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Overview on Analysis Methods of Telmisartan in Pharmaceutical Preparation and Biological Matrices

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ABSTRACT

Angiotensin II type 1 receptor antagonists were broadly employed to remedydiverse issues along with hypertension, coronary heart failure, myocardial infarction, and diabetic nephropathy. Telmisartan is a strong, long-lasting nonpeptide antagonist of the angiotensin II receptor type 1 that's the brand new preference for the remedy of critical hypertension, with its very high lipophilicity, unique telmisartan features, plus a high volume of distribution, provides clinical advantages for penetration into target tissues and organs. Various analytical strategies are expanded in each biological fluid and dosage form to estimate the activity of the prescribed drug.This drug has been assigned within biological formulations and fluids by various methods according to spectrophotometry, high-performance liquid activity with ultraviolet and fluorimetry detection, liquid chromatography and tandem mass spectrometry, densitometry, immune test methods, ultra-performance liquid chromatography methods, titrimetric methods of analysis, and electrochemical methods such as voltammetry and polarography.

Keywords: Telmisartan, pharmaceutical preparation, biological matrices, telmisartan analysis

I. INTRODUCTION

Telmisartan is a type 1 AII receptor antagonist, a strong and long-lasting nonpeptide employed for the medication of essential hypertension. Telmisartan has very high lipophilicity, high volume of distribution, and Telmisartan's unique characteristics suggest that Telmisartan provides clinical advantages for penetration into target tissues and organs. Telmisartan is not a prodrug preparation that includes an extended terminal elimination half-life than other commercially available sartans; therefore,Telmisartan is appropriate for the once-daily dose. In clinical trials in hypertensive patients, Telmisartan has been shown to reduce blood pressure and comparable to other members, such as ACE inhibitors, beta-blockers, and calcium antagonists. This test provides safety to placebo and tolerability of Telmisartan in hypertensive patients. This drug is superior to other sartans and should be a possible replacement treatment for hypertension[1].

Telmisartan (Micardis®, Pritor®),a very selective type 1 hypertension receptor antagonist, is used at the hypertension medication, suitable for monotherapy and in conjunction with alternative medicine agents. The removal of the long half-life of Telmisartan from the drug led to an effective reduction in blood pressure over a 24-hour dosing interval. Clinical trials, as well as clinical practice, show that Telmisartan, either as monotherapy or in conjunction with other antihypertensive agents, provides semi-permanent antihypertensive properties and is well tolerated in a vast spectrum of hypertensive patients, including the elderly and those with type 2 diabetes mellitus which coexist with metabolic syndrome and kidney disorders. Regardless of its effect on blood pressure, Telmisartan exhibits a beneficial impact on internal secretion resistance, macromolecular levels, left ventricular hypertrophy (LVH), and kidney organ function. The consistent drug efficacy of the drug over an unlimited total count interval of 24 hours and the long-term worsening effects of physical phenomena, combined with its favorable tolerability profile, means that Telmisartan may also be a valuable first-line treatment option for hypertension management [2].

Telmisartan determination is commonly used by various methods such as spectrophotometry, high-performanceultraviolet and fluorimetry liquid chromatography, liquid chromatography-tandem mass spectrometry, densitometry, and ultra-performance liquid chromatography, titrimetric testing methods, and

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electrochemical methods such as voltammetry in formulations and biological fluids.

CLINICAL BACKGROUND

Telmisartan is employed in the treatment of high blood pressure and decrease cardiovascular risk. Medicine is given orally, and once a dose, the hypotensive effect peaks within 24 hours at intervals of 3 hours. Within around four to eight weeks after beginning treatment, most hypotensive effects occur. For hypertension, Telmisartan is administered once daily at an initial dose of 40 mg. This may, if necessary, accumulate up to a maximum dose of 80 mg once daily. For patients with impaired liver or organ excretion, lower doses have to be recalculated[3].

