A Concise Review on Analytical Methods for Estimation of Benidipine HCL, Telmisartan and Chlorthalidone in Pharmaceutical Dosage Form

Dr. Tamilselvi N[1], Prakash M[2], Velmurugan M[3]
[1,2,3]*Department of Pharmaceutical Analysis, KMCH College of Pharmacy*

Abstract-Hypertension, other call for high blood pressure, is a not unusual condition characterized by abnormally high blood vessel pressure. Numerous people go through with high blood pressure (HT), especially as they get older. It's far a huge risk issue for cardiovascular mortality and morbidity however is not a sickness in and of itself Benidipine, telmisartan and chlorthalidone which decrease blood stress efficiently. It desires qualitative and quantitative estimation inside the pharmaceutical formulation. Therefore, the main goal of this estimation of benidipine HCl, chlorthalidone and telmisartan within the pharmaceutical method is in each qualitative and quantitative terms in this assessment article, we have short UV/Vis Spectroscopy, High-performance liquid chromatography (HPLC), high-performance thin-layer chromatography (HPTLC), Ultra performance liquid chromatography (UPLC), etc. Based totally methods for estimation of benidipine HCl, chlorthalidone, telmisartan for individual and different drug combination. In end, this review article will help to investigate scholars for similarly approach improvement for drug estimation in pharmaceutical dosage form.

Keywords: Benidipine HCl (BEN), Chlorthalidone (CHL), Telmisartan (TEL), Analytical Method, UV Spectrometry, HPLC, HPTLC, UPLC.

INTRODUCTION

Benidipine HCl is designated chemically as O5-methyl O3-[(3R)-1-(phenylmethyl) piperidin-3-yl] 2,6- dimethyl-4- (3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate, hydrochloride (Figure 1) is a compound of the Piperidines class and Calcium Channel Blockers is used as an antiarrhythmic agent. It acts by inhibiting the Calcium Channel blocker. It's a triple L-, T-, and N- form calcium channel blocker. It is reno- and cardioprotective.

Chlorthalidone designated chemically as (RS)-2-Chloro-5-(1-hydroxy-3-oxo-2,3-dihydro-1H-isoindol-1- yl) benzene-1-sulfonamide (Figure 2) is a compound of Thiazide Diuretic class and is used as Antihypertensive agent and Diuretic drug[11.] It acts by inhibits sodium ion transport across the renal tubular epithelium in the cortical diluting segment of the ascending limb of the loop of Henle. Through cumulative the delivery of sodium to the distal renal tubule, Chlorthalidone indirectly increases potassium excretion via the sodium-potassium exchange mechanism.

Telmisartan is designated chemically as 2({[4Methyl6(1methyl1H1,3benzodiazol2yl) 2propyl1H1,3benzodiazo l1yl] methyl} phenyl) benzoic acid (Figure 3) is a compound of the Azoles class and is an angiotensin II receptor antagonist which has been used for the treatment of HT. It interferes with the binding of angiotensin II 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 excites the synthesis too release of aldosterone, blockage of its effects results in decreases in systemic vascular resistance.

Telmisartan is not prevents the angiotensin converting enzyme, other hormone receptors, or ion channels. Studies also propose that telmisartan is a fractional agonist of PPARγ, which is a recognized target for antidiabetic drugs. This recommends that telmisartan can expand carbohydrate and lipid metabolism, as well as control insulin resistance without causing the side effects that are associated with full PPARγ activators.

PHYSICAL AND CHEMICAL PROPERTY

Benidipine HCl is yellow to yellow crystalline powder. Its chemically 5-O-[(3R)-1-benzylpiperidin-3-yl] 3-O-methyl (4R)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate Molecular formula of

benidipine is $C_{28}H_{32}ClN_3O_6$. Molecular weight is 505.6 g/mol. It is insoluble in water, slightly soluble in methanol, soluble in DMSO and DMF, PKa was 7.34 [1]

