Research Article
ISSN: 0974-6943

Rupali Hirave et al. / Journal of Pharmacy Research 2010, 3(10),2400-2401

Available online through
www.jpronline.info

RP-HPLC method for simultaneous estimation of Atorvastatin Calcium and Fenofibrate in tablet dosage forms.

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Received on: 08-06-2010; Revised on: 22-07-2010; Accepted on:12-09-2010

ABSTRACT

A reverse phase high performance liquid chromatographic method was developed for simultaneous estimation of atorvastatin calcium and fenofibarte in tablet formulation. The separation was achieved by HiQ sil C-8 (4.6×250mm) column with a mobile phase consisting of methanol: water pH 3.2 (90:10v/v), at a flow rate of 1ml/min. Detection was carried out at 260 nm. Retention time of atorvastatin calcium and fenofibrate was found to be 3.32 and 4.51 min, respectively. The method has been validated for linearity, accuracy and precision. Developed method was found to be accurate, precise, selective and rapid for simultaneous estimation of atorvastatin calcium and fenofibrate in tablets.

Key words: RP-HPLC, simultaneous determination, atorvastatin calcium, fenofibrate, development and validation.

INTRODUCTION

Atorvastatin calcium (ß R, d R)-2-(4-fluorophenyl)-ß,d-dihydroxy-5-(1-methylethyl)-3-phenyl-4-(phenyl amino) carbonyl)-1 H-pyrrole-1-hepatonic acid as the calcium salt belongs to the group of statins.[1] All the statins, including atorvastatin reduce the production of cholesterol in the liver by the competitive inhibition of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase the rate limiting enzyme in the biosynthesis of cholesterol.[3] Fenofibrate is 2-[4-(4-chlorobenzoyl) phenoxy]-2-methyl-propanoic acid, 1-methylethyl ester.[2] It is indicated for the treatment of hypercholesterolemia and mixed dyslipidemia.[3] Tablet formulation containing 10 mg of atorvastatin calcium 160 mg of fenofibrate is available. (Atorlip-F) The literature survey revealed some HPLC methods[5-13] & Spectrophotometric[14-16] methods for determination of atorvastatin calcium and Fenofibrate individually and in combination with other drugs. The present work describes the development of simple, precise, and accurate isocratic reverse phase HPLC method for simultaneous estimation of atorvastatin calcium and fenofibrate in tables.

Experimental

Chemicals: The drug sample, atorvastatin calcium and fenofibrate were obtained as gift samples from the Emcure Pharmaceuticals Ltd, Pune. Acetonitrile and Methanol (HPLC Grade) were purchased from Merk Chemical division Ltd. Mumbai. Triple distilled water was used for analysis.

Equipments: A gradient HPLC (JASCO PU-2080) was used equipped with Intelligent HPLC pumps UV-2075, and Intelligent UV / VIS Detector.

Chromatographic conditions: Chromatographic conditions were obtained by using a stainless steel column HiQ Sil C-8 (4.6 × 250 mm). A mixture of methanol and water in the ratio of (90: 10% v/v) was used as a mobile phase and the pH was adjusted to 3.2 with o-phosphoric acid. It was filtered through 0.45µ membrane filter and degassed. The flow rate of mobile phase was maintained at 1 ml/min. Detection was carried out at 260 nm at 25^0.

Preparation of standard stock solutions: The standard stock solution was prepared to contain 100 µg/ml of atorvastatin calcium and fenofibrate in a mixture of methanol and water (90:10v/v) as diluents. From the standard stock solution, a mixed standard solution was prepared using mobile phase to get the final concentration of 4 µg/ml atorvastatin calcium and 64 µg/ml fenofibrate and chromatograph was recorded and results are shown in **Fig no.1.**

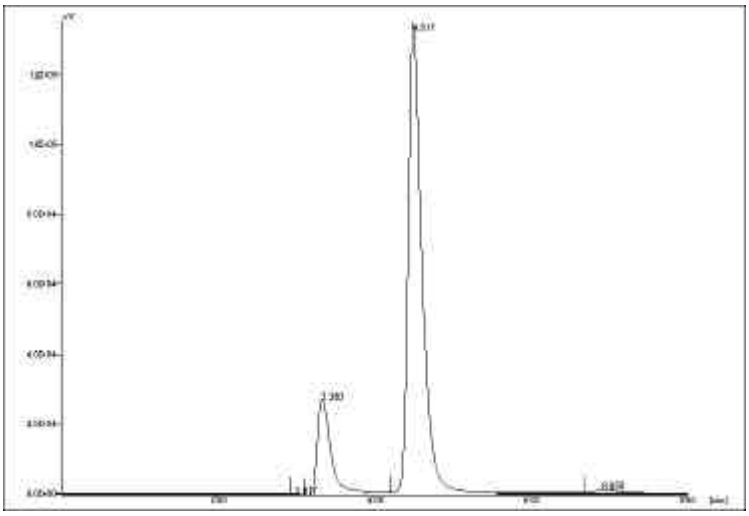

Fig no.1. *Chromatogram of standard solution.*

Analysis of formulation: Twenty tablets of Atorlip-F each tablet containing 10 mg of atorvastatin calcium and 160 mg of fenofibrate were weighed and finely powdered. Powder equivalent to 10 mg of atorvastatin calcium and 160 mg of fenofibrate were weighed and transferred to a 100 ml dried volumetric flask. Sufficient amount of mobile phase was added to dissolve the content and shaked for 20 min. The volume was made up to 100 ml with mobile phase, filtered & degassed through membrane filter. From these solution appropriate dilutions of atorovastatin calcium and fenofibrate were made to get the final concentrations of 4 µg/ml atorvastatin calcium and 64 µg/ml fenofibrate. Results are shown in **table no.1** the chromatogram recorded is shown in **fig.2**.