Telmisartan is a highly selective receptor for angiotensin II type 1 receptor.The multicenter, randomized, double-blind clinical trial in patients with mild to moderate hypertension was considerably simpler than the larger placebo (n> 100).Telmisartan reduced systolic blood pressure and diastolic blood pressure to 15.5 and 10.5 mmHg, respectively, at a dose of 20 to 160 mg once daily. The greatest decrease in blood pressure occurs at the 40 to 80 mg/day dose [4].

DATA COLLECTION

In preparing this review article, the technique used is to use literature study by searching for sources or literature in the form of primary data in official books and international journals for the last 20 years (2000 - 2020). In addition, in making this review article, data search was carried out using online media with the keyword telmisartan, telmisartan analysis, pharmaceutical preparations, biological matrices. The main reference searches used in this review article were through trusted webs such as Science Direct, Google Scholar, and other trusted published journals.

SPECTROPHOTOMETRY METHOD

This article describes the occurrence and validation of first-order derived UV spectrophotometric methodologies for the determination of Telmisartan in pharmaceutical formulations. Standard solutions and 0.1 M hydroxide in the ultraviolet light spectrophotometric method, the quantitative determination of the drug is dispensed at 295 nm with a dimensional variation of 4 - 20 µg/mL and the determination of the drug at 311 nm with a first-order derivative of the spectrophotometric method with a linearity range of 4 - 20 µg/mL [5].

EstimatingTelmisartan in tablet formulations, modest, quick, sensitive, accurate, and economical spectrophotometric methods have been used. It has been confirmed throughout the study that the drug's acid solution forms colored ionic bonds with chloroform-soluble bromocresol green (BCG).For the development of colorimetric methods of drug analysis, these medicinal properties can beused. At 440 nm, the Telmisartan complex with BCG demonstrates $\lambda_{max,}$ and this method has been validated statistically.The recovery analysis confers satiate results that indicate that no additives and excipients interfere with the review method.A modest, precise, and reproducible projection method is useful in analyzing tablet formulations [6].

This article describes a modest, precise, and correct spectrophotometric method with measurementsusing Shimadzu's expanded and validated UV/Vis spectrophotometer to estimate Telmisartan in bulk and tablet dosage types. Telmisartan zero-order spectrum with 0.1 N NaOH shows the A (1%,1cm) value at 234 nmwas found to be 912.028. The percentrecovery was found to be nearly 100% indicatingreproducibility and accuracy of the method. The calibration graphwas found to be linear (r^2 =0.999) over the concentration range of 4-24 µg/mL. The proposed method was simple, precise, and economicaland can be adopted for routine qualitycontrol of drugs[7].

Telmisartan is also estimated by spectrophotometric methods in bulk drugs and pharmaceutical formulations. In the acidic and alkaline media found in the ultraviolet radiation spectrum, Telmisartan is two distinct types.The spectral variance was achieved by storing Telmisartan in the reference cell at 0.01 N NaOH and Telmisartan in the sample cell at 0.01 N HNO_3. There are two characteristic summits with positive and negative absorbances at 295 and 327 nm.The difference in absorbance between the two was measured to see the previously expected amplitude toward the concentration. In variations of 2 - 12 µg/mL, this technique was found to be linear [8].

Telmisartan examination using direct UV spectrophotometric techniques has developed a UV estimation method for Telmisartan in tablet formulations. The wavelength (λ_{max}) chosen for

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Telmisartan is 230 nm. The linearity of this drug at the selected wavelength is between 1 and 8 µg/mL. During this method, the beer law is obeyed with a correlation of 0.999 [9].

This article explains that telmisartan estimation in bulk dosage form and tablets has been expanded and is valid using the ultraviolet radiation spectrophotometric method. The telmisartan spectrum for 0.1 N NaOH and H_2O (20:80) shows The A (1%, 1cm) value at 295.0 nm was found to be 1109.167. With different concentrations of 2- 10 µg/mL, the standardization graph was found to be linear (r^2 = 0.999). The recovery percentage was found to be almost 100 %, showing the method's reproducibility and precision.For precision, accuracy, specificity, complexity, and durability, the projected methods have been validated. In routine analysis, this way can be adopted [10].