Chlorthalidone is white powder. It is a type of thiazide diuretic used to treat hypertension. Its chemically (RS) 2-Chloro-5-(1-hydroxy-3-oxo-2,3-dihydro-1H-isoindol1-yl) benzene-1-sulfonamide. Molecular formula of chlorthalidone is $C_{14}H_{11}ClN_2O_4S$. Water, methanol, alcohol, DMSO, and methanol were all solvents for chlorthalidone. PKa was 9.57 [2]

Telmisartan a white or almost white, crystalline powder. Its chemically 2-[4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl] methyl] phenyl] benzoic acid Molecular formula of telmisartan is $C_{33}H_{30}N_4O_2$. Molecular weight i 505.6 g/mol. It is insoluble in water, slightly soluble in methanol, soluble in DMSO and DMF), PKa was 4.1 [3]

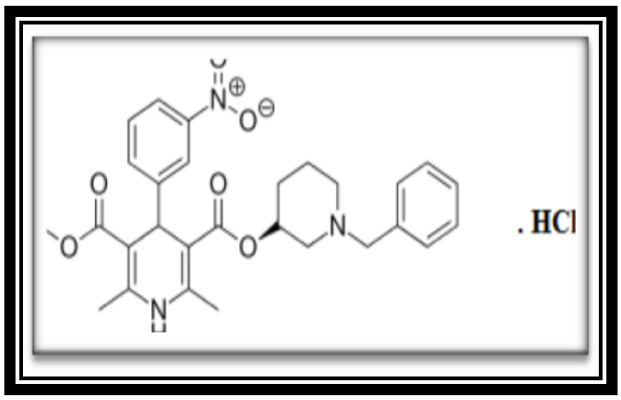

Figure 1) chemical structure of benidipine HCl

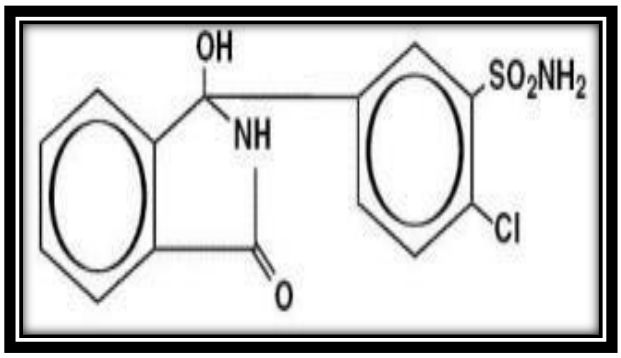

Figure 2) chemical structure of chlorthalidone

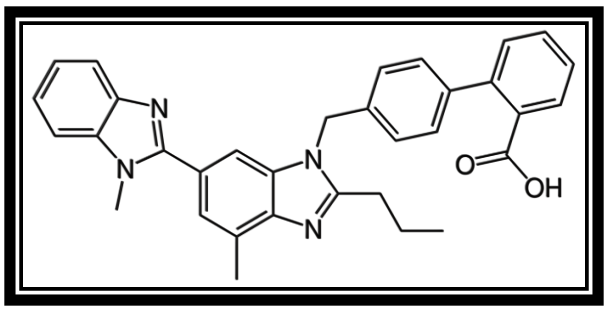

Figure 3) chemical structure of telmisartan

ANALYTICAL METHOD DEVELOPMENT

Development and validation of analytical methods play a crucial role in pharmaceutical product assembly as well as medication discovery and advancement. It comprises determining a drug substance's toxicity and purity. Development of analytical methods is the process of choosing an exact assay method to ascertain a formulation's composition. It involves demonstrating that an analytical technique can be used in a lab to determine the concentration of future samples. The procedures and acceptance criteria outlined in the ICH guidelines Q2 must be applied when developing analytical techniques in GMP and GLP environments (R1).

