Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 13 [5] April 2024:13-22

Online ISSN 2277-1808
Journal's URL: http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

Efonidipine HCL Ethanolate, Telmisartan, and Chlorthalidone: A Review of Analytical Methods

Jash Sonawane[1]*, Vaishali Patel[2]
[1]Department of Quality Assurance, Parul Institute of Pharmacy & Research, Parul University Limda, Vadodara 391760, Gujarat, India.
[2]Department of Quality Assurance, Parul Institute of Pharmacy & Research, Parul University Limda, Vadodara 391760, Gujarat, India.
***Corresponding Author**: 2208232130012@paruluniversity.ac.in

ABSTRACT
Analytical method development estimates the Quality, identity, potency, and purity of the drug and further considered in validation-based methods which are suitable and aligned with the intended use and is applied further in Formulation. Efonidipine Hydrochloride Ethanolate, Telmisartan, and Chlorthalidone were approved by CDSCO in 2019 for the treatment of Hypertensive patients. This combination improves the medication for Stage II Hypertension. Efonidipine Hydrochloride Ethanolate is Calcium channel blocker and chemically 2-(N-benzylanilino) ethyl-5-(5,5-dimethyl-2-oxo-1,3,5-dioxaphosphinan-2-yl)-2,6-dimethyl-4- (3) -nitrophenyl)-1,4-dihydropyridine-3-carboxylate; ethanol; hydrochloride. Telmisartan is an angiotensin receptor blocker (ARB) and chemically 2- [4-[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl] phenyl] benzoic acid. Chlorthalidone is a diuretic used to treat hypertension or edema caused by heart failure, renal failure, and other conditions, and chemically 2-chloro-5-(1-hydroxy-3- oxo- 2H-isoindol-1-yl) benzene sulfonamide. This review focuses on recent developments in analytical method development for Efonidipine Hydrochloride Ethanolate, Telmisartan, and Chlorthalidone, and there are methods like UV spectrophotometry and HPLC reported for this combination. It provides information about different analytical method development like UV spectrophotometry, HPLC, and LC-MS performed using degradate products which are identified by using HPLC and characterized by LC-Q-TOF-MS methods reported for Efonidipine Hydrochloride Ethanolate, Telmisartan, and Chlorthalidone for individual and with other drugs combination. The diverse analytical techniques employed contribute to the ongoing progress in pharmaceutical research and development.
Keywords: *Efonidipine Hydrochloride Ethanolate, Telmisartan, Chlorthalidone, Analytical techniques, UV-Spectrophotometry, HPLC, Stability indicating RP-HPLC*

Received 10.01.2024 Revised 12.02.2024 Accepted 12.04.2024

INTRODUCTION

Hypertension, often known as high blood pressure, is a long-term medical condition characterized by persistently high blood pressure in the arteries. A silent killer is a chronic medical disease defined by a sustained rise in systolic or diastolic blood pressure exceeding 140/90 mmHg. Pheochromocytoma, hyperthyroidism, hyperaldosteronism, primary renal failure, and aortic coarctation are among the illnesses that increase arterial pressure. To meet treatment objectives, the majority of hypertension patients need a combination of antihypertensive drugs. About 70 % of high blood pressure people need more than one blood pressure medication to bring their readings down to the recommended range. For the treatment of hypertension, ACE inhibitors, diuretics, angiotensin II type 1 receptor blockers (ARBs), -blockers, renal inhibitors, calcium channel blockers, and CNS sympatholytic may be used singly or in combination. A drug from the Dihydropyridine family called efonidipine hydrochloride ethanol inhibits L and T-type calcium channels. L calcium channels and T calcium channels are blocked by it. The presence of a phosphonate nucleus at the fifth position of the dihydropyridine chain sets it apart from other dihydropyridines. Its effects are diuretic and vasodilator. It barely has any inotropic effects. Without increasing intraglomerular pressure, it increases the rate of glomerular filtration. It minimizes proteinuria and relaxes both the efferent and afferent arterioles. It has qualities that can shield the kidney and heart from harm. Efondipine hydrochloride ethanol provides additional advantages. In comparison to Amlodipine, Nifedipine, and Cilindidipine. [1], [2], [3] Efonidipine hydrochloride ethanolate is a crystalline powder that ranges from pale yellow to greenish yellow. IUPAC name of Efonidipine hydrochloride ethanolate 2-(N-benzylanilino)

ethyl-5-(5,5-dimethyl-2-oxo-1,3,25-dioxaphosphinan-2-yl)-2,6-dimethyl-4- (3) -nitrophenyl)-1,4-dihydropyridine-3-carboxylate; ethanol; hydrochloride. C36H45ClN3O8P is the chemical formula, and the mass of it is 714.2 g/mol. Efonidipine Hydrochloride Solubility Ethanolate is nearly insoluble in water, somewhat dissolves in Dimethylformamide, and just slightly soluble in methanol. Efonidipine Hydrochloride Ethanolate's chemical structure is given below Figure 1. [4], [5]

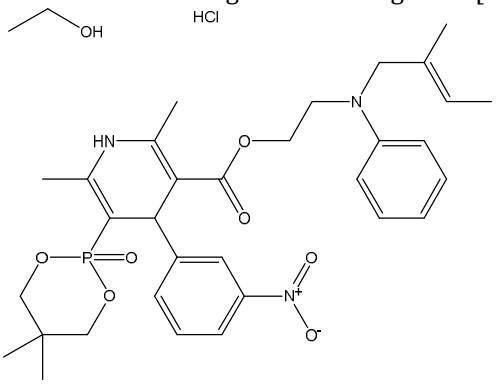

Figure 1: Efonidipine Hydrochloride Ethanolate's Structure

Telmisartan belongs to the Angiotensin II antagonist family of medications. By binding reversibly and selectively to receptors in vascular smooth muscle and the adrenal gland, it blocks angiotensin II from bonding to the angiotensin II AT1 receptor. Because angiotensin II is a vascular constrictor that simultaneously stimulates aldosterone synthesis and release, inhibiting its activities lowers the resistance of the systemic vascular system Telmisartan has no effect on the angiotensin-converting enzyme (ACE), receptors for hormones, or channelization of ions. Telmisartan is White to slightly yellowish solid. Telmisartan's IUPAC designation is 2-[4-[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl] phenyl] benzoic acid. C33H30N4O2 is the chemical formula, and the molecular weight is 514.6 g/mol. Telmisartan is very hydrophobic in water, ethanol and methanol are hardly soluble, and dichloromethane is weakly soluble. Telmisartan's chemical structure is shown below in Figure 2. [6], [7]