Several spectrophotometry methods have been used for telmisartan analysis, either as raw material or in pharmaceutical dosage forms (Table 1).

Table 1: Telmisartan analysis using spectrophotometry

No	Sample	Solvent	Wavelength	Range of Concentration	Reference
1	Pure and pharmaceutical dosage form	Sodium Hydroxide	295 nm	4 - 20 µg/mL	[5]
2	Tablet	Bromocresol green	440 nm	4 - 20 µg/mL	[6]
3	Bulk, tablet	NaOH, Distilled water	234 nm	4 - 24 µg/mL	[7]
4	Bulk	NaOH	295 nm 327 nm	2 - 12 µg/mL	[8]
5	Tablet	Sodium Hydroxide	230 nm	1 - 8 µg/mL	[9]
6	Bulk, tablet	NaOH, Distilled water	234 nm	2 - 10 µg/mL	[10]

HIGH-PERFORMANCE THIN-LAYER CHROMATOGRAPHY METHOD

Several research uses this method for telmisartan determination, furthermore as several stability studies conducted by the researchers. The tests performed to show the steadiness, and also the pathway of drug degradation must be studied. This HP-TLC method makes it possible to calculate Telmisartan in pharmaceutical tablets quickly, accurately, and reproducibly, without distraction from excipients and in the presence of its acid and oxidative degradation items.This approach works much better than the methods published for deciding Telmisartan. The way has been thoroughly tested and is ideal for laboratories and quality control, where thrift and velocity are crucial.A study using this technique typically assesses the chastity of drugs by detecting the associated impurities from different sources. It is possible to improve the kinetics of telmisartan degradation for estimation in plasma and other biological fluids during the analysis. It can distinguish the drug from its degradation products and because this could be considered a sign of stability[11].

The modest, selective, accurate, and stable thin layer chromatography (HP-TLC) method shows high efficiency in the densitometric determination of Telmisartan both as a bulk drug and formulations expanded and validated in compliance with the international conference on harmonization guidelines (ICH).TLC procedure was optimized to develop a stability-indicating assay method. The mobile phase consisting of ethyl acetate: dichloroethane: methanol (6:2:1 v/v) gave a sharp and well-defined peak at R_f value of 0.68. The linear regression data for the calibration curve (n = 6) showed a good linear relationship over the concentration range 300 – 1800 ng/spot with respect to the peak area. No significant difference was observed in the slopes of standard curves.The repeatability of the sample application and measurement of peak area was expressed in terms of % RSD, and results revealed intra-day and inter-day variation of Telmisartan at three different

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concentration levels 600, 900, and 1200 ng/spot.The standard deviation of peak areas was calculated for the parameter, and the % RSD was less than 2%. The low value of % RSD shown indicated the robustness of the method.The proposed method for extracting and estimatingTelmisartanfrom pharmaceutical dosage form drug afforded 99 – 101% recovery. The method can determine the purity of the drug available from various sources by detecting the various impurities[12].

HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY METHOD

The HPLC method has expanded fast, responsive, selective, and validated testingquantitative determination of Telmisartan in human plasma. The pretreatment of a plasma sample consists of the extraction of the precipitated protein with methanol. There was no intervening endogenous compoundblank plasma in Telmisartan at the retention period.This method is validated within the concentration range of 40–1600 ng/ml, showing a better linear response,and the correlation coefficient is 0.9998.The extraction process's recovery was 82.4, 79.96, and 81.13 %, respectively, in the HQC, MQC, and LQC telmisartan samples. The sum means recovery value was found to be 81.16 %.Under various storage and processing conditions, Telmisartan was found stable.The observations state that the method developed is incredibly appropriate and applicable for the telmisartan antihypertensive research program [13].

