WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 9, 1149-1155. Research Article ISSN 2277– 7105

RP HPLC METHOD DEVELOPMENT AND ITS VALIDATION FOR SIMULTANEOUS DETERMINATION OF TELMISARTAN AND FINOFIBRATE

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Article Received on
06 June 2019,

Revised on 26 June 2019,
Accepted on 16 July 2019,

DOI: 10.20959/wjpr20199-15498

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ABSTRACT

A reversed phase liquid chromatographic method with UV detection 290 nm for Telmisartan and Finofibrate assay in human plasma was developed and validated. chromatographic separations was achieved on Phenomenex(c-18 250 mm x 4.60 mm) column kept at 4-35tem with mobile phase (methenoal:water) at a flow rate of 1ml /mint the method was validated for its specificity, linearity, accuracy, LOD, LOQ and robustness based on ICH guidelines. The validation studies revealed satisfactory reasarch proposed method has been applied for the quantification of telmisartan and Finofibratein commercial samples.

KEYWORDS: RP-HPLC, Telmisartan and Finofibrate, retention time, validations-linearity, accuracy, precision.

1. INTRODUCTION

Telmisartan, chemically [(1,4 dimethyl-2- propyl[2,6-bi 1h benzimidazol]-1-yl) methyl]-]1'-biphenyl-2 carboxylic acid is a vasoconstrictor and aldosterone which is used for the treatment of antihypertension.[5]

Finofibrate, chemically 2-[4-(4-chloro-benzoyl)phenoxy]-2-methyl-propanoic acid,1-methyl ethyl ester, is a lipid lowering agent and active metabolites of fenofibrate. which is used for the treatment of antihyperlipidemic.[6]

A number of analytical method have been report in the literature for the assay Telmisartan and Finofibrate.[1-3] These methods include reversed phase high-performance liquid chromatography(RP-HPLC).[7-10] The present study is aimed at developing and validating a

fast, sensitive, and cost-effective method for the quantification of Telmisartan and Finofibrate.[4,11,12]

2. EXPERIMENTAL STUDY

2.1. Reagent and samples- Analytical grade, phosphoric acid, acetonitrile, and water were purchased from(Mumbai, India). Pure Telmisartan and finofibrate active substance obtained from cipla pharmaceutical company, India.

2.2. Instrumentation- chromatographic System consiste of HPLC analyses carried out on an apparatus Shimadzu-lc-10A TVS, Phenomenex(c-18 250 mm x 4.60 mm) column, injector (with 20 ml loop size).[15] Spinchrom software was used for processing and acquisition. The mobile phase consisted of methanol:water (90:10). It was filtered through a 0.22 um filter and then pumped at of flow rate 1ml /mint. the injection volume 20ml and the uv detection was performed at 290 mm.

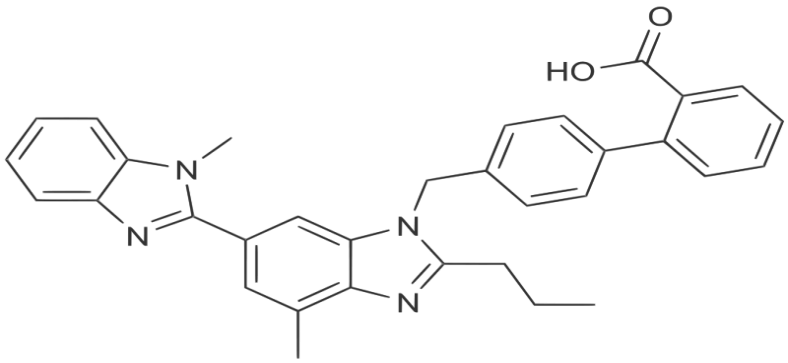


Figure 1: Chemical Structure of Telmisartan.

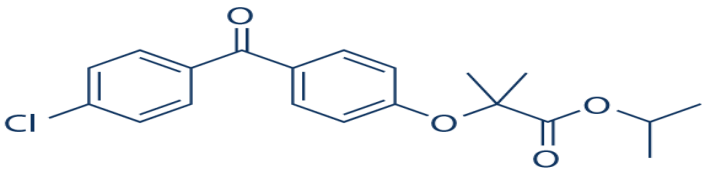


Figure 2: Chemical structure of Finofibrate.

2.3. Preparation of Reference Solution-A Stock standard Solution of Telmisartan and Finofibrate was Prepared by dissolving 100mg of pure drug in a 100ml volumetric flask using HPLC grade water. The drug was dissolved 70ml water and diluted up to the mark with the same solvent to get the solution containing.