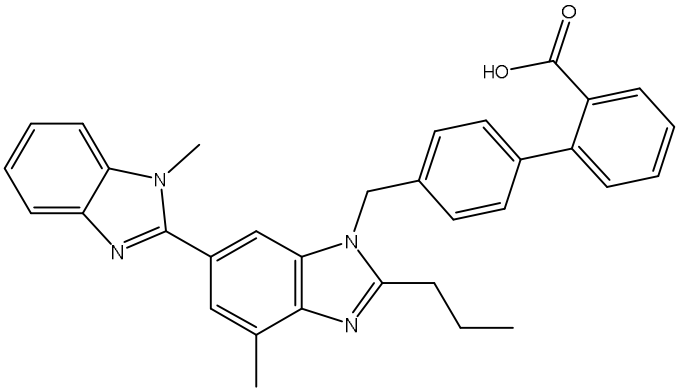

Figure 2: Telmisartan's structure

Chlorthalidone is basically dissolves in methanol, marginally dispersed in alcohol, and almost insoluble in water, ether, and chloroform. By blocking the Na+/Cl symporter in the ascending limb of Henle's cortical diluting segment, chlorthalidone limits sodium and chloride reabsorption. Reduced sodium reabsorption causes sodium-driven diuresis, osmotic which results in a reduction in extracellular fluid and plasma volume. a prescription drug used to treat high blood pressure (hypertension). Lowering cholesterol levels helps to avoid strokes, heart attacks, and kidney problems. It is also used to remove excess salt and water from the body as a result of ailments such as heart failure, liver problems, and renal disease. Chlorthalidone is a crystalline powder that is white or pale yellow-white in color. Chlorthalidone's IUPAC name is 2-chloro-5-(1-hydroxy-3-oxo-2H-isoindol-1-yl) benzene sulfonamide. C14H11ClN2O4S is the chemical formula, and the molecular mass is 338.8 g/mol. Chlorthalidone is soluble in water and more soluble in aq sol of NaOH; it is soluble in heated ethanol; it is mildly dissolves in ether and chloroform; and it is soluble in methanol. The chemical structure of Chlorthalidone is given below in Figure 3. [8], [9]

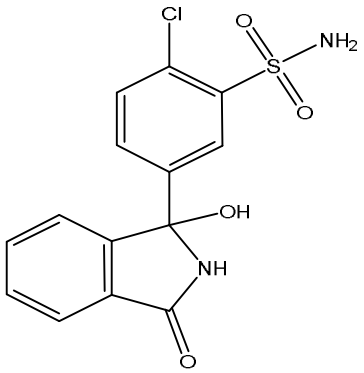

Figure 3: Chlorthalidone's Structure

Efonidipine hydrochloride ethanolate isn't a drug that is listed in any pharmacopeia.

REPORTED METHOD FOR EFONIDIPINE HYDROCHLORIDE ETHANOLATE

In an experiment by **Bhalerao SS and Jawarkar SG**[10], Development of a New Bio-Analytical Method for Efonidipine in Human Plasma Using RP-HPLC, simple, selective, precise, fast and precise according to the ICH recommendations. A Zodiac-100 C8 (150 x 4.6 mm ID) column was used for RP-HPLC., mobile phase was acetonitrile: methanol (90:10, V/V) With a flow rate of 10 minutes, using wavelength detection at 250 nm. Efonidipine HCL Ethanolate elute time was measured to be 4.027 min. The established method's validation was carried out in compliance with the ICH and EMA recommendations. Method verification showed that the method was fast, exact, dependable, reliable, and consistent. Linearity is seen in the 3.12-50 ppm range, with a correlation value of 0.9997. In another study conducted by **Pandya** CP and Rajput [11] the estimation of Efonidipine Hydrochloride Ethanolate was performed using the NMR and LC-Q-TQF-MS for the Forced degradation of efonidipine hydrochloride ethanolate, characterization compounds from degradation in order to create and validate a simple strategy and a precise, exact, and technique. Acetate buffer (10 mm), created by dissolve 770 milligrams of ammonium acetate in 1,000 milliliters of double-distilled water, used as the mobile phase for the suggested procedure. The column utilized was a Thermo Hypersil C18 column (250 4.6 mm, 5). Acetic acid was used to bring the pH level down to 5.8, the flow rate was held constant at 1 mL min^{-1}, the detection wavelength was 254 nm, and the mobile phase served as the diluent. According to ICH criteria, the proposed method's linearity, precision, reliability, limit of detection, and adaptability were all validated. The HPLC system was injected with solutions with concentrations ranging from 20 g mL^{-1} to 120 g mL^{-1}. A replica of the linearity sample was injected. The R2 value was equal to 0.999. The recovery rate was found to be 99.7–100.25 %. The quantification limit was 1.24 g mL^{-1}, while the detection limit was 0.41 g mL^{-1}. The results of the forced deterioration investigation showed that acid hydrolysis, followed by alkaline, oxidation, heat, photolysis, and neutral, is the primary pathway for degradation. The developed approach came to the conclusion that efonidipine HCl ethanolate was unstable under acidic and basic circumstances but stable under neutral, photolytic, thermal, and oxidative stress conditions.

Rajput AS, Jha DK, Gurram S, Shah DS, and Amin PD [12], they created a straightforward RP-HPLC technique in their study to measure the amount of Efonidipine Hydrochloride Ethanolate in the generated solid dispersions. In the experiment, a suitable detachment was performed using a photodiode array detector to analyze the effluent at 252 nm on an Agilent Eclipsed XDB-C18 column (4.6 250 mm), packed with 5 µm particles, acetonitrile: phosphate buffer (85:15) V/V with adjusted pH 2.5 as the mobile phase, and the flow rate was 1.2 mL min^{-1}. According to their results, the linearity for Efonidipine Hydrochloride Ethanolate was found in the wide range of 2.5 - 100 microgram $milliliter^{-1}$ (R2 = 0.9997) respectively. The percentage recovery must meet an acceptability threshold of 98-102 %. Precision tests and deviation values were carried out. The relative standard was less than 2. The approach was discovered to be resilient. Overall, it was demonstrated that the recommended method was exact, accurate, and strong, and it could be utilized to estimate Efonidipine Hydrochloride Ethanolate in solid dispersions treated with HME.