This test is meant to be expanded and validate an accurate, precise, and fast method for estimating Telmisartan as an active pharmaceutical ingredient (API) additionally as within the dosage form of agglomerate tablets and balls made by RP-HPLC. The method developed is modest, accurate, precise, and sensitive.Method development consists of selecting suitable wavelengths and choice of stationary and mobile phases.HPLC with a programmable UV-Visible variable wavelength detector, and the separation was achieved on Isocratic HPLC. A mixture of Acetonitrile: Phosphate buffer in the ratio of 90:10 v/v was prepared and used as a mobile phase. The summit absorbance of Telmisartan was found to be maximal at 296 nm. The method proposed was applied to the assay of tablets containing spherical agglomerates of Telmisartan. Telmisartan spherical agglomeration result assay was 18.52 [14].

This article develops and validates a modest, selective, and precise reverse-phasehigh-performance liquid chromatography (RP-HPLC) method that demonstrates the analytical stability of Telmisartan in pure and pharmaceutical dosage forms. The chromatographic conditions comprised a reversed-phase C_{18} column (4.6150 mm, 3.5 m, Make: XTerra), with a mobile phase composed of buffer and methanol (40:60 v/v pH to 3.0 with orthophosphoric acid). The detection was allotted at 230 nm with a flow of 0.5 mL/min. The retention time for Telmisartan was 2.6 min. The regression analysis data for the calibration plot showed a nice linear relationship within the concentration range of 20 - 100. During this test, the coefficient of correlation, slope, and intercept values were 0.9998, 2.326, and 6.708, respectively [15].

Telmisartan determination (TELM) has been expanded and validated in tablet dosage form employing the high-performance liquid chromatography (RP-HPLC) method. Various buffers, including phosphate, acetate, and citrate for mobile phase preparation and the chromatographic conditions, were designed for better resolution. It was concluded that the phosphate buffer (10 mM phosphate buffer pH at 3.0) provided preferable peak shapes than its compared of acetate and citrate. HPLC has been validated according to the ICH approach in terms of accuracy, precision, specificity, and linearity. The method developed shows its suitability for routine TELM analysis in tablet dosage form [16].

A very selective, sensitive, and quickmechanism of determination using high-performance liquid chromatography with tandem mass spectrometry detection on Telmisartan is performed in human plasma.Zorbax extender gave the best chromatography out of a range of C_{18} columns evaluated. The telmisartan test it proven linear with a LOD of 0.05 ng/ml over the concentration range of 0.5-600.0 ng/ml ($r > 0.996$). Intra- and inter-day precision was 4.5-6.7 % and 3.6-8.1 % and accuracy was 88.9-111.0 %, respectively.The results show that the ionization of Telmisartan and the internal standard were significantly no influenced by endogenous substances. Telmisartan was stable with mean recoveries of 94.3-105.6 % of nominal concentrations in all conditions evaluated[17].

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A rapid HPLC method with a monolithic column using fluorescence detection has been expanded to determineTelmisartan in human plasma. Sample preparation was done out by protein deposition with acetonitrile and naproxen employed as IS. During this method, the compounds used are detected by fluorescence detection using an excitation wavelength of 300 nm and an emission wavelength of 385 nm. The downside of the approach was that the domain of linearity was not high enough, so required dilution and reanalysis were at specific samples. It was successfully applied to a bioequivalence analysis after complete validation[18].

The HPLC method will be reproduced for quantitative telmisartan analysis. The drug is separated from its degradation product in column C_{18} at room temperature with methanol-water 80:20 v/v, pH 4.0 (adjusted for addition of orthophosphoric acid), as a mobile phase with a rate of flow of 1.0 mL/min. Under these conditions, the telmisartan retention time was 4.85 ± 0.05 min. The quantification was carried out based on the height area achieved by UV detection at 225 nm and a linear calibration plot at a 10 - 60 µg/mL concentration range. This method is applied to pharmaceutical formulations; then, there is no chromatographic interference of tablet excipients. This method is validated for accuracy, robustness, recovery, detection limit, and quantification limit. The drug undergoes acid and alkaline hydrolysis and oxidation, dry heat, wet heat, and photodegradation. This method can effectively separate the drug from its degradation products, which is considered a sign of stability [19].

