World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: https://wjpsonline.com/
Research Article

METHOD DEVELOPMENT AND VALIDATION OF TELMISARTAN BY USING RP-HPLC

[1]Ganta Bhargavi, [1]Kintail Gowthami, [1]Paidisetti Pravallika, [1]Vasantha Pushpa kumari, [1]Pudi sindhura, [2]P.R. Sudha Rani, [3]Dr. K. Atchuta Kumar.

[1]B. Pharmacy, Srinivasarao College of Pharmacy, Affiliated to Andhra University, Visakhapatnam, Andhra Pradesh, India.

[2]M. pharmacy, Department of Pharmaceutical analysis, Assistant Professor, Srinivasarao College of Pharmacy, Affiliated to Andhra University, Visakhapatnam, Andhra Pradesh, India.

[3]Department of Pharmacognosy, Principal, Srinivasarao College of Pharmacy, Affiliated to Andhra University, Visakhapatnam, Andhra Pradesh, India

Received: 28-08-2024 / Revised Accepted: 01-09-2024 / Published: 09-09-2024

ABSTRACT:

A straightforward, reliable reverse phase RP-HPLC technique has been devised and verified for the quantification of Telmisartan in both bulk and pharmaceutical dose forms. Chromotography was estimated by Stationary phase is STD Ascentis C18 (250mm×4.6mm 5µm) for elutant separation, and the Mobile phase is 0.01N Kh2Po4 and Acetonitrile in the ratio of 8:2 at a flow rate 0.5ml/min was maintained, maximum wave length at 296.0 nm, Temperature was set to 30oC. The average retention time of Telmisartan were found to be 5.100 min respectively. By injecting the standard six times, the system suitability characteristics were evaluated, and the results were significantly below the acceptance requirement (Limit of less than 2). A linearity analysis was conducted between 25% and 150% levels, and the R2 value was found to be 0.999. Several validation criteria, including precision, accuracy, LOD, LOQ, and robustness, were determined to be within accepted limits. % recovery was obtained as 99.49% for Telmisartan respectively. The approach was discovered to be simple, accurate, sensitive, quick, and cost effective, with a runtime of less than 30 minutes. In practice, this approach may also be used to determine assay in tablet formulation.

Keyword: Telmisartan, RP-HPLC, Method Validation, optimized.

INTRODUCTION

The major adjustable risk variable for all-cause mortality and morbidity globally is systemic arterial hypertension, which is also linked to an elevated risk of cardiovascular disease (CVD). Although proper

Address for Correspondence: P.R. Sudha Rani**,** M. pharmacy, Department of Pharmaceutical analysis, Assistant Professor, Srinivasarao College of Pharmacy, Affiliated to Andhra University, Visakhapatnam, Andhra Pradesh, India.; **E-Mail:** ramasudharanipalla@gmail.com

How to Cite this Article: P.R. Sudha Rani. Method Development and Validation Of Telmisartan By Using Rp-Hplc. World J Pharm Sci 2024; 12(03): 18-27; https://doi.org/10.54037/WJPS.2022.100905

treatment of hypertension decreases the global burden of disease and death, less than half of persons with hypertension are aware of their condition, and many more are aware but not treated or poorly managed.[1,2,3] The development of hypertension is influenced by the intricate interaction of environmental and pathophysiological determinants that impact many systems, together with hereditary susceptibility. The evaluation of patients with hypertension involves precise measurement of standardized blood pressure (BP), appraisal of patients anticipated risk of atherosclerotic cardiovascular disease (CVD) [4,5,] identification of target organ damage, detection of secondary causes of hypertension, and assessment of comorbidities such as CVD and kidney disease. [6.7,8] Implementing lifestyle adjustments, such as dietary adjustments and higher levels of physical exercise, can effectively reduce blood pressure and avoid the development of hypertension and its cardiovascular disease consequences. [9] Antihypertensive drugs such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, dihydropyridine calcium channel blockers, and thiazide diuretics are highly efficient in reducing blood pressure and avoiding cardiovascular disease (CVD) outcomes in the majority of patients. [10]