According to a study by Solanki D, Patel D, and Meshram D [13] for two simple, accurate, and cost-effective UV spectrophotometric approaches in synthetic compounds, A UV spectroscopic approach was developed for the simultaneous quantification of chlorthalidone, and efonidipine hydrochloride ethanolate. The technique 1 is a simultaneous equations method based on absorption measurements of efonidipine hydrochloride ethanolate and chlorthalidone at 251 and 227 nm, respectively, i.e. max. technique 2 is a first-order derivative based on efonidipine hydrochloride ethanolate absorbance measurements at 283.2 nm (chlorthalidone ZCP) and chlorthalidone absorbance readings at 250.8 nm (efonidipine hydrochloride

ethanolate ZCP). Linearity was observed for efonidipine hydrochloride ethanolate at concentrations ranging from 6.4 to 38.4 ug $mL^{-1}$and for chlorthalidone at concentrations ranging from 2 to 12 ug mL^{-1} using methanol as a solvent. Recall studies determined that the approaches accuracy was 98-102 % for both medications. Studies of reproducibility and average precision were used to assess the approaches' accuracy. The % RSD numbers were determined to be less than 2, indicating that the proof procedures were correct. An F test was used to compare the two techniques. As per ICH Q2 R1 standards, the outcomes were statistically verified and judged to be adequate.

Adeshra SD and Meshram DB[14], in their study developed the RP-HPLC process development and simultaneous estimation validation of telmisartan and efonidipine hydrochloride ethanolate within their synthetic mixture. The approach was verified and found to be straightforward, sensitive, accurate, and exact. The separation via chromatography was accomplished by Phenomenex Kinetex 5µ C18 150 * 4.6mm column with a flow rate of 1 mL min^{-1} and a detecting wavelength of 253 nm, a mixture of acetonitrile:25 mm phosphate buffer (pH 4.9) in the ratio of 45:55 V/V serves as the mobile phase. The retention duration of medicines was noted to be 7.77 minutes and 4.10 minutes for Efonidipine hydrochloride ethanolate and Telmisartan, using optimal chromatographic conditions. Over concentration ranges of 5–30 and 10–60 g mL^{-1}, respectively, the calibration curve for efonidipine hydrochloride ethanolate and telmisartan were linear. The suggested method is precise and accurate between a recovery rate of 99.75 % and 100.10 %.

Dudhrejia A, Patel A, Chavda J, Gol D, and Koli P[15], 2022, established and validated a simple, reliable, specific, and reproducible technique for estimating Efonidipine Hydrochloride Ethanolate with Telmisartan within a synthetic combination. Both drugs were quantified using the first-order derivative of the overlay spectra. This method involved determining both drugs at their respective zero crossing point working wavelengths, which were 231.00 nm for Efonidipine hydrochloride ethanolate and 238.60 nm for Telmisartan using methanol as diluent. The ICH Q2R1 guideline was followed for method validation. For Efonidipine Hydrochloride Ethanolate, in concentration levels of 2-18 g mL^{-1}, and for Telmisartan, in ranges of 4-36 g mL^{-1}, the Beer-Lambert's law was followed. Efonidipine Hydrochloride Ethanolate recovered at a rate of 98-101 %, whereas Telmisartan recovered at a rate of 98.46-99.77 %. According to the accuracy and repeatability study, the % relative standard deviation was less than 1 %. Both medications may be checked in quality control laboratories using this simple and precise approach.

Patel bd[16] created an RP-HPLC technique for the synchronized analysis of Efonidipine hydrochloride ethanolate with Telmisartan in Tablet Dosage Form in their study. The Method 2^3 Factorial Design by evaluating the effect of three independent variables i.e., pH, flow rate and mobile phase composition. Retention time, area, resolution, number of theoretical plates, and tailing factor were selected as response factor. The effective separation was achieved using HPLC system with PDA detector, C18 column Inertsil (150 x 4.6 mm, 5 m), acetonitrile (60:40 % V/V) mobile phase, and 1.0 mL min^{-1} flow rate with detection at 254 nm. Telmisartan and efonidipine hydrochloride ethanolate showed excellent crisp peaks with retention times of 2.720 and 4.430 min, respectively. A linear calibration curve was displayed in the amount ranges of 10–30 g mL^{-1} and 20–60 g mL^{-1}. Drug assay percentages for Telmisartan and Efonidipine Hydrochloride Ethanolate were 99.361 % and 102.341, respectively.

Official methods for telmisartan.

Official in IP 2022[17]

Chromatographic Method with a stationary phase as stainless-steel column 15 cm*4.6 mm packed with Octadecylsilane bonded to porous silica (5 µm) (Inertsil ODS-3), a mixture of 60 vol of a buffer solution was prepared by dissolving 2.72gm of Potassium Dihydrogen Phosphate in 1000 mL of water; add 2 mL of triethylamine and adjust the pH to 2.4 with orthophosphoric acid and 40 volumes of ACN as Mobile Phase at a flow rate of 1mL min^{-1}. Using a 20mL injection volume, the wavelength of 298 nm was found.

Reported Method for Telmisartan

In their work, Rao MB, Nagendrakumar A, Sivanadh M, and Rao GV[18] (2012) created and verified a straightforward, specific, accurate, and exact reversed-phase high-performance liquid chromatography technique for the assessment of telmisartan dosage as a tablet. A chromosil C18 (250 mm x 4.6 mm, 5 m) column was used to achieve the anticipated separation and peak form. To achieve good drug separation under isocratic conditions, a number of solvent mixtures, including methanol, water, and acetonitrile, were explored as mobile phases on the chromosyl-C18 column. The most acceptable of all combinations was an 80:05:15 V/V mixture of methanol, 0.1 % orthophosphoric acid, and acetonitrile, as the resultant chromatographic peak became sharper and clearer, with nearly no tail. The emission was measured at 256 nm and the flow rate was 1.5 mL min^{-1}. Telmisartan had a retention time of 2.7 minutes. The process was confirmed to be exact and accurate. Telmisartan recovery from tablet formulation was found to be 99.41 %. The quantitative concentration of telmisartan in the formulation of the suggested method's tablet was successfully ascertained.

In an experiment by Londhe SV, Kaul N, Agrawal H, and Mahadik KR [19], (2019) For the quantitative measurement of telmisartan, High-performance liquid chromatography (HPLC) has a procedure that is sensitive and repeatable. The drug was isolated from its breakdown products on a C18 column using a mobile phase of methanol: water 80:20 (V/V), pH 4.0 (adjusted by the addition of orthophosphoric acid), at a flow rate of 1.0 mL min^{-1} at room temperature. Under these conditions, telmisartan had a retention time of 4.85-0.05 minutes. Utilizing UV detection at 225 nm, the peak area was measured; calibration curves were linear in the concentration range of 10–60 g mL^{-1}. When the technique was used to construct a pharmaceutical formulation, the excipients in the tablet did not produce chromatographic interference. The method's precision, robustness, recovery, and identification and quantification limits were all confirmed. The drug was subjected to oxidation, acid and base hydrolysis, dry heat, wet heat, and photodegradation conditions. Because the approach successfully isolated the medicine from its breakdown products, it may be used to predict drug stability.