Several liquid chromatography methods have been used for telmisartan analysis, both raw material and pharmaceutical dosage forms (Table 2).

Table 2: Telmisartan analysis using liquid chromatography.

No	Sample	Column	Mobile Phase and [Flow Rate]	Detection	Reference
1	Human plasma	Phenomenex LUNA C_{18}, column (250 × 4.6 mm i.d, 5µm)	Sodium dihydrogen phosphate buffer (pH:3.0): acetonitrile (42:58 v/v) [1.2 mL/min]	Ultraviolet (UV)-PDA detector at 297 nm	[13]
2	Tablet	Column oven (Jasco), and a Reverse Phase C_{18} (phenyl) (25 cm × 4.6 mm i.d., 5 µm)	Acetonitrile: buffer in the ratio of 90:10 v/v [0.8 mL/min]	UV detector at 296 nm	[14]
3	Pure and pharmaceutical dosage form	Reversed phase C_{18} column (4.6150 mm, 3.5 m, XTerra)	Buffer and methanol (40:60 v/v, pH 3.0 with ortho phosphoric acid) [0.5 mL/min]	UV detector at 230 nm	[15]
4	Tablet	Waters symmetry column 250 × 4.6 mm, 5µ	10 mM potassium dihydrogen phosphate (pH 3.5): acetonitrile (64:40) [1.0 mL/min]	UV detector at 230 nm	[16]
5	Human plasma	Zorbax extend C_{18} column	Methanol 10 mM ammonium acetate (85:15 v/v) to pH 4.5 [1.0 mL/min]	Q-trap TM LC–MS/MS	[17]
6	Human plasma	Monolithic analytical column,	Acetonitrile and naproxen	Fluorescence detection	[18]

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		Chromolith® (RP-18e 100mm × 4.6 mm, Merck, Germany)	[3 mL/min]	λ_{ex} 300 nm λ_{em} 385 nm	
7	Tablet	Column C_{18}	Methanol-water (80:20 v/v) pH 4.0 [1.0 mL/min]	UV detector at 225 nm	[19]
8	Rat Plasma	Phenomenex Luna® C_8 column	Methanol and acetonitrile (70:30 v/v) [1 mL/min]	Shimadzu LC SOLUTION (PDA)	[20]
9	Tablet	Chromosil C_{18} (250 mm × 4.6 mm, 5 µm) column	Methanol : 0.1 % orthophosphoric acid : acetonitrile (80:5:15 v/v/v) [1.5 mL/min]	Spectrophotometer UV detector at 256 nm	[21]

Telmisartan determination in little volumes of mouse plasma has been expanded and validated employing a simple and special inverted phase bioanalytical HPLC method. A precise, reproducible method for the estimation of drug samplescould be used to analyze drugs in bulk drug delivery with the system in vitro and in vivo. From primarybackpressure, peak resolution, summit shape, and reproducibility of daily retention times, chromatographic conditions were selected.The intra-day and inter-day precisions results indicate that the method developed to quantify TLM in plasma samples was accurate and precise.This technique can also be used in bulk and pharmaceutical dosage forms for TLM quality-control tests[20].

This article discusses the estimation of Telmisartan employing the reversed-phase HPLC method in tablet dosage form developed and validated. The optimum detection wavelength hasbeen set at 256 nm, where the detectors have much stronger drugresponses. The calibration curve was obtained for a series of concentrations in the 2 - 12 µg/ml range, and it was found to be linear. The robustness test found no significantchanges were made in chromatograms, which showed that the system developed was strong. Telmisartan recovery from tablet formulation was found to be 99.41 %. That proposed method is accurate, precise, and rapid and is successfully applied to estimateTelmisartan in bulk and pharmaceutical formulations without interference and with good sensitivity[21].