2.4. Sample preparation- From a drug, 1ml of the test sample was transferred into a 100ml volumentric flask, sonicated with mobile phase for 10minutes, and made up to the volume with the same solvent mixture. This solution was diluted to 10 ug/ml to get 50ug/ml with the solvent mobile phase. A 20ul aliquot was injected into the chromatographic system for analysis.

2.5. Method development- The developed method was valted according to the ICH guidelines for its specificity, accuracy, precision, limit of detection(LOD), limit of quantification(LOQ), and robustness.[13,14]

3. RESULTS AND DISCUSSION

The objective of present work is to develop RP-HPLC method for simultaneous determination of Telmisartan and Fenofibrate and its validation.

For determination of Telmisartan and Fenofibrate series of mixed standards were prepared in the concentration range of linearity. The calibration curve was plotted between concentration and AUC observed at the selected wavelength.

RESULTS OF VALIDATION PARAMETERS

The developed method was validated and results respect to the various validation parameters are given below:

3.1. Linearity

The results of linearity analysis indicates that the drug components are linear with respect to the concentration range applied in the method.

Table No 3.1: Comparison of Statistical Data for Linearity.

Data for Linearity	TELMISARTAN	FENOFIBRATE
Correlation Coefficient (r^2)	0.9994	0.9993
Slope (m)	63672.3	71107.9
Y-Intercept	19146.7	38463.1
Linearity rang (µg/ml)	5-25	10-50

3.2. Accuracy

Accuracy for the developed method was studied and results show that the percent recovery was found within the limit and RSD was found to be < 2.

Table No 3.2: Statistical Data for Accuracy.

Statistical data	TELMISARTAN	FENOFIBRATE
% Mean	100.25	100.2
SD	0.232	0.123
%R.S.D.	0.002	0.001

3.3. Precision

Similar to accuracy, precision was also determined to assure the repeatability of the method. The R.S.D. was found < 2.0, which lie within the limit (table 6.3.).

Table No 3.3: Statistical Data for Precision.

Statistical parameter	TELMISARTAN		FENOFIBRATE	
	S.D.	%R.S.D	S.D.	%R.S.D
Repeatability	0.31	0.003	0.17	0.001
Intermediate Precision				
(a) Day to Day	1.79	0.17	0.05	0.013
(b) Analyst to Analyst	0.17	0. 001	0.37	0. 003

3.4. Robustness

To assess the acceptability of the method under the slight variation in the conditions, analysis was carried out. The analysis is carried out in slightly changed mobile phase. In place of methanol: water 90:10, the methanol: water is taken in the ratio of 90:10 and method is found robust as RSD is again found < 2.0.

Table No 3.4: Statistical Data for Robustness.

Parameters	TELMISARTAN		FENOFIBRATE	
	85:15	95:5	85:15	95:5
S.D.	0.314	0.284	0.291	0.44
% R.S.D.	0.002	0.002	0.002	0.004

DISCUSSION

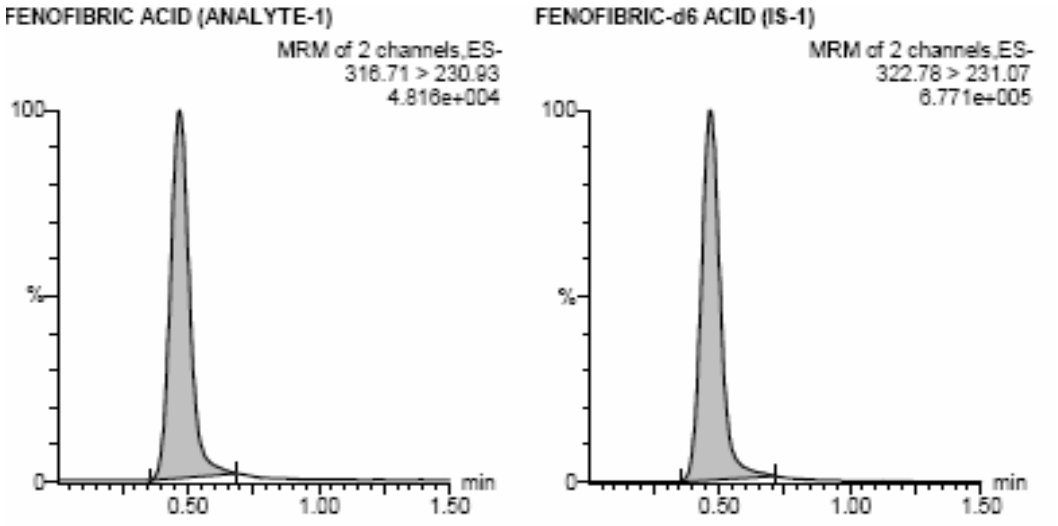
An analytical method for simultaneously measuring concentration of TLS and FNF is very useful for quality control of formulation containing these two drugs.