According to Chaudhary BR and Dave JB[20] (2017), For the simultaneous evaluation of both medications in bulk API and fixed-dose combination, a unique Stability-indicating RP-HPLC technique was created. A column from the Agilent Extend C18(150 mm 4.6 mm id, 5 m particle size) underwent separation with a gradient elution ratio of 75:25, % V/V. Using acetonitrile as the mobile phase and a disodium hydrogen phosphate buffer with a pH of 6.5, the detection wavelength is 235 nm. The retention times for chlortalidone and telmisartan were 3.82 and 14.23 minutes, respectively. The linearity ranges were 6-18 mcg mL^{-1} and 20-60 mcg mL^{-1}. Chlorthalidone and telmisartan had percentage recoveries of 99.19-101.19 % and 99.19-101.91 %, respectively. The established approach sufficiently distinguishes probable degradation products that arise under stressed settings, confirming the method's specificity.

Chlorthalidone decomposed extensively under acidic and basic circumstances, but very marginally in oxidative, neutral, and photolytic settings, while remaining stable in thermal temperatures. Telmisartan degraded significantly under neutral conditions, moderately under acidic, basic, and heat settings, and did not degrade at all under oxidative or photolytic conditions. The suggested approach was verified in accordance with ICH recommendations, and it may now be used to evaluate the medicine telmisartan and chlorthalidone tablets.

Vanaja N, Preethi C, Manjunath SY, and Pal K[21]
, (2015) in their study a novel RP-HPLC technique for the simultaneous measurement of telmisartan and chlorthalidone in pharmaceutical formulation was created and validated. Chlorthalidone and Telmisartan had retention periods of 3.640min and 4.937min, respectively. Linearity ranges for Telmisartan and Chlorthalidone were determined to be 20-100g mL^{-1} and 6.25-31.25g mL^{-1}, respectively. Telmisartan and Chlorthalidone have LOD ranges of 0.3074 and 0.9316 g mL^{-1} and LOQ ranges of 0.0579 and 0.1756g mL^{-1}, respectively. Theoretical plates and tailing factors for Chlorthalidone and Telmisartan were found to be 5648.33 and 1.58, and 6141.47 and 1.71, respectively. ICH guidelines were used to validate this method.

Prajapati P, Patel A, and Shah S[22], (2022) a new RP-HPLC Method for Estimation of Multiple FDC Products of Telmisartan Using Enhanced AQbD Approach. The chromatographic separation was achieved by shimpack ODS C_{18} (250 mm L,4.6 mm ID, 5.0 µm) column, Acetonitrile: 0.1 %V/V triethylamine, mobile phase, flow rate of 1 mL/min, detection wavelength of 220 nm, pH adjusted to 6.2 with perchloric acid. Ramipril, amlodipine besylate, atorvastatin, and telmisartan peak retention times were reported be 2.79 0.02, 3.44 0.02, 5.12 0.02, and 8.45 0.02 min. The correlation coefficient for each drug's linearity curve was found to be greater than 0.995, the peak areas of ramipril, telmisartan, atorvastatin, and amlodipine besylate over concentration ranges of 40-200, 320-1600, 80-400, and 40-200 ng/injection, respectively, show a solid linear relationship. The suggested method's accuracy, precision, robustness, linearity, and range, among other validation characteristics, were assessed and found to be within acceptable bounds.

Panda M, Dadi V, Yarraguntla SR, and Rao KV[23], (2023) a novel reverse phase high performance liquid chromatography was created and verified. based analytical technique that was discovered to be easy in their study as well as for the quick simultaneous measurement of telmisartan and azelnidipine in dosage form for medications. Separation was carried out on an Intersil C18 column (250 x 4.6 mm, i.d., 5 m) with a mobile phase of 70 volumes acetonitrile and 30 volumes 5 mM phosphate buffer, pH 4.6. Isocratic elution was used for the chromatographic analysis, with a flow rate of 1 mL min^{-1}. Linearity experienced in the concentration ranges of 10-50 ug mL^{-1} for azelnidipine and 20-100 ug $mL^{-1}$for telmisartan when detected with UV detector at 255 nm. Azelnidipine recovery rate was 99.48-100.22 % while the telmisartan with UV recovery rate was 99.62-99.88 %. The dosage was unaffected by excipients. For parameter correctness, precision, specificity, robustness, detection limits, and quantification, the technique was verified in accordance with the ICH criteria. Based on the recovery data, the proposed RP-HPLC technique was used to the analysis of commercial azelnidipine and telmisartan medicines and proven to be successful.

In their investigation, Gandu S, Ravinder M, Gandla K, and Narmada G[24], (2022) For the simultaneous estimation of metoprolol and telmisartan in tablet dosage form, a precise, accurate, and repeatable RP-

HPLC and UV Spectrophotometric Method was created and validated. On an X-tera C8 column (100mm*4.6mm*5), the chromatographic separation was carried out using a mobile phase of 0.05M sodium phosphate buffer pH 2.8 and methanol in a 35:65 ratio at a flow rate of 1.2mL min^{-1}. At a wavelength of 226 nm, the detection was made. Metoprolol and Telmisartan had retention times of 2.338 sec and 5.559 sec. The ultraviolet approach involves simultaneously calculating equations based on measurements of the absorbance of metoprolol and telmisartan at two different wavelengths, 223 nm and 296 nm, respectively. Beer's rule was followed at concentrations of 1.25-6.25g mL^{-1} for Metoprolol and 2-10g mL^{-1} for Telmisartan. According to ICH guidelines, the methods created were validated.

In an experiment by Chaitanya DB and Ajitha M[25], (2022) a new technique of high-performance reverse-phase liquid chromatography of Azelnidipine and Telmisartan was established, for the simultaneous estimate of Azelnidipine and Telmisartan in bulk and pharmaceutical dose form, a straightforward, accurate, and precise approach was created. A standard Denali C18 150mm x 4.6 mm, 5 chromatogram was used. The flow rate was kept at 1.0 mL/min for the mobile phase, which contained 0.1 % OPA in a 60:40 mixture of acetonitrile. 0.1 % OPA was the buffer employed in this technique. A 30°C temperature was established for the column.The chosen optimized wavelength was 242.0 nm. Azelnidipine and telmisartan were shown to have retention times of 2.116 and 3.188 minutes, respectively. It was discovered that the %RSD of the azelnidipine and telmisartan systems were 1.6 % and 1.0 %, respectively. Azelnidipine and telmisartan both had recovery rates of 100.15 % and 100.20 %, respectively. For azelnidipine and telmisartan, the LOD and LOQ values derived from the regression models were 0.04, 0.13 and 0.38, 1.14, respectively. The storage and working periods were lowered, making the devised approach easy and cost-effective for application in regular quality control trials in industry.