Description: - Telmisartan is a commonly used antihypertensive medication that has shown desirable safety and tolerability characteristics, either taken alone or in combination with other treatments. Among the ARBs, this one has several pharmacological characteristics that set it apart—the longest plasma half-life, most lipophilicity, and highest receptor binding affinity in its class. The wide prescription of telmisartan for cardiovascular risk reduction in individuals with atherothrombotic disease or diabetic mellitus (DM) with end-organ damage is well-established.[11,12] Telmisartan has been shown to enhance insulin sensitivity in hypertensive patients. Additionally, its capacity to agonistically stimulate PPARγ leads to improvements in vascular inflammation, reduction of visceral fat, increase of serum adiponectin, and reduction of elevated blood pressure in essential hypertensive patients. Based on a meta-analysis, telmisartan treatment may decrease the left ventricular mass index more effectively than other antihypertensive medication treatments in hypertensive patients. [13] This effect is generally independent of its blood pressure lowering mechanism. Hence, it is important to take into account the supplementary advantages provided by telmisartan treatment, such as its agonistic effects on PPARγ and its stimulating impact on adiponectin synthesis, in order to enable patients to get benefits from these effects.[14,15]

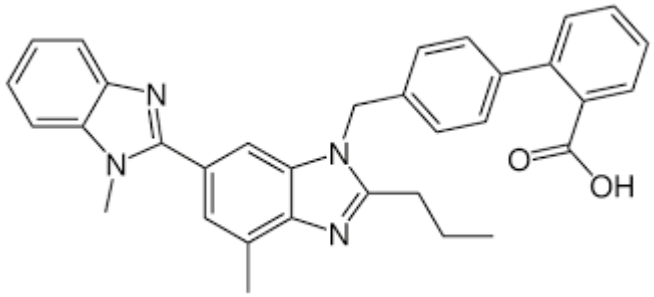

Figure-1: Structures of Telmisartan

One of the most effective separation analytical methods for determining drug estimation is high performance liquid chromatography. Some RP-HPLC [17, 18, 19, 20, 21] methods for estimating Telmisartan drugs and a few other anti-antihypertensive drugs individually or in combination dosage forms have been described in the literature. More economical methods were discovered in the literature review, so a simple, cost-effective stability-indicating simultaneous estimation of Telmisartan by RP-HPLC in pharmaceutical dosage form must be developed and validated in accordance with ICH (Q2 specification) [16].

Materials and Reagents

Telmisartan pure drugs were obtained from Spectrum Pharma research solutions. The HPLC grade methanol and acetonitrile procured from Rankem chemical division, India. Sodium hydrogen phosphate procured from Rankem, India and Pure milli-Q water is used with the help of 0.45µ Millipore filters (Rankem, India).

Instrumentation and Chromatographic Conditions

WATERS HPLC, model: 2690 SYSTEM with UV detector was used for the development and method validation, with an automated sample injector. Std Ascentis (250mm×4.6mm 5µm) column was used for the separation. 0101N Kh2Po4 used as mobile phase A and Acetonitrile is used as mobile phase B (80:20

Ratio). Analysis was carried out in isocratic mode with flow rate of 0.5 mL/min and injection volume was 20 µL. The column temperature was 30°C; the run time was 20.0 min. The data was acquired at detection wavelength 296.0nm and using the software Empower 2.

Preparation of Solutions

Diluent: Mixed Water and Acetonitrile in the ratio of 50:50v/v.

Preparation of buffer

Buffer (0.01N Kh2Po4): Accurately weighed 1.36gm of Potassium dihyrogen Ortho phosphate in a 1000ml of Volumetric flask add about 900ml of milli-Q water added and degas to sonicate and finally make up the volume with water (4.8-pH).

Preparation of Standard solution: Accurately Weighed and transferred 50mg of Telmisartan into 50 ml clean dry volumetric flasks, add 25ml of diluent, sonicated for 10 minutes and make up to the final volume with diluents. (1000µg/ml Telmisartan). 5ml from the above stock solution was taken into a 50ml volumetric flask and made up to 50ml. (100µg/ml Of Telmisartan)

Preparation of Sample stock solution: Accurately weighed equivalent weight of the powder(50mg) sample transfer into a 50ml volumetric flask, 50ml of diluents was added and sonicated for 25 min, further the volume was made up with diluent and filtered by 0.45µ milli-Q filters (1000µg/ml Telmisartan), 5ml of filtered sample stock solution was transferred to 50ml volumetric flask and made up with diluent. (100µg/ml of Telmisartan)

Method Validation

The validation of HPLC method was carried out for the simultaneous estimation of Telmisartan drug substance as per the ICH guidelines to demonstrate that the method is proposed for the routine analysis.