ULTRA-PERFORMANCE LIQUID CHROMATOGRAPHY METHOD

The stability and accuracy of this method are demonstrated by the development of the gradient reverse-phase ultra-performance liquid chromatographic (RP-UPLC) method for the quantitative estimation of the purity of Telmisartan drug ingredients and medicinal products in bulk samples and pharmaceutical dosage forms with the presence of product degradation and impurities.The development for this method uses a BEH C_{18} (100 mm × 2.1 mm, 1.7 µ) water aquatic column with a mobile phase containing a gradient time program for solvents A and B.The wavelength selected for monitoring the eluted compound was observed within 10 min at 290 nm, during which Telmisartan and seven impurities were divided correctly. During this test, it was found that Telmisartan significantly decreased when subjected to numerous stress conditions. In this method, the degradation product comes from mostly peaks and impurities, a sign of steadiness. This method has been validated in line with international conference guidelines on harmonization (ICH) with a precision of relevance, specificity, linearity, accuracy, the limit of detection (LOD), and limit of quantification (LOQ) [22].

TITRIMETRIC METHODS

A simple and straightforward titrimetric approach has been extended and validated for the stipulation of widely used angiotensin II receptor antagonists (ARA-IIs). In this process, Telmisartan's acid-base titration is directly applied in an ethanol blend: water (1:1) as a solvent using a regular sodium hydroxide water solution as the titrant with employing phenolphthalein as an indicator and potentiometrically employing a combined pH electrode. This method features a

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relative variance of below 2 % for all ARA-II studied and is accurate and precise. This method shows that it can be applied to testing commercial drugs containing ARA-II, which has been tested above. Testing the validity of this method was carried out using a standard additional recovery study for the drug, and the results were satisfactory. This method obtained results followingthe results obtained from the UV spectrophotometric method. In analyzing using the UV spectrophotometric method, ethanol was used as a solvent and the wavelength used was 296 nm to determine telmisartan drug. The simple, fast, and precise titrimetric method aim to regulate drug quality [23].

VOLTAMMETRY METHOD

Telmisartan has electrochemical behavior, and also the optimum conditions for the test were checked employed square wave voltammetry and cyclic voltammetry. All assays during this method are supported a quasi-reversible electrochemical reduction signal and controlled TS adsorption at about 1.50 V versus Ag/AgCl at pH 10.0 within the Britton-Robinson buffer. The summit current is known to shift linearly, and even the peak current shifts with a concentrate from 1.69 nM (0.87 mg/L) to 27.5 nM (14.15 mg/L). The method has a lower detection limit than other electrochemical and the yield of the t- and F-tests showed that the variations between the two methods were negligible at a confidence level of 95 %, suggesting that there were no substantial differences between the performance of the two methods in terms of performance their accuracy, precision, and recovery.The result proposed method might be alternatives to the HPLC techniques [24].

A hanging mercury drop electrode was investigated for the voltammetric activity of Telmisartan adsorptive stripped. The catalytic wave of hydrogen -1.5 V generated by this compound in a Britton Robinson buffer with a pH of 10.38 encompasses a high summit current with adsorptive accumulation on the electrodes. A sensitive new technique for the stipulation of Telmisartan can be used in adsorptive stripping voltammetry with catalytic hydrogen waves.There is no significant impact on the response of the catalytic hydrogen wave of Telmisartan to the SWAdSV, then the proposed procedure selective. The high value of the correlation coefficient (r = 0.996) indicates the good linearity of the concentration graph. Determination of Telmisartan in pharmaceutical tablets and human plasma using the proposed electrochemical procedure was successfully implemented. The SWAdSV method developed obtained results such as the results obtained from the reported analytical techniques[25].