Gholve R, Pekamwar S, Wadher S and Kalyankar T[26] (2021) For the simultaneous measurement of telmisartan and rosuvastatin calcium in bulk and tablet form in their investigation, they created and validated a novel stability-indicator chromatographic approach. RP-HPLC elution was performed at 242.0 nm using an Oyster ODS3 column (150 x 4.6 mm, 5 µm) isocratically with a mobile phase containing 10 mM phosphate buffer and 1.1 g octane-1-sulfonic acid sodium salt, which the pH was set to 2.5 (adjusted with 5 % OPA), and acetonitrile 500:500 V/V was fed through the column at a flow rate of 1.0 mL/min while it was kept at room temperature (about 25 °C). The proposed method was validated according to ICH Q2 guidelines. After 2,553 and 4,505 minutes, telmisartan and rosuvastatin were eluted, respectively. For telmisartan, The technique is linear from 99.9073 to 299.7218 ug mL^{-1} (R2 = 1.000) and linear from 23.6841 to 71.0522 ug mL^{-1} (R2 = 0.999) for rosuvastatin. At three separate levels, the average percent recovery for telmisartan was 100.51, 99.76, and 99.14 %, while for rosuvastatin it was 99.68, 99.72, and 98.56 %. The method's repeatability and average accuracy were determined to be within acceptable ranges. According to the solution stability data, the mobile phase was stable for 2 days; standard and test preparations may be kept at ambient temperature and in the refrigerator (2-8 °C) for 1 night. The forced degradation research findings also reveal that the approach is stable, indicating that it can differentiate the peak of active analytes from the degradation product.

Patel B, Chaudhary A, and Gami S[27] devised a new RP-HPLC technique for the simultaneous measurement of chlorthalidone, telmisartan, and benidipine chloride in their combination formulation in another study. An RP-HPLC chromatographic approach was developed for the simultaneous evaluation of chlorthalidone, telmisartan, and benidipine hydrochloride. They created a mixed dose form. The separation was performed on a C18 (25 cm x 0.46 cm) Hypersil BDS column with a mobile phase of buffer (pH 3.0): methanol (50:50 V/V) at a flow rate of 1 mL/min. The wavelength of detection was 230 nm.. Chlorthalidone, benidipine HCl, and telmisartan had retention periods of 4.887 minutes, 6.690 minutes, and 8.813 minutes, respectively. The linearity, precision, and specificity of the approach were all confirmed. Linearity was seen with benidipine hydrochloride 2-6 g mL^{-1}, telmisartan 20-60 g mL^{-1}, and chlorthalidone 6.25-18.75 g mL^{-1}. For the simultaneous measurement of chlorthalidone, telmisartan, and benidipine chloride in their combination formulation, the devised approach was found to be accurate, precise, and fast.

In another study conducted by Dalal D, Kant R, and Yadav M[28], The RP-HPLC drug estimation technique was picked since it is suggested for use with ionic and mild to non-polar compounds. In terms of stability, efficiency, and reproducibility, reverse-phase chromatography is straightforward, specific, and better. The C_{18} is used to separate Telmisartan and Benidipine Hydrochloride. The particle size in the column was set to be 250 x 4.6 mm,5 m. Various solvent solutions were tried and mixed for best performance in the mobile phase. Telmisartan (40 g mL^{-1}) and Benidipine hydrochloride (4 g mL^{-1}) are two drugs that can be used together. Because it had an outstanding peak and considerable level of resolution, the concentration range (8-40 and 0.5-4 g mL^{-1}) of acetonitrile in buffer at pH 4: Water (70:30) was used. The Mobile phase running at 1mL/min, the photodiode at 215 nm, and both analytes were detected using array detectors. The approach was verified in human plasma at various concentrations.

According to a study by Deshpande SV, Waman JS, Patil AR, and Kapse BP[29], Development and Validation of a Simple, Accurate, and Precise UV-Spectrophotometry Method for Simultaneous Estimation of Telmisartan and Hydrochlorothiazide in Bulk Drug and Pharmaceutical Dosage Form. These medications' wavelengths were 295.5 nm and 273.0 nm, respectively. Telmisartan has a linearity at 10-90 g $mL^{-1}$and Hydrochlorothiazide has a linearity of 5-60 g mL^{-1}. These medications' concentrations were determined in a laboratory combination of reference standards and commercial formulations. Recovery studies proved the suggested method's accuracy. The method's precision was determined by the values being within an acceptable range. As a result, the suggested method and results were validated in accordance with ICH recommendations. Statistical research demonstrates that the approach for calculating Telmisartan and Hydrochlorothiazide at the same time is repeatable and efficient.

Pattanik SK and Pradhan KK [30] devised in their work, they used an easy, selective, and highly accurate HPTLC method to quantify Telmisartan and Gallic acid at the same time. The separation was accomplished using aluminium-backed silica gel 60F254 TLC plates (20cm10cm, thickness-0.2mm) as columns and acetate: methanol: chloroform: acetic acid in the ratio 4:2:2:0.2 (V/V/V/V) as mobile phase. Medications were treated to various stress conditions (Acid, Alkali, Oxidative, Thermal, and Photolytic) for 8 hrs and examined at 2 h intervals during the forced degradation experiment. Detection and quantification were performed densitometrically (between 200-400nm). Calibration plots revealed a strong inverse relation, with correlation coefficient (R2) values of 0.9902 for GA and 0.9933 for TEL. The peak area of both medications was in the 200-1200ng/spot concentration range. The Rf value for GA was 0.60, the LOD was 5.494 Ng/spot, and the LOQ was 16.65 Ng/spot. The Rf value for TEL was 0.67, the LOD was 19.877 Ng/spot, and the LOQ was 60.235 Ng/spot. TEL was shown to be degraded up to 12.5 % in alkaline solution and completely degraded in GA, but in an oxidative environment, TEL and GA degraded at 30 % and 30.55 %, respectively. The established approach has been validated in compliance with ICH requirements, and the forced degradation study will help with pharmaceutical stability and formulation development.