System suitability: The system suitability was performed for every validation parameter by injecting of system suitability solution containing Telmisartan 100µg/ml. System suitability chromatogram was shown in figure 2 and values are mentioned in the table 1.

Table 1: system Suitability Parameter

S no	Telmisartan		
Inj	RT(min)	USP Plate Count	Tailing
1	5.156	4654	0.8
2	5.150	4647	0.8
3	5.145	4637	0.9
4	5.146	4637	0.8
5	5.149	4647	0.8
6	2.557	4648	0.8

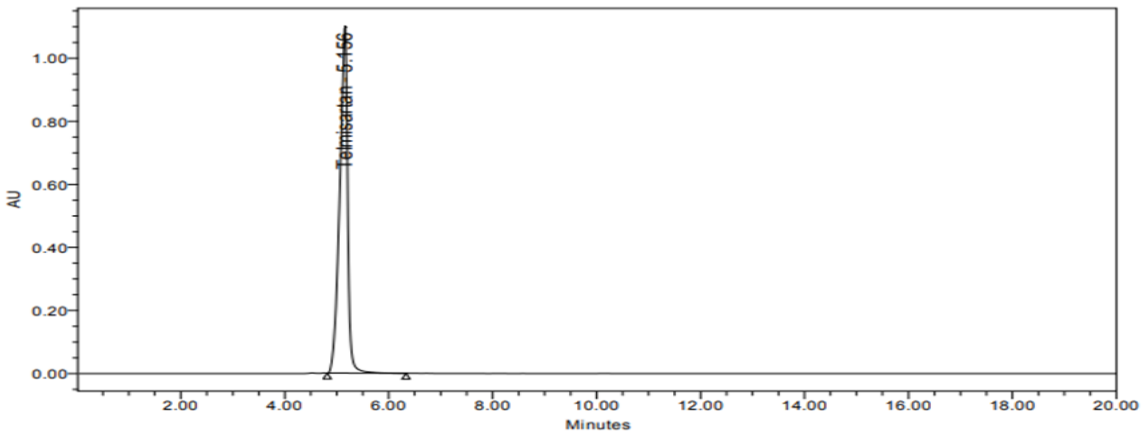

