical instrument that measures the amount of visible and ultraviolet (UV) light absorbed by a sample. It is widely used in chemistry, biochemistry, and various other fields for identifying and quantifying chemicals in different types of samples.

### HPTLC

High-Performance Thin Layer Chromatography, is an advanced form of standard Thin Layer Chromatography (TLC) that provides significantly enhanced separation

efficiency. It is utilized for both qualitative and quantitative analysis of mixtures, particularly in fields such as environmental analysis, food science, and pharmaceuticals. When compared to conventional TLC methods, HP-TLC delivers more accurate sample application, quicker development times, and better resolution.

### RP-UPLC

Reversed-phase ultra-performance liquid chromatography, commonly known as RP-UPLC, is a technique used to identify and separate components in a mixture. This fast, accurate, and reproducible method has

a wide range of applications, including food safety, drug development, and quality control.

**Table 2: UV- spectrophotometric methods for Benidipine HCl and Telmisartan.**

S. No	Title	Method	Materials & Description	Ref. No
1.	Kumar M <a href="#">et al.</a> , (2018)	Shimadzu UV-1800 double beam spectrophotometer	<b>Wavelength:</b> 236 nm <b>Solvent:</b> Methanol <b>Concentration Range:</b> 3 to 18 µg/ml <b>Linearity (R<sup>2</sup>):</b> 0.9999	[14]
2.	Mohanbhai PL <a href="#">et al.</a> , (2018)	Double beam UV- visible spectrophotometer (Shimadzu, model 1601) having two matched quartz cells with 1cm light path and Digital analytical balance (Shimadzu ATX 224)	<b>Wavelength:</b> 355nm <b>Solvent:</b> Methanol <b>Concentration Range:</b> 1- 3.5µg/ml <b>Linearity (R<sup>2</sup>):</b> 0.9938	[15]
3	Nagabathula R <a href="#">et al.</a> , (2019)	Double beam UV/Vis spectrophotometer, Systronics UV- 1100	<b>Wavelength:</b> 297 nm <b>Solvent:</b> Telmisartan in tri ethyl amine, methanol, distilled water in ratios of 5:10:85 <b>Concentration Range:</b> 10- 50µg/mL <b>Linearity (R<sup>2</sup>):</b> 0.999	[16]
4.	Chohan MS <a href="#">et al.</a> , (2022)	UV-Vis spectrophotometer (Shimadzu 1650, Japan)	<b>Wavelength:</b> 239.8nm(BEN) and 233.1 nm(TEL) <b>Solvent:</b> ethanol <b>Concentration Range:</b> 0.5– 10g mL <sup>-1</sup> (BEN) and 1–24 g mL <sup>-1</sup> (TEL) <b>Linearity (R<sup>2</sup>):</b> 0.9998	[17]
5.	Patel K <a href="#">et al.</a> , (2018)	A Shimadzu model 1800 with software UV Probe version 2.3.1)	<b>Wavelength:</b> 228.36- 245.39 nm(BEN) 280.21-315.39 nm(TEL) <b>Solvent:</b> methanol <b>Concentration Range:</b>	[18]

**Table 3: HPTLC method for Benidipine HCl and Telmisartan.**

SL.No	Title	Stationary phase[S.P]	Mobile phase [M.P], Flow rate [F.R] & Injection Volume[L.V]	Retention factor & Wavelength	Ref. No
1.	Mandal LB <a href="#">et al.</a> , (2023)	<b>HPTLC plates pre-coated with silica gel 60F254</b>	<b>MP:</b> Methanol: Acetonitrile (1:9 v/v) <b>Concentration range:</b> 200–1000 ng/band (BEN) 2000 and 10000 ng/band (TEL)	<b>R<sub>f</sub> :</b> 0.890 ± 0.010 5(BEN) 0.173 ± 0.015 1(TEL) <b>W:</b> 237 nm	[19]

**Table 2: RP-UPLC method for simultaneous estimation of Benidipine HCl and Telmisartan.**

SL No	Title	column	Mobile phase [M.P], Flow rate [F.R] & Injection Volume[L.V]	Retention time & Wavelength	Ref. No
1.	Kumar RH <a href="#">et al.</a> , (2024)	HSS C18 column (50 mm×2.1 mm, 1.8 µm)	<b>MP:</b> 60:40 (% v/v) mixture of 0.01N KH <sub>2</sub> PO <sub>4</sub> buffer and ACN (pH 3.0) <b>FR:</b> 0.3 ml/min	<b>RT:</b> 0.933min (BEN) 1.106min(TE L) <b>W:</b> 269 nm	[20]

## CONCLUSION

Essential hypertension is a common chronic condition that has a significant effect on cardiovascular and kidney health. Managing this condition effectively often involves using antihypertensive medications such as Benidipine Hydrochloride, a calcium channel blocker, and Telmisartan, an angiotensin II receptor blocker. When used together, these medications improve treatment outcomes by addressing different mechanisms that regulate blood pressure. To ensure proper dosage, stability, and quality in pharmaceutical formulations, various analytical techniques have been developed for their simultaneous estimation.

Methods like UV spectroscopy, RP-HPLC, HPTLC, and RP-UPLC have been validated for their accuracy, sensitivity, and reliability in drug analysis. These analytical methods not only support drug development and regulatory compliance but also play a crucial role in ensuring the safe and effective treatment of hypertension. Future developments in analytical techniques may further enhance these estimation methods, leading to greater accuracy, shorter analysis times, and improved overall quality assurance for antihypertensive drugs.

## ABBREVIATION

**RP-HPLC:** Reversed-Phase High-Performance Liquid Chromatography, **UV:** Ultraviolet, **HPLC:** High Performance Liquid Chromatography, **HPTLC:** High Performance Thin-Layer Chromatography, **BEN:** Benidipine HCl, **TEL:** Telmisartan, **ODS:** Octadecyl-silica column, **HSS:** Hollow Structural Sections column, **pH:** Potential of Hydrogen, **µl:** microliter, **mL:** millilitre, **MP:** Mobile Phase, **RT:** Retention Time, **IV:** Injection Volume, **W:** Wavelength, **Rf:** Retention factor.

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