In a study conducted by Ramesh I, Subramani H, Kuppusamy S, and Kamatham S [31], A unique technique Stability Indicating RP-HPLC Method for the simultaneous estimation of hydrochlorothiazide, telmisartan, and Amlodipine in bulk and combined tablet dosage form was devised, a unique, easy, and accurate RP-HPLC approach was developed for the simultaneous measurement of pharmaceuticals in a bilayer tablet containing Hydrochlorothiazide, Telmisartan, and Amlodipine. The mobile phase was monobasic sodium phosphate dihydrate phosphate buffer and acetonitrile (60:40), the stationary phase was Intersil C18 (250 mm 4.6 mm i.d., 5 m particle size) column, and at a detection wavelength of 257 nm, the flow rate was 1.0 mL/min. Hydrochlorothiazide, telmisartan, and Amlodipine have recorded retention periods of 4.0, 8.6, and 13.3 minutes. This technique has been validated in accordance with ICH standards. The approach provides good resolution between the drugs while having a short retention time. The results of the validation parameters reveal that the proposed technique is simple, specific, precise, reliable, robust, unique, and selective. As a result, the outcomes of the proposed study support the assumption that the established technique is an effective strategy for calculating the doses of hydrochlorothiazide, telmisartan, and amlodipine in tablet form at the same time. The outcomes of the proposed study support the notion that the method developed is an accurate method for concurrently assessing the amounts of hydrochlorothiazide, telmisartan and amlodipine in a multilayer Tablet dosage form.

OFFICIAL METHODS FOR CHLORTHALIDONE

Official in IP 2022[32]

Stainless steel column 25 cm 4.6 mm, packed with octysilane bonded to porous silica gel (5 m), buffer solution prepared by mice dissolving 1.32 g of diammonium hydrogen orthophosphate in 900 mL of water, adjusted to pH 5.5 with dilute orthophosphoric acid, and dilute to 1000 mL with water as Mobile phase A and methanol as Mobile phase B at a flow rate of 1.4 mL min^{-1}. The wavelength detection was performed at 220nm with a 20 µL injection volume.

Reported Methods for Chlorthalidone

Another study by Kharat C, Shirsat VA, Kodgule YM and Kodgule M[33] (2020) developed a revised reversed-phase HPLC technique for the simultaneous identification and quantification of pharmacopoeia-listed and indoor processes & degraders. Impurities of chlorthalidone in bulk pharmaceuticals and dosage formulations. A C8 column (particle size 5 µm, 250 4.6 mm;) was used for chromatographic separation, with a flow rate of 1.4 mL/min and an observation wavelength of 220 nm. A C8 column (particle size 5 µm, A buffer solution (diammonium hydrogen orthophosphate (10 mM, pH 5.5) was used in mobile phase A and a C8 column (particle size 5 µm, methanol in a 65:35 (V/V) ratio, while mobile phase B was made up of a buffer solution and methanol in a 50:50 (V/V) ratio. The linearity for chlorthalidone was found to be between 1 and 2.8 g mL^{-1}, while the levels of both intrinsic impurities were between 0.75 and 2.1 g mL^{-1}. Chlorthalidone and the phase II and phase III pollutants had R2 values of 0.9985, 0.9985, and 0.9986, respectively. Stress conditions, including acid, alkali,photolysis, heat, and oxidation , were

applied to the API and formulation. Additional validation studies for specificity , limit of quantitation (LOQ), limit of detection (LOD), linearity, precision, accuracy, and robustness were carried out while the experiment was still in progress. In order to better separate all known and unknown contaminants with acceptable resolution and rejection factor, an enhanced RP-HPLC technique was created.

Singh B, Patel DK, and Ghosh SK[34] organized their research with the goal of establishing Reverse-phase high-performance liquid chromatography is a straightforward, accurate, and focused method for finding chlorthalidone in pharmaceutical formulations. As a consequence of their efforts, the Chlorthalidone peak was eluted utilizing the mobile phase at 10.82 min. The calibration curve was a linear combination of 50 mM disodium hydrogen phosphate: methanol: acetonitrile in a ratio of 70:30:05 (pH adjusted to 3.5 with orthophosphoric acid) with a flow rate of 1 mL min^{-1} and the eluates were monitored at 220 °C. °C. etc. A C18 column (particle size 5 µm, 250 x 4 mm,) was used for other chromatographic conditions. Between 0.1 and 3.2 g mL^{-1}, the calibration curve was determined to be linear. The calculated intraday coefficients of variation were 3.3085 and interday coefficients of variation were 0.3702, respectively. It has been proven to validate the method and can be used to determine chlorthalidone in pharmaceuticals according to ICH regulations. 50 mM disodium hydrogen phosphate: methanol: acetonitrile: 05 (pH adjusted to 3.5 with orthophosphoric acid) was used as the calibration curve, and the eluents were seen at a wavelength of 220 nm. A C18 column (particle size 5 µm ,250 x 4 mm) was used for other chromatographic conditions. Between 0.1 and 3.2 g mL^{-1}, the calibration curve was determined to be linear. The calculated intraday coefficients of variation were 3.3085 and interday coefficients of variation were 0.3702. It has been proven to validate the method and can be used to determine chlorthalidone in pharmaceuticals according to ICH guidelines.

Gandhi SV and Sanklecha AP[35] conducted research in which they aimed to design and verify a simple, accurate, and Chlorthalidone tablet dose analysis using the HPLC method. The technique was created to evaluate the qualitative and quantitative properties of chlorthalidone in tablet dose form. A HiQ Sil C8 (4.6 mm x 250 mm x 5 m) for chromatographic separation, a 20 MM potassium dihydrogen orthophosphate buffer, pH 4.0: methanol (30:70 % V/V) column was utilized. The eluate was measured at 230 nm while the mobile phase was pumped at a rate of 1.0 mL/min. Retention lasted for 3.334 and 0.042 minutes. In the concentration range of 5–30 g mL^{-1}, linearity was noted with an R2 correlation value of 0.9915. All parameters were evaluated in accordance with ICH recommendations and determined to be appropriate for routine drug analysis in dosage form.

In a study conducted by Kachave RN, Sonawane MS, and Patil SD [36], a method was developed for the estimation of Chlorthalidone in both bulk medicine sold in stores and Individual tablet batches are analyzed using an Agilent C18 column (250 x 4.6 mm) with a diode array detector at a detection wavelength of 275 nm using the Stability Indicating RP-HPLC technique. The mobile phase was used as a Water: Methanol (30:70 V/V) with pH adjusted to 4.8 with glacial acetic acid at a flow rate of f 1 mL min^{-1}. As a result of the procedure, the chromatogram is separated and indicates the retention time of 2.79 min. The recovery of Chlorthalidone was found to be between 99.0 % and 101.0 %. The created approach underwent ICH recommendations validation as well. Chlorthalidone was tested for linearity in the 5–25 g mL^{-1} range with a 0.990 correlation value. Both 0.40g $mL^{-1}$and 1.20g mL^{-1}were found to be the analytical and detection limits, respectively. Acidic, alkaline, oxidative, photolytic, and thermal breakdown stress conditions were all applied to chlorthalidone. Chlorthalidone is more affected by acidic conditions than by oxidation. It is less affected by alkaline conditions, heat, and light. The approach is straightforward, dependable, delicate, and accurate. It can distinguish between the medicine and the substance that results from the drug's breakdown under various stress situations. This enables it to be used as a stability-indicating tool for identifying Chlorthalidone in both bulk and medicinal dosage form.