Figure 2: System suitability Chromatogram of Telmisartan

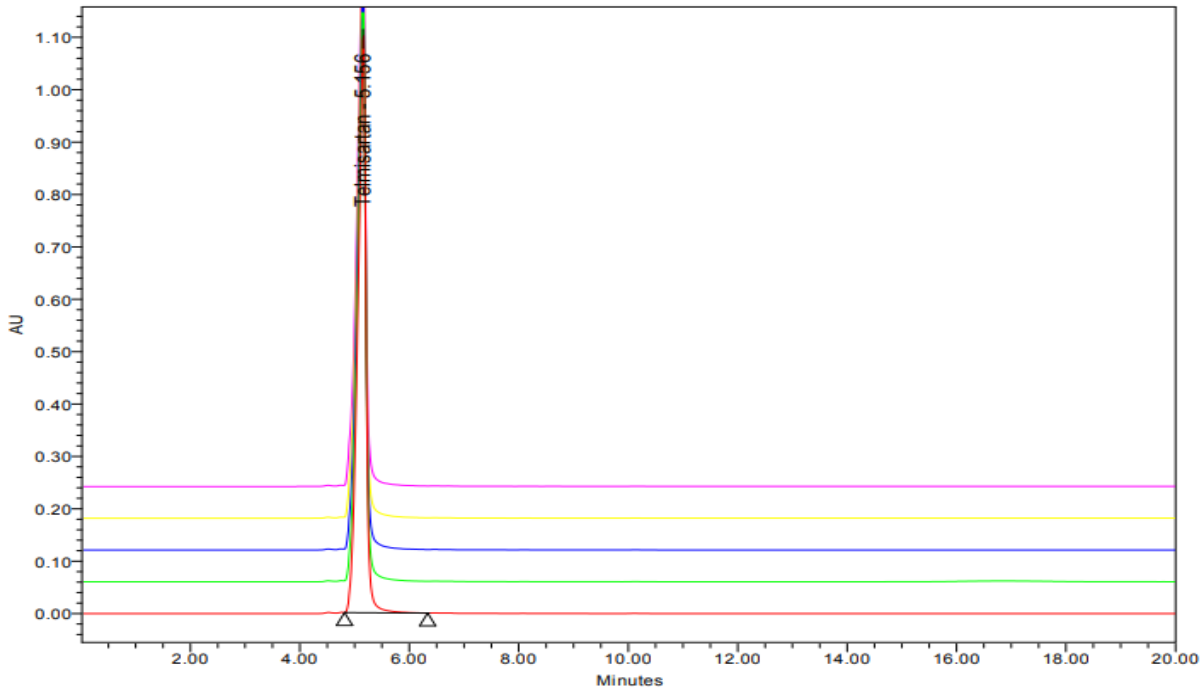

Figure 3: Overlay of System suitability

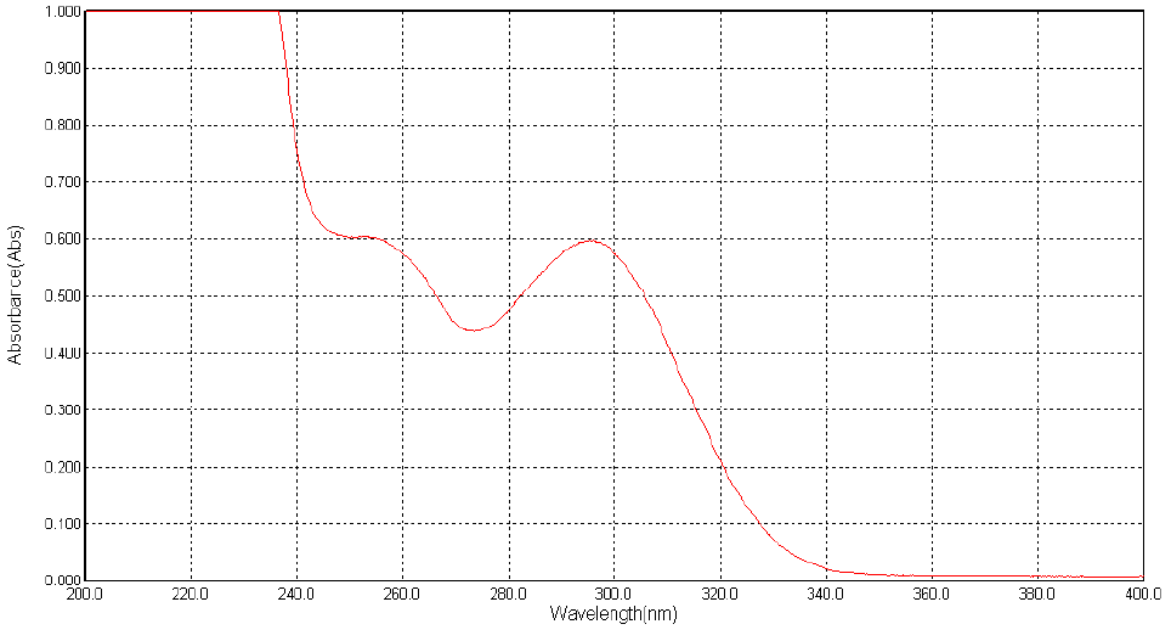

Figure 4: Uv spectrum of Telmisartan by UV

Specificity (Selectivity): Checking of the interference in the optimized method. We should not found interfering peaks in blank and placebo at retention times of these drugs in this method. So, this method was said to be specific.

Representative chromatogram is shown in Figure 3 and experimental data is given in Table 2