Table no.1 Analysis of test formulation

Sr. no.	Amount present in(mg)		Amount found in(mg)		% Label claim	
	Atorovastatin calcium	Fenofibrate	Atorovastatin calcium	Fenofibrate	Atorovastatin calcium	Fenofibrate
1	10	160	10.07	160.6	100.74	100.40
2	10	160	9.92	159.2	99.26	99.65
3	10	160	9.93	159.16	99.34	99.48
4	10	160	9.96	160.8	99.62	100.55
5	10	160	9.95	160.9	99.56	100.61

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Table No.2 Recovery study

Drug	Amount Added [%]	Amount Added [µg/ml]	Amount Recovery ± S.D. [µg/ml, n=3]	Amount Recovery [%]	% R.S.D.
Atovastatin calcium	80	3.2	7.12 ± 0.34	99.12	0.35
	100	4	7.88 ± 0.31	98.91	0.31
	120	4. 8	8.83 ± 0.18	100.81	0.18
Fenofibrate	80	51.2	114.29 ± 0.21	99.23	0.21
	100	64	127.14 ± 0.21	99.14	0.21
	120	76.8	139.46 ± 0.40	99.05	0.13

Table 3: System suitability Parameters

Name	RT (min)	Area (µV.sec)	Plates	Resolution	Asymmetry	% RSD
Atorovastatin calcium	3.35	216988.54	2872	1.676	1.261	0.012680
Fenofibrate	4.51	3226540.11	4092	4.546	1.621	0.073019

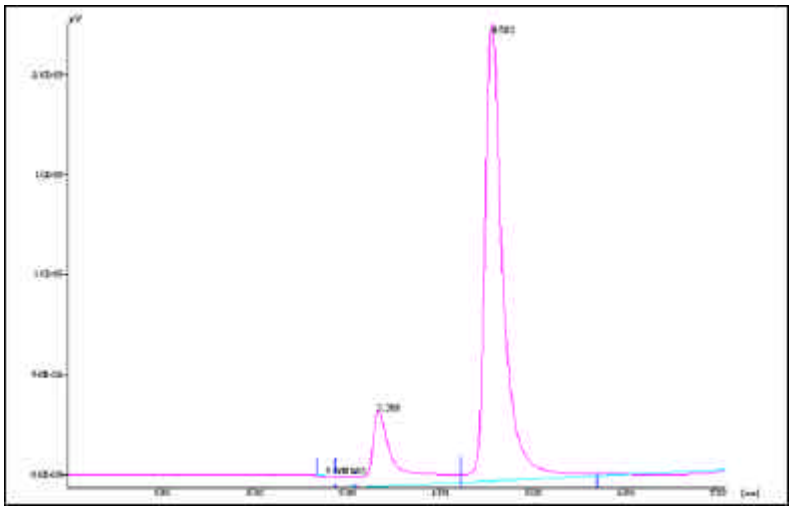

Fig no.2. Chromatogram of sample solution.

RESULT & DISCUSSION:

The retention time of atorvastatin calcium and fenofibrate was found to be 3.32 and 4.51 min respectively. The proposed method was validated as per ICH guideline. Each of the sample was injected 5 times and the same retention time was observed in all the cases. Linearity: Linearity of atorvastatin calcium and fenofibrate was determined by plotting peak area versus concentration. The response was found to be linear in the range of 10-50 µg/ml for atorvastatin calcium and 16-80 µg/ml for fenofibrate. Correlation coefficient ' r ' values (n=5) for both atorvastatin calcium and fenofibrate were 0.999. Accuracy of the method was calculated by recovery studies (n=3) at three levels. Standard drug solutions containing drugs in the range of 1-5 µg/ml for atorvastatin calcium and 16-80 µg/ml for fenofibrate were added to previous analysed test solution. Amount of drug recovered at each level (n=3) was determined. Percent recovery at each level were found to be 99.61 % & 99.14 % for atorvastatin calcium & fenofibrate respectively Results are shown in **table no.2.** High percentage recovery showed that the method is free from interference of excipients used in formulations. The method is simple with short runtime of 8 min.

CONCLUSION:

The results of the study indicate that the proposed HPLC method was simple, precise, highly accurate, specific and less time consuming.

ACKNOWLGEMENT

The authors are thankful to Emcure Pharmaceuticals Ltd, Pune. For providing gift samples and Principal, Appasaheb Birnale College of Pharmacy Sangli for providing facilities to perform the research work.

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Source of support: Nil, Conflict of interest: None Declared