P. H. Sakpal and A. R. Chabukswar [37] used the Stability Indicating RP-HPLC technique to estimate amlodipine and chlorthalidone in bulk and tablet dosage form. The Octadecylsilane C18 column (5 m, 25 cm 4.6 mm) was used for chromatography. At pH 3, 0.1 % formic acid: methanol: acetonitrile (50:5:45 V/V) was adjusted with orthophosphoric acid as mobile phase at a flow rate of 1 mL min^{-1}, and the effluent was monitored at 266 nm. Amlodipine and chlorthalidone had drug retention times of 6.32 and 5.32 minutes, respectively. The calibration curves produced at each retention period are 2.5-7.5 g mL^{-1} and 06-18 g mL^{-1}, respectively, with regression coefficients of 0.9990 and 0.9940 for amlodipine and chlorthalidone. The designed and verified approach is dependable, simple, precise, and accurate, and it is straightforward to use in laboratories.

CONCLUSION

The provided study is based on a literature review on the development of analytical methods for Efonidipine Hydrochloride Ethanolate, Telmisartan, and Chlorthalidone when used in conjunction with UV,

IR, and HPLC. Only HPLC and LC/MS/MS techniques for Efonidipine Hydrochloride Ethanolate were published on an individual drug basis, whereas UV, HPLC, Stability indicating HPLC, HPTLC, and UPLC methods were given for estimation of Telmisartan and Chlorthalidone for individual drug and along with other drugs. There is therefore scope to design and validate a stability indicating HPLC for the combination of Chlorthalidone, Telmisartan, and Efonidipine Hydrochloride Ethanolate. This review gave an overview of the most recent analytical techniques for analyzing Efonidipine Hydrochloride Ethanolate, Telmisartan, and Chlorthalidone. The information will be helpful to researchers working on formulation development, bioanalytical research, and quality control projects in the future.

REFERENCE

1. Tripathi KD, (2017). "Essentials of Medical Pharmacology", Jaypee Brothers Medical Publisher (P) Ltd., vol. 8, pp. 604-615. DOI: 10.5005/jp/books/10282
2. Sharma HL and Sharma KK, (2023)."Principle of Pharmacology", Paras Medical Publisher, vol. 3, pp. 262-265, 2017.
3. Pathophysiology of Hypertension, 2023. http://pathophysiology530.weebly.com/pathophysiology.htmL. Accessed Aug. 22, 2023.
4. National Center for Biotechnology Information. PubChem Compound Summary for CID 163838, Efonidipine hydrochloride ethanolate. https://pubchem.ncbi.nlm.nih.gov/compound/Efonidipine-hydrochloride-ethanolate. Accessed Aug. 22, 2023.
5. Drug profile, "Efonidipine Hydrochloride Ethanolate", https://newdrugapprovals.org/tag/efonidipine-hydrochloride-ethanolate. Accessed Aug. 23, 2023.
6. National Center for Biotechnology Information. PubChem Compound Summary for CID 65999, Telmisartan; https://pubchem.ncbi.nlm.nih.gov/compound/Telmisartan. Accessed Aug. 23, 2023.
7. Drug profile, "Telmisartan", https://go.drugbank.com/drugs/DB0096. Accessed Aug. 23, 2023.
8. National Center for Biotechnology Information; 2004-. PubChem Compound Summary for CID 2732, Chlorthalidone; https://pubchem.ncbi.nlm.nih.gov/compound/Chlorthalidone. Accessed Aug. 23, 2023.
9. Drug profile, "Chlorthalidone", https://go.drugbank.com/drugs/DB00310. Accessed Aug. 23, 2023.
10. Bhalerao SS and Jawarkar SG, "Bio-analytical method development for efonidipine in human plasma by using RP-HPLC", International Research Journal of Modernization in Engineering Technology and Science, vol. 5, no. 5, pp. 7983-7989, 2023. DOI: 10.56726/IRJMETS40755
11. Pandya CP and Rajput SJ, (2020). "Forced degradation study of efonidipine HCl ethanolate, characterization of degradation products by LC-Q-TOF-MS and NMR," Journal of Applied Pharmaceutical Science, vol. 10, no. 4, pp. 75-99, DOI: 10.7324/JAPS.2020.104012
12. Rajput AS, Jha DK, Gurram S, Shah DS, Amin PD, (2020). "RP-HPLC method development and validation for the quantification of Efonidipine hydrochloride in HME processed solid dispersions," Future Journal of Pharmaceutical Sciences, vol. 6, no. 1, pp. 1-9. DOI: 10.1186/s43094-020-00094-2
13. Solanki D, Patel D, Meshram D, (2022). "Development and validation of UV Spectrophotometric method for simultaneous estimation of Efonidipine hydrochloride ethanolate and Chlorthalidone in their synthetic mixture," Drug Analytical Research. vol. 6, no. 1, pp. 27-34. DOI: 10.22456/2527-2616.125170
14. Adeshra SD, Meshram DB, (2022). "RP-HPLC Method Development and Validation for Simultaneous Estimation of Efonidipine Hydrochloride Ethanolate and Telmisartan in Their Synthetic Mixture," International Journal of Pharmaceutics and Drug Analysis. vol. 9, no. 3, pp. 190-195. DOI: 10.22456/2527-2616.12517
15. Dudhrejia A, Patel A, Chavda J, Gol D, Koli P, (2022). "Spectrophotometric simultaneous determination of Efonidipine hydrochloride ethanolate and telmistran in synthetic mixture by first order derivative method," Journal of medical pharmaceutical and allied sciences, vol. 11, no. 2, pp. 4547-4551. DOI: 10.55522/ jmpas.V11I2.2427
16. Patel BD (2022). 2^3 factorial design for optimization of Hplc-pda method for the simultaneous estimation of efonidipine hydrochloride ethanolate and telmisartan in tablet dosage form," Journal For Basic Sciences, vol. 22, no. 12, pp. 1383-1392.
17. Indian pharmacopeia, Government of India, ministry of Health and Family Welfare, The Indian pharmacopeia Commission, Ghaziabad, 9th edition vol. 2, pp. 3726, 2022.
18. Rao MB, Nagendrakumar A, Sivanadh M, Rao GV, (2012). "Validated RP-HPLC method for the estimation of telmisartan in tablet formulation," Pharmaceutical Research, vol. 2, no. 2, pp. 50-55. DOI: 10.1093/chromsci/ bmab070
19. Londhe SV, Kaul N, Agrawal H, Mahadik KR, (2010). "Stability-indicating RP-HPLC method for analysis of telmisartan in the bulk drug and in formulations," Acta Chromatographic, vol. 22, no. 4, pp. 539-548.DOI: 10.5958/2231-5675.2020.00002.2
20. Chaudhary BR, Dave JB, (2017). "Development and validation of stability indicating gradient RP-HPLC method for simultaneous estimation of telmisartan and chlorthalidone in bulk API and fixed dose combination," World Journal of Pharmaceutical Research, vol. 6, no. 10, pp. 1015-1029 DOI: 10.20959/wjpr201710-9417
21. Vanaja N, Preethi C, Manjunath SY, Pal K, (2015). "Method development and validation for simultaneous estimation of telmisartan and chlorthalidone by RP-HPLC in pharmaceutical dosage form," Asian Journal of Pharmaceutical Analysis, vol. 5, no. 4, pp. 171-177, DOI: 10.5958/2231-5675.2015.00027.7