Table 2: Specificity data

Sample name	Retention time(mins)
Telmisartan	5.100

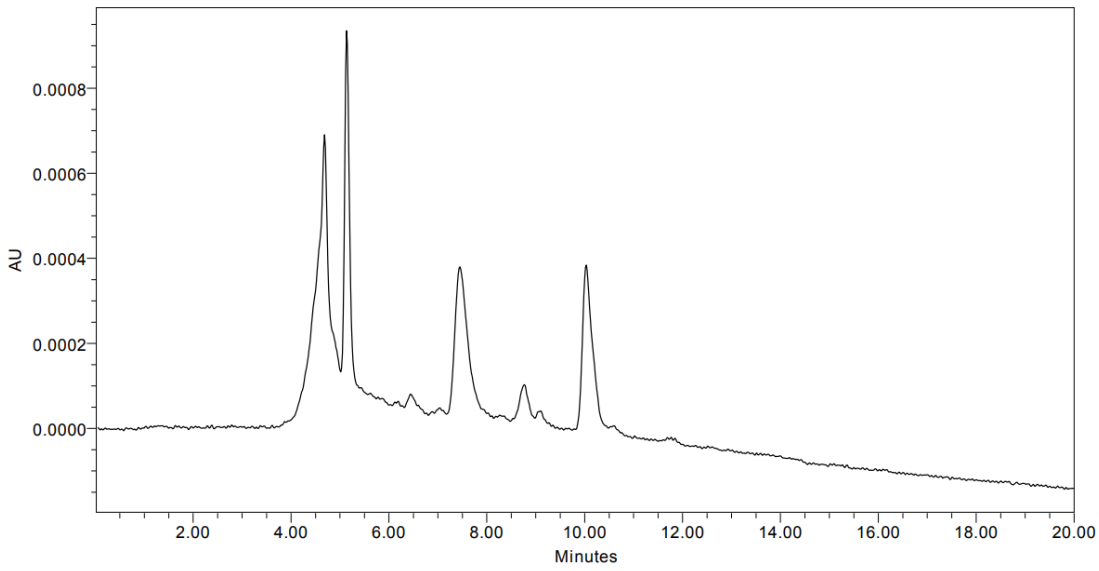

Figure 5: Typical representation of HPLC Chromatogram of Telmisartan

Linearity: The method's linearity was demonstrated for Telmisartan by analyzing solutions ranging from 80% to 100% of the specification limit (Table 3). Telmisartan had a correlation coefficient of 0.999. This demonstrates good linearity (Figures 6)

Table 3: Linearity data

PPM	Areas
50.4	5781657
75.6	9599632
100.8	11625060
126	14764001
151.2	17295772
Correlation coefficient	1.00

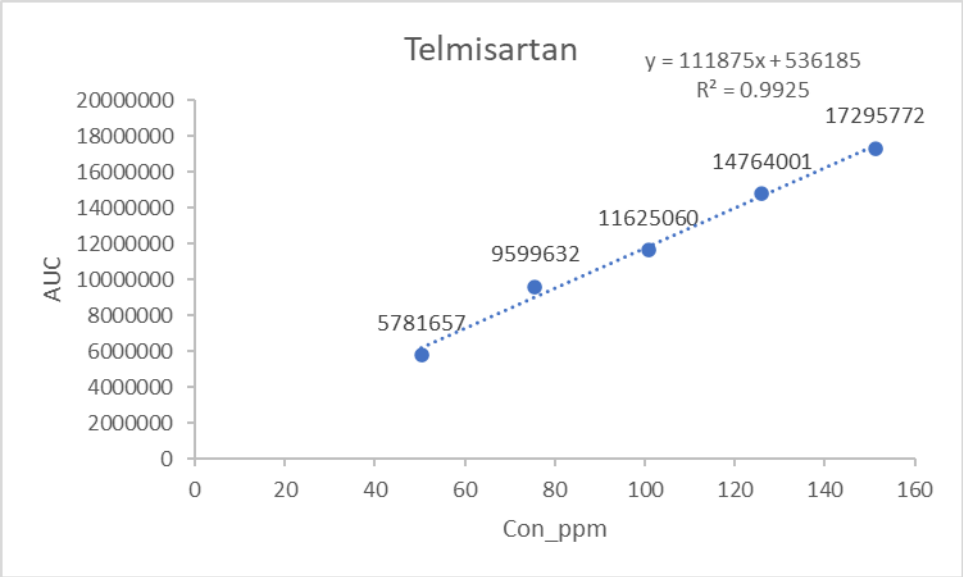

Fig 6: Linearity plot

Accuracy: The accuracy of the method was determined by using solutions containing spiked samples of Telmisartan at 50%, 100% and 150% of the working strength. All the solutions were prepared in triplicate and analyzed. The percentage recovery results obtained for each impurity was listed in Table 4.