In the discovery, development, and production of pharmaceuticals, analytical method development and validation are crucial processes. The following literature review reveals that single and combined approach has been described for the combination of benidipine HCl, telmisartan and chlorthalidone. Various analytical methods have been reported for the estimation of Benidipine HCl, chlorthalidone and telmisartan was alone as well as in combination with other drugs. From the literature survey, few methods for benidipine HCl, chlorthalidone and telmisartan like spectrophotometric methods[5-9,] and UPLC[10], HPLC methods for estimation of benidipine along with combinations of telmisartan and chlorthalidone[10], Qbd approches[11] stability indicating HPLC methods with Telmisartan[12-15], RP- HPLC methods with other drugs [16-25]

Reported methods for assessment of BEN, CHL and TEL

S.NO	TITLE/METHOD	DISCRIPTION	RF.NO
1	Development and validation of an UV spectrophotometric method for simultaneous determination of cilnidipine and chlorthalidone	LOD: 0.4174 µg/mL and 0.068 µg/ml LOQ: 1.264 µg/ml and 0.206 µg/ml Wavelength selection: Cilnidipine are 271.83 nm and 278.34 nm and Chlorthalidone are 233.83 nm and 250.0 nm Linearity: f 2-10mg/mL (r2=0.9990) for Cilnidipine and 2.5 - 12.5mg/mL (r2 = 0.9986) for Chlorthalidone	6

		Solvent: methanol	
2	RP-HPLC method development and validation for simultaneous estimation of benidipine hydrochloride, telmisartan and chlorthalidone in tablet	Stationary Phase- C_{18} hypersil BDS column (25 cm × 0.46 cm) Mobile Phase-the mixture of buffer (pH 3.0): methanol (50:50)v/v Flow rate- 1.0 ml / min Wavelength: 230 nm, RT: CLD, BPH, and TEL were found to be 4.887 min, 6.690 min and 8.813, respectively. Linearity: BPH 2-6 µg/ml, for TEL 20-60 µg/ml and CLD 6.25-18.75 µg /ml.	10
3	Development of UV spectrophotometric method for the determination of benidipine hydrochloride by using quality by design (QBD) approach	A UV spectrophotometric method was developed on Shimadzu UV-1800 double beam spectrophotometer using methanol as solvent, Wavelength: 236 nm, Linearity: range 3 to 18 µg/ml with high correlation co efficient 0.999 LOD and LOQ: 0.20µg/ml and 0.60µg/ml respectively. The mean recovery: 100.35 % with low (% RSD) value.	11
4	Stability indicating reverse-phase high-performance liquid chromatography method development and validation for simultaneous estimation of telmisartan and benidipine hcl in pharmaceutical dosage form	Stationary Phase-C_{18} column, (250×4.6 mm), Mobile Phase- buffer: methanol (50:50) pH:4.0 Flow rate- 1.0 ml / min, Wavelength: 210 nm, Linearity: BPH 2-6 µg/ml, TEL 20-60 µg/ml. The percentage recoveries-TEL 100.46% and BPH 100.08% were, respectively	12
5	Simple and stability indicating RP-HPLC assay method development and validation of telmisartan in bulk and dosage form	Stationary Phase-C18 (150x4.6 mm) Mobile Phase- Acetonitrile and 0.1ml Phosphoric acid and 0.2ml Try Ethyl Amine Buffer (35:65) v/v Flow rate- 1.2 ml / min, Wavelength: 234 nm, RT: 5.33 min Linearity: 0.1 – 0.6 mg/ml (25% to 150%) with correlation coefficient (r2) 0.99 The method is accurate with 99.85% - 99.98% recovery for telmisartan and precise	13
6	Stability indicating HPLC method development and validation for the simultaneous estimation of benedipine HCl and telmisartan in its pharmaceutical dosage form	Stationary Phase- Phenomenax C18 Column (250×4.6 mm, 5µm particle size) Mobile Phase- Methanol: Acetonitrile: water in the ratio of 70:20:10 v/v/v, Flow rate- 0.8 ml / min, Wavelength: 237 nm, Retention time: 2.51 min for BPH and 3.22 min for TEL.	14
7	Method development and validation for simultaneous estimation of telmisartan and chlorthalidone by RP-HPLC in pharmaceutical dosage form	Column: CAPCELL C18 (250mm x 4.6mm id ,5 µm) Mobile phase: potassium di hydrogen ortho phosphate buffer: acetonitrile: methanol (35: 45: 20) % v/v/v Flow rate: 0.8ml/min Linearity: 20-100 µg/ml and 6.25-31.25 µg/ml for telmisartan and chlorthalidone Retention time: 3.640min and 4.937min for chlorthalidone and telmisartan	16
8	HPLC method development and validation for estimation of chlorthalidone in tablet dosage form	Stationary Phase-HiQ Sil C8 (4.6 mm*250 mm* 5µm) Mobile phase -potassium dihydrogen orthophosphate buffer pH 4.0: methanol (30:70 % v/v), Flow rate -1ml / min Wavelength: 230 nm, Retention time: 3.334min, Linearity: the concentration range of 5-30 µg/ml with a correlation coefficient (r2) of 0.99	18
9	Sensitivity Enhanced Ecofriendly UV Spectrophotometric Methods for Quality Control of Telmisartan and Benidipine Formulations: Comparison of Whiteness and Greenness with HPLC Methods	LOD:(0.088–0.139 µg mL−1 for BEN and 0.256–0.288 µg mL−1 for TEL) LOQ: (0.293–0.465 µg mL−1 for BEN and 0.801–0.962 µg mL−1 for TEL) The accuracy and precision were confirmed by the good recovery percent (98.37%–100.6%), with low percent relative	25