POLAROGRAPHY

Polarography yield in ca. -1.30 V shows the reduction wave in the absence by H_2O_2 was called a catalytic hydrogen wave, and the reducing wave amplified by H_2O_2iscalled a parallel catalytic hydrogen wave.The employment of parallel catalytic hydrogen waves could enhance the analytical sensitivity of Telmisartan native catalytic hydrogen waves. Telmisartan determination by linear polarographic sweep was expanded, supported by parallel catalytic hydrogen waves and a new technique in pharmaceutical capsule forms and biological serum samples without interference from additives and endogenoussubstances. Parallel catalytic waves decrease with increasing pH and will growwith an increase in the buffer concentration. This shows that the core of the electrode reaction of the parallel catalytic waves in the presence of H_2O_2 is the same as the catalytic hydrogen wave in the absence ofH_2O_2.The proposed method provides advantages in simplicity, speed, and reproducibility over CZE and MEKC [26].

Research on the polarographic behavior of Telmisartan in 0.8 mol/L NH_3H_2O-NH_4Cl (pH 8.9) as supporting electrolyte showed that the reduction summit got at ca. -1.30 V, which corresponds to a catalytic hydrogen swell. Telmisartan determination by linear polarographic sweep, which is a new method developed that supports parallel catalytic hydrogen waves. The calibration curve is linear within the range 2.0×10^{-7} to 3.0×10^{-6} mol/L, and also the detection limit is 1.0×10^{-7} mol/L. The new method using within the determination of Telmisartan in capsules and biological samples carried the absence of pre-separation [27].

ANALYSIS OF TELMISARTAN AND AMLODIPINE MIXTURE

Analysis of telmisartan and amlodipine besylate in tablets, the developed HPTLC technique is reliable, relevant, precise, and robust without the intervention of any excipients. Densitometric analysis of telmisartan and amlodipine besylate was performed at 326 nm. Adequate separation of the two medicine enabled the event of a selective and specific methodology

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of research. The solvent system consist tetrahydrofuran: dichloroethane: methanol: ammonia (6.0:2.0:1.0:0.4 v/v).The statistical analysis shows that the approach is reproducible and selective for the simultaneous calculation as a bulk drug solution and in pharmaceutical formulations of telmisartan and amlodipine besylate[28].

The routine analysis of Telmisartan and amlodipine in pharmaceutical dosage types,employing a UV detector, developed with the RP-HPLC approach. Separation on a column of Nucleodur® C_{18} 5µm (250 x 4.6 mm ID) in a mobile phase consisting of acetonitrile: buffer (55:45) at pH 4.5 ± 0.1, the flow rate of 1.3 mL/min at 238 nm. The test result for Telmisartan and amlodipine tablets were found to be 98.71 ± 0.24 %. The way has been used, and it is known that there is no interference from excipients or endogenous substances at the simultaneous estimation of these two compounds in tablets and bulk drugs [29].

ANALYSIS OF TELMISARTAN AND RAMIPRIL MIXTURE

Identification of Telmisartan and ramipril in pharmaceutical dosage forms employing a modest isocratic HPLC method has been expanded and validated. This method was optimized using an Inertsil ODS column C_{18}, five µ, 250 mm x 4.60 mm id with a 1.5 mL/min flow using PDA detection on 210 nm.The mobile phase consists of buffered potassium in hydrogen phosphate having a pH of 2.8 and acetonitrile with a ratio of 60:40 each used for separation. Linearity was seen by regression toward the mean equation method for Telmisartan and ramipril in several concentration ranges. This method has good linearity because the correlation coefficient of this drug is close to 1.0. The HPLC method is expanded and validated for simultaneous estimation of Telmisartan and ramipril employed linearity, range, accuracy, and precision.The yieldof simultaneous drug analysis of medication in tablet formulations using the proposed method is accurate, precise, reproducible, and specific [30].