Table 4: %Recovery data

%Level	%Recovery
	Telmisartan
50% Level	99.95
	99.24
	99.29
100%Level	100.57
	100.09
	101.04
150%Level	99.53
	98.31
	98.08
Mean%	**99.56**

Method Precision: The precision of the method was determined by analyzing a sample of Telmisartan. (Six individual sample preparations). Data obtained is summarized in Table 5

Table 5: precision data

Injection	Telmisartan
1	11680760
2	11781442
3	11565426
4	11689575
5	11664390
6	11784668
Avg	**11694377**
Std dev	**81815.45**
%RSD	**0.7**

The % RSD for the peak areas of Telmisartan obtained from six replicate injections of standard solution was within the limit.

ASSAY OF MARKETED FORMULATION

Standard solution a

nd sample solution were injected separately into the system and chromatograms were recorded and drug present in sample was calculated using before mentioned formula. Data obtained is summarized in Table 6 and Chromotogram fig in 6

Fig.6 Telmisartan tablets IP

Table 6: Assay data

Sample No	%Assay
1	99.06
2	99.20
AVG	**99.13**
STDEV	**0.10**
%RSD	**0.1**

		AT	WS	1	50	10	p	AvWt		
	% Assay = --------X--------X-------X------- X -------X --------X ----------X ----------X100									
		AS	50	10	1	5	100	L.C		
AT		Average Peak area of in test solution								
AS		Mean peak area of in standard solution								
WS		Weight of working standard taken in mg								
P		Potency of working standard in % on dried basis								
L.C		Label Claim								

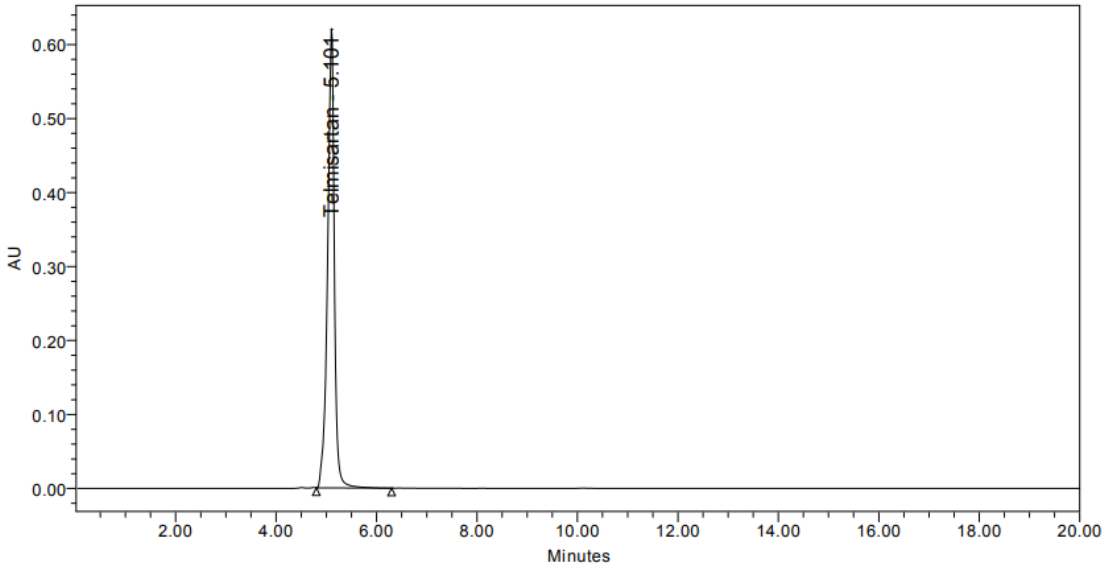

Fig 7: Chromotogram of Assay sample

CONCLUSION

According to the results of the preceding tests, the newly proposed technique for simultaneous estimation of Telmisartan was discovered to be simple, precise, and accurate, with high resolution, a shorter retention period, and separated degradants. The proposed method is inexpensive and could be used for routine evaluations in the pharmaceutical industry.

ACKNOWLEDGMENTS:

The authors are thankful to the Department of Pharmaceutical analysis, Srinivasarao college of Pharmacy, Affiliated to Andhra University, Mrs. P.R. Sudharani, Asst. Professor and Dr. K. Atchuta Kumar, Department of Pharmacognosy, Principal, Srinivasarao college of Pharmacy, Affiliated to Andhra University, Visakhapatnam, Andhra Pradesh, India and Spectrum Pharma Research Solutions, Hyderabad, Telangana, India.