		error (0.67%–1.70%) and less than 2 percent relative standard deviation, respectively	
10	Method development and validation for simultaneous estimation of benidipine hydrochloride and metoprolol succinate in tablet	Stationary phase: C18 (250 mm x 4.6 mm, 5 µm) Hypersil BDS Column Mobile Phase: Potassium Dihydrogen Phosphate Buffer (pH 4.0): Methanol (65: 35% v/v) as Wavelength: 269 nm. Correlation coefficient for Metoprolol succinate and Benidipine Hydrochloride was found 0.9995 and 0.9997 respectively. The RT values for Metoprolol succinate and Benidipine Hydrochloride were found to be 3.4 and 5.9 min respectively	26

CONCLUSION

This article gives an idea about enhanced activity of benidipine hcl, telmisartan and chlorthalidone from other drugs. The presented review provides information about the various methods available in the literature for the determination of benidipine hcl, telmisartan and chlorthalidone. The different analytical methods are reported for the individual and other combination like UV spectroscopy, HPLC, HPTLC. This article also provides with pharmacological action, chemical structure, solubility, etc. of benidipine hcl, telmisartan and chlorthalidone. The given literature review focus that there is a single method reported for each drug and their combination. This review will assist the upcoming analytical method to develop the new combination and also gives the evidence about its characteristics of both drug.

REFERENCE

[1] Drug profile for Benidipine HCl: www.drugbank.ca/drugs/DB09231

[2] Drug profile for Chlorthalidone: http://www.drugbank.ca/drugs/DB00310

[3] Drug profile for Telmisartan: www.drugbank.ca/drugs/DB00966

[4] Kang W, et.al, “Analysis of benidipine enantiomers in human plasma by chromatography using a macro cyclic antibiotic (Vancomycin) chiral stationary phase column” Journal of Chromatography. 2005, 814, 75-81.

[5] Buridi K, el.al, “Validated Visible Spectrophotometric Methods Development of The Determination of Benidipine Hydrochloride Based on Complex and Internal Salt Formation Reactions” Journal of Institution of pharmaceutical and life sciences, 2012, 2(1), 25-33.

[6] Snehal N. Patel et al.” Development and validation of an UV spectrophotometric method for simultaneous determination of cilnidipine and chlorthalidone” Journal of Pharmacy Research. 2015,9(1),41-45

[7] Niraimathi V., Jerad SA, Kumar SI, “UV Spectrophotometric Methods for the Estimation of Chlorthalidone in Bulk and Oral Dosage Form.” Indo American Journal of pharmaceuticals 2013, 3(9), 7160-7167.

[8] Jat RK, Sharma S, Chippa RC, Singh R, “Quantitative Estimation of Telmisartan in Bulk Drug and Tablets by UV Spectroscopy” International Journal Of drug and research Technology., 2012, 2(3),268-272.

[9] Atici EB, Karliga B, " Identification, synthesis and characterization of process related impurities of Benidipine hydrochloride, stress-testing/stability studies and HPLC/UPLC method validations” Journal of Pharmaceutical Analysis, 2015, 5, 265-268.