Using the thin layer liquid chromatography (TLC) process, a simultaneous estimate of Telmisartan and ramipril in combined dosage forms was expanded and validated. This way does not require the components to be isolated from the previous sample. The method was performed in TLC of precast silica gel on aluminum plate $60F_{254}$ (10 cm × 10 cm, identified previously as methanol and activated at 60 °C for five min before chromatography). The mobilephase Acetone: Benzene: Ethyl acetate (5:3:2, v/v/v) gave good resolution with Rf values of 0.35 and 0.68 forramipril and Telmisartan, respectively. The method was accurate with a % recovery of 99.9% – 100.48% for ramipril and 99.07% –99.62% for Telmisartan. The system developed can be employed in the tablet dosage form for routine analysis of the drug material[31].

ANALYSIS OF TELMISARTAN AND HYDROCHLOROTHIAZIDE MIXTURE

Four methods can determine the new combination of antihypertensive drugs TELM and HCT.The first method is first derivativespectrophotometry (^{1}D) using a zero-crossing technique and wavelength for HCT 241.6 nm and TELM 227.6 nm within the simultaneous determinate of TELM and HCT in a binary mixture. The zero order absorption spectra of 12.5 µg/ml^{-1} for telmisartan and 2.0 µg/ml^{-1}for hydrochlorothiazide in methanol. The first-derivative spectrum of Telmisartan with a yield of 12.5 µg/ml^{-1} and for hydrochlorothiazide 2 µg/ml^{-1} in methanol.The first derivative of ratio spectrophotometry(^{1}DD) is the second method, where the amplitudes were measured for TELM at 242.7 nm and HCT at 274.9 nm. The third technique is based on the isolation of the two drugs by TLC, accompanied by densitometric measurements at 295 nm for TELM and225 nm for HCT.The fourth approach is TELM spectrofluorimetric determination, based on the measurement of native drug fluorescence in 1 M sodium hydroxide at λ excitation 230 nm and emission at 365 nm. The methods suggested have been successfully implemented to determinebulk powder and pharmaceutical formulations [32].

The RP-HPLC method proposed for the simultaneous estimation of Telmisartan and hydrochlorothiazide within the combined dosage form is modest, exact, strong, and fast. Methanol and acetonitrile (70:30 v/v) were used because the mobile phase with a rate of flow of 1 mL/min and a detection wavelength of 270 nm. Rabeprazole is also employed as an internal standard. Retention times for telmisartan 1.79 + 0.01 min, hydrochlorothiazide 2.80 + 0.01 min and rabeprazole 3.19 + 0.01 min. The RP-HPLC method proposed for the simultaneous estimation of

Telmisartan and hydrochlorothiazide within the combined dosage form is modest, exact, strong, and fast. This way fit for quality control of raw materials and formulations or combined dosage forms [33].

The determination of Telmisartan and hydrochlorothiazide in human plasma has been extended and validated using analytical, sensitive, and selective rapid liquid chromatography-tandem mass spectrometry methods. On the sample preparation and analysis, extraction was distributed within the liquid and followed by liquid chromatography-tandem spectrometry analysis and electrospray ionization interface. Compounds were analyzed on an Aquasil-C_{18} (250 × 4.6 mm × 5 µm) column with the mobile phase of pH 4.5 Acetate solution, methanol, and acetonitrile within the ratio of 60:20:20 (v/v) in isocratic condition at a rate of flow 0.5 mL/min for 10 min. Retention times obtained is 4.39 min for telmisartan and 5.73 min for hydrochlorothiazide. The way used was validated in step with the ICH guidelines to study various linearity, precision, accuracy, recovery, and stability. The LC/ MS/MS method developed was successfully utilized to determineTelmisartan and hydrochlorothiazide in human plasma [34].

II. CONCLUSION

Overall, various analytical methods have been used to determine telmisartan levels. Spectrophotometry, high-performance liquid chromatography with ultraviolet and fluorimetric detection, liquid chromatography combined with tandem mass spectrometry, densitometry, ultra-performance liquid chromatography methods, titrimetric analysis methods, and electrochemical methods such as voltammetry and polarography, which are simple and easy to apply. However, the HPLC and HP-TLC analysis methods are often used in research because they can detect samples with low concentrations. The HPLC and HP-TLC methods can be applied in a mixture of Telmisartan with other drugs.

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