REFERENCES

1. Luft FC Twins in Cardiovascular Genetic Research. Hypertension 37, 350–356 (2001).
2. Fagard R et al. Heritability of Conventional and Ambulatory Blood Pressures : A Study in Twins. Hypertension 26, 919–924 (1995).
3. Liu C et al. Meta-analysis identifies common and rare variants influencing blood pressure and overlapping with metabolic trait loci. Nat. Genet 48, 1162–1170 (2016).
4. Maass PG et al. PDE3A mutations cause autosomal dominant hypertension with brachydactyly. Nat. Genet 47, 647–653 (2015).
5. Blood Pressure Lowering Treatment Trialists' Collaboration. Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data. Lancet 384, 591–598 (2014).
6. Rose G & Day S The population mean predicts the number of deviant individuals. BMJ 301, 1031–4 (1990).
7. Rapsomaniki E et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. Lancet 383, 1899–1911 (2014).
8. Hall ME & Hall JE Pathogenesis of Hypertension. Hypertension: A Companion to Braunwald's Heart Disease 33–51 (2018). doi: 10.1016/b978-0-323-42973-3.00005-6
9. V, Berkowitz DE & Nyhan D Vascular stiffness and increased pulse pressure in the aging cardiovascular system. Cardiol. Res. Pract 2011, 263585 (2011).

10. Ehret GB et al. The genetics of blood pressure regulation and its target organs from association studies in 342,415 individuals. Nat. Genet 48, 1171–1184 (2016).
11. H. Takagi et al. Blood pressure-independent effects of telmisartan on regression of left ventricular mass: a meta-analysis and meta-regression of randomized controlled trials, Int J Cardiol(2013).
12. Galzerano D, Capogrosso C, Di Michele S, Galzerano A, Paparello P, Lama D, Gaudio C: New standards in hypertension and cardiovascular risk management: focus on telmisartan. Vasc Health Risk Manag. 2010 Mar 24;6:113-33.
13. FDA Approved Drug Products: MICARDIS (telmisartan) tablets for oral use.
14. Smith DH: Treatment of hypertension with an angiotensin II-receptor antagonist compared with an angiotensin-converting enzyme inhibitor: a review of clinical studies of telmisartan and enalapril. Clin Ther. 2002 Oct;24(10):1484-501.
15. Sharpe M, Jarvis B, Goa KL: Telmisartan: a review of its use in hypertension. Drugs. 2001;61(10):1501-29.
16. Deepti Jain et all.., ICH guideline practice: application of validated RP-HPLC-DAD method for determination of tapentadol hydrochloride in dosage form, Journal of Analytical Science and Technology, Published: 18 July 2013.
17. Ashok P, Narenderan ST, Meyyanathan SN, Babu B, Vadivelan R. DEVELOPMENT AND VALIDATION OF A RP-HPLC METHOD FOR ESTIMATION OF TELMISARTAN IN HUMAN PLASMA. Int J App Pharm [Internet]. 2019 Jan. 7 [cited 2024 Jul. 9];11(1):237-40. Available from: https://journals.innovareacademics.in/index.php/ijap/article/view/30513
18. Raju VB, Gandhi BM, Sumanth KS, Srinivas K, Neeraja TN. RP-HPLC method development and validation for simultaneous estimation of telmisartan and ramipril in pure and pharmaceutical dosage forms. Asian Journal of Research in Chemistry. 2017;10(2):179-85.
19. Vanaja N, Preethi C, Manjunath SY, Pal K. 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):171-7.
20. Upendra B, Hemant D, Kumar DA. RP-HPLC Method development and validation for estimation of telmisartan in bulk and tablet dosage form. International Journal of Drug Regulatory Affairs. 2013 Aug 1;1(2):61-4.
21. Kumar SA, Venkateshwar R, Jupally T, Kumar M. Development and Validation of a Stability Indicating RP-HPLC method for simultaneous determination of Telmisartan and Amlodipine in combined dosage form. Asian J Pharm Clin Res. 2014 Jan 1;7(1):32-5.