The developed method has the advantage of determining both the drugs over the reported methods, which are for their individual measurement. The assay is entirely isocratic involving only two stable solvent components with low volatility. A pH adjusted water and methanol, the use of pH adjusted aqueous mobile phase, while no buffering at pH 3, works well in the assay, which added, further in the simplicity of the method.

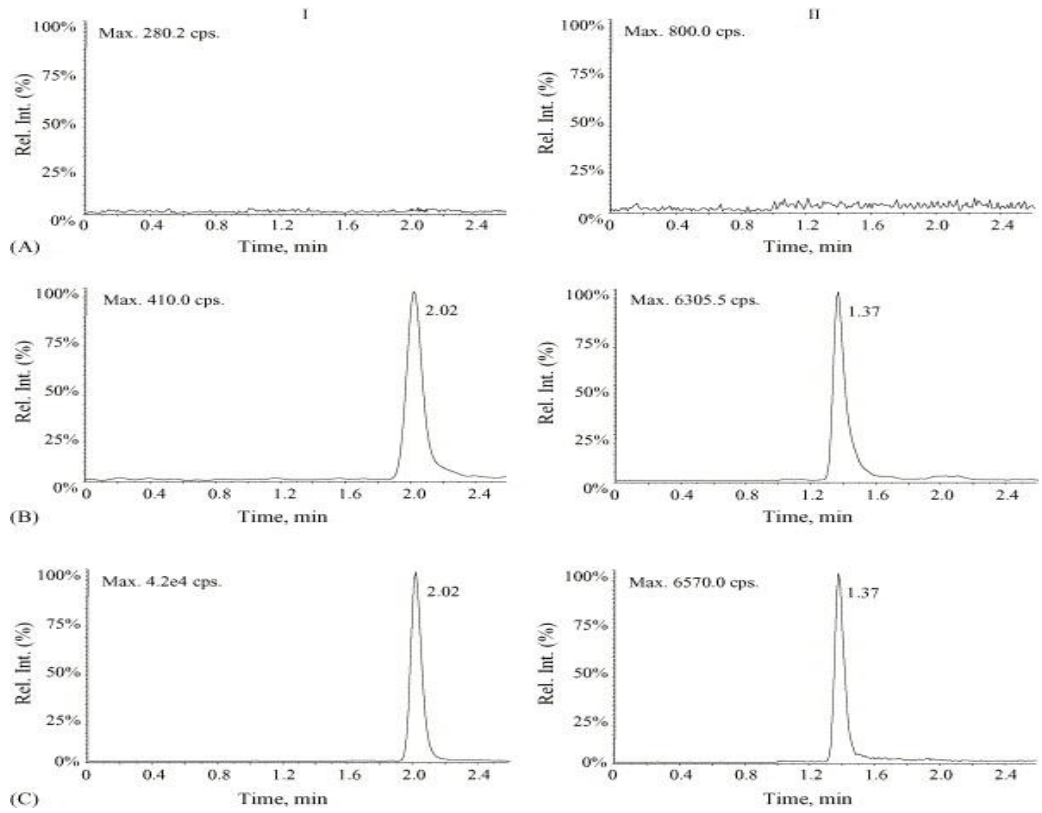
The background blank baseline is clean with little interference from mobile phase peaks. Also, equilibrium is rapid, absorbance at 290nm is transparent and runtime is less than 7 min.

VALIDATION

The developed method was fully validated according to ICH guidelines in respect of linearity, accuracy and precision and robustness. It was found robust for organic content of 80 to 95%.



(A) Determination offinofibric acid in human plasma.



(B) Determination of telmisartan in human Plasma.

4. CONCLUSION

In present research work a successful attempt was made for estimation of telmisartan and Fenofibrate by High Performance Liquid Chromatography (HPLC). The method was developed by experimentation based on through literature survey and ascertained by statistical parameter of sampling. The simplicity, rapidity reproducibility and economy of the proposed method completely fulfill the objective of the research work.

Retention time **Telmisartan** **Fenofibrate**	- 3.819 -6.565

Under optimized conditions, Telmisartan and Fenofibrate showed good selectivity and resolution, which can be well understood, looking at the validation data for the developed method are given as follows -

VALIDATION PARAMETERS	TELMISARTAN	FENOFIBRATE
Linearity(r2)	0.9994	0.9993
Precision (%RSD)		
Repeatability	0.003	0.001
Analyst variation	0.001	0.003
Inter day Variation	0.003	0.0005
Accuracy by recovery study (%found)	100.25	100.26
Robustness (%RSD)	0.004	0.008

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