22. Prajapati P, Patel A, Shah S, (2022). "Application of DoE-based analytical QRM to development of the multipurpose RP-HPLC method for estimation of multiple FDC products of telmisartan using enhanced AQbD approach," Journal of Chromatographic Science, vol. 60, no. 6, pp. 525-537 DOI: 10.1093/chromsci/bmab070
23. Panda M, Dadi V, Yarraguntla SR, Rao KV, (2023). "RP-HPLC Method for Determination of Azelnidipine and Telmisartan in Pharmaceutical Dosage Form," Research Journal of Pharmacy and Technology, vol. 16, no. 2, pp. 509-513. DOI: 10.52711/0974-360X.2023.00086
24. Gandu S, Ravinder M, Gandla K, Narmada G, (2022). "Simultaneous Estimation of Metoprolol and Telmisartan in Combined Tablet Dosage Form by Using RP-HPLC and UV Spectrophotometry," Asian Journal of Pharmaceutical Research and Development, vol. 10, no. 4, pp. 22-33. DOI: 10.22270/ajprd.v10i4.1153
25. Chaitanya DB, Ajitha M, (2022). "Stability Indicating RP-HPLC Method Development and Validation for simultaneous estimation of Azelnidipine and Telmisartan in Bulk and Pharmaceutical Dosage Form," World Journal of Pharmaceutical Sciences, vol. 10, no. 1, pp. 121-127, DOI: 10.54037/WJPS.100113
26. Gholve R, Pekamwar S, Wadher S, Kalyankar T, (2021). "Stability-indicating RP-HPLC method development and validation for simultaneous estimation of telmisartan and rosuvastatin calcium in bulk and in tablet dosage form," Future Journal of Pharmaceutical Sciences, vol. 7, pp. 1-5. DOI: 10.1186/s43094-021-00369-2
27. Patel B, "Chaudhary A, and Gami S. (2019). RP-HPLC method development and validation for simultaneous estimation of benidipine hydrochloride, telmisartan and chlorthalidone in Tablet," Journal of Emerging Technologies and Innovative Research, vol. 6, no. 3, pp. 110-134.
28. Dalal D, Kant R, and Yadav M, (2023). "Simultaneous estimation of fixed dosage combination of telmisartan and benidipine hydrochloride in human plasma by HPLC-UV," Eur. Chem. Bull, vol. 12, no. 5, pp. 3300-3307. DOI: 10.48047/ecb/2023.12.si5a.0218
29. Deshpande SV, Waman JS, Patil AR, and Kapse BP, (2015). "Development and Validation for Simultaneous Estimation of Telmisartan and Hydro-chlorothiazide in Bulk Drug and Pharmaceu-tical Dosage Form by Uv-Spectrophotometry," International Journal of Pharmaceutics and Drug Analysis, vol. 3, no. 12, pp. 265-362.
30. Pattanik SK, Pradhan KK, (2022). "Development and Validation of Stability Indicating Hptlc Method for Simultaneous Estimation of Telmisartan and Gallic Acid as Per Ich Q1a (R2)," Analytical chemistry journal, DOI: 10.2139/ssrn.4233902
31. Ramesh I, Subramani H, Kuppusamy S, Kamatham S, (2022). "Stability Indicating Rp-Hplc Method Development and Validation for The Simultaneous Estimation of Hydrochlorothiazide, Amlodipine and Telmisartan in Bulk and Combined Tablet Dosage Form," NeuroQuantology, vol. 20, no. 15, pp. 346-357. DOI: 10.14704/ NQ.2022.20.15.NQ88035
32. Indian Pharmacopoeia, Government of India, Ministry of Health and Family Welfare, The Indian Pharmacopoeia Commission, Ghaziabad, 9th edition vol. 2, pp. 1863, 2022.
33. Kharat C, Shirsat VA, Kodgule YM, Kodgule M, "A validated RP-HPLC stability method for the estimation of chlorthalidone and its process-related impurities in an API and tablet formulation," International Journal of Analytical Chemistry, 2020. DOI: 10.1155/2020/3593805
34. Singh B, Patel DK, Ghosh SK, (2009). "A reversed-phase high performance liquid chromatographic method for determination of chlorthalidone in pharmaceutical formulation," Int J Pharm Pharm Sci, vol. 1, no. 2, pp. 24-29.
35. Gandhi SV, Sanklecha AP, (2019). "HPLC method development and validation for estimation of chlorthalidone in tablet dosage form," Journal of Drug Delivery and Therapeutics, vol. 9, no. 4, pp. 53-56.DOI: 10.22270/jddt.v9i4.3127
36. Kachave RN, Sonawane MS, Patil SD, (2022). "Development and Validation of Stability Indicating Rp-Hplc Method For Determination Of Chlorthalidone," Journal of Pharmaceutical Negative Results, vol. 13, no. 6, pp. 4416-4423, 2022. DOI: 10.47750/pnr.13.S06.583
37. P. H. Sakpal and A. R. Chabukswar, (2020). "Stability Indicating RP-HPLC Method Development and Validation for Simultaneous Estimation of Amlodipine and Chlorthalidone in Bulk and Tablet Dosage Form," International Journal of Pharmaceutical Sciences and Research, vol. 11, no. 5, pp. 2161-2168, DOI: 10.13040/IJPSR.0975-8232.

CITATION OF THIS ARTICLE

Jash S, Vaishali P. Efonidipine HCL Ethanolate, Telmisartan, and Chlorthalidone: A Review of Analytical Methods. Bull. Env. Pharmacol. Life Sci., Vol 13 [5] April 2024: 13-22