[10] Patel, Bhoomi and Chaudhary, RP-HPLC Method Development and Validation for Simultaneous Estimation of Benidipine Hydrochloride, Telmisartan and Chlorthalidone in Tablet Journal of Emerging Technologies and Innovative Research2019, 6(3);110-11

[11] Manish Kumar et.al development of UV spectrophotometric method for the determination of benidipine hydrochloride by using quality by design (QBD) approach, International Journal of Applied PHarmaceutics,2018, 10(4):92

[12] Naim M, Ahmed A, Khan GJ, “Stability indicating reverse-phase high- performance liquid chromatography method development and validation for simultaneous estimation of Telmisartan and Benidipine hydrochloride in pharmaceutical dosage form” Asian journal of Pharmaceutical and Clinical. Research, 2018, 11(5), 342-350.

[13] Raghu Babu.K, Simple and stability indicating

RP-HPLC assay method development and validation of telmisartan in bulk and dosage form Der pharmacia Lettre, 2015, 7 (4);274-280

[14] Chandgude et.al Stability indicating reverse-phase high- performance liquid chromatography method development and validation for simultaneous estimation of telmisartan and benidipine hydrochloride in pharmaceutical dosage form 2018Asian Journal of Pharmaceutical and Clinical Research 11(5);342-350

[15] Sravani M, "Estimation of Benedipine by using HPLC" International journal of Pharmaceuticals and Chemical Research, 2017, 3(4), 775-806.

[16] Vanaja et.al "method development and validation for simultaneous estimation of telmisartan and chlorthalidone by RP-HPLC in pharmaceutical dosage form" Asian journal of pharmaceutical analysis, 2015; 5(4): 171-177.

[17] Singh B et.al "A reversed-phase high performance liquid chromatographic Method for determination of chlorthalidone in Pharmaceutical formulation." International journal of Pharmaceuticals And pharmaceutical sciences .2009, 1(2), 24-29.

[18] Santosh Vilaschand HPLC Method Development and Validation for Estimation of Chlorthalidone in Tablet Dosage Form journal of drug delivery and therapeutics 2019,9(4);342-351

[19] Sheth A, Patel CN, Shah N, "simultaneous estimation of chlorthalidone and olmesartan medoxomil from bulk and commercial products using a validated reverse phase high performance liquid chromatographic technique." Invention pages . 2013.7(2),232-237.

[20] Madhu BK, Bikshal BK, "Reverse phase-HPLC method development and validation for the simultaneous estimation of azilsartan medoxomil and chlortalidone in pharmaceutical dosage forms." Journal of Atoms and Mols 2012, 2(1), 117–126.

[21] Hari Prasad P, Reddy SY. and kumar RB, "Simultaneous estimation of metoprolol tartrate and chlorthalidone by using RP-HPLC and method development as per ICH guidelines" PHarmaceutical and Chemicals.2013, 5(5),139-143

[22] Jain PG, et.al, "Development and validation of RP-HPLC method for simultaneous estimation of Benidipine hydrochloride and Telmisartan in tablet" World Journal of Pharmacy and Pharmaceutical Sciences, 2018, 7(5), 751-762

[23] Wankhede SB, tajnemr, Gupta KR, "RPHPLC method for simultaneous estimation of telmisartan and hydrochlorothiazide in tablet dosage form" Indian Journal Pharmceutical. Sciences., 2007, 69(2),298-300

[24] Kurade VP, Pai MG, Gude R, "RPHPLC estimation of ramipril and telmisartan in tablets" Indian Journal Pharmaceutical. Science. 2009, 71(2),148-151

[25] Muhammad Shahzad Chohan, Sensitivity Enhanced Ecofriendly UV Spectrophotometric Methods for Quality Control of Telmisartan and Benidipine Formulations: Comparison of Whiteness and Greenness with HPLC Methods, national library medicine 2022 Jun 14;19(12):7260

[26] Dhaval M Patel,Method Development and Validation for Simultaneous Estimation of Benidipine Hydrochloride and Metoprolol Succinate in Tablet, journal of drug delivery and therapeutics,2019 9(6),1- 4