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Research Article

Development and Validation of Fenofibrate in Bulk and Tablets using UV-Spectroscopy: An Anti-Hypercholesterolemic Agent

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A B S T R A C T

The spectrophotometry provides versatile techniques for analyse drug in multi component pharmaceutical formulation in presence of various interferences. Simple, accurate, sensitive, precise and rapid UV-Spectrophotometric methods have been developed for the estimation of fenofibrate in bulk and tablet dosage form formulation. To determine the absorption maximum, the drug fenofibrate were scanned in wavelength range of 200-400nm in spectra measurement mode using the double beam UV-Spectrophotometer, 290 nm was selected as a sampling wavelength in DMF as solvent. Beer's limit was obeyed in the range of 2-10 µg/ml for fenofibrate. The correlation coefficient found to be satisfactory. Validation parameters such as its accuracy, linearity, precision, limit of detection (LOD), and limit of quantitation (LOQ) was studied for proposed method according to the ICH guidelines. Results of all parameters were found to be satisfactory. The proposed method can be used effectively for routine analysis and estimation of fenofibrate in bulk and dosage form. The result demonstrated that the proposed method is accurate, precise and reproducible.

Key words: Fenofibrate, lipid regulating agent, hypercholesterolemia, UV-Spectroscopy.

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INTRODUCTION

Fenofibrate is official drug Indian Pharmacopoeia. It is a member of fibrate/fibric acid class. Fenofibrate has IUPAC name as - propane-2-yl-2-{4-[4-chlorophenyl)-carbonyl] phenoxy}-2-methyl propanoate. The molecular formula is $C_{20}H_{21}ClO_4$ and molecular weight is 360.83 g/mol. It is used as a lipid regulating agent in the patients which a reat the risk of cardiovascular disorders. Fenofibrate act by increasing lipolysis and triglycerides rich particles are eliminated from plasma by activating lipoprotein lipase and by reducing a poprote in C-III production. Apoprotein C-III is an inhibitor of lipoprotein lipase activity. It causes reduction in in both LDL (low density lipoprotein) and VLDL (very low-density lipoprotein) levels. Fenofibrate also increases the level of high-density lipoprotein (HDL). It is indicated for the treatment of hypercholesterolemia and mixed dyslipidemia[1,2].

Fenofibrate is a member of fibrate class with lipid-regulating action commonly referred to as fibric acid derivative. It is almost white crystalline powder, which is stable under ordinary conditions with melting point 79-82 ^{0}C.

It is virtually water insoluble (<0.3 µg/ml) but slightly soluble in alcohol and has relatively high octanol/water partition coefficient (log P 4.6). Fenofibrate is mainly used to reduce the amounts of low-density lipoprotein (LDL) cholesterol,total cholesterol, triglyceride and apolipoprotein-B, and increase the amounts of high-density lipoprotein (HDL) cholesterol in the blood. Fenofibrate is a prodrug which is converted rapidly after oral administration through the hydrolysis of the ester bond to fenofibric acid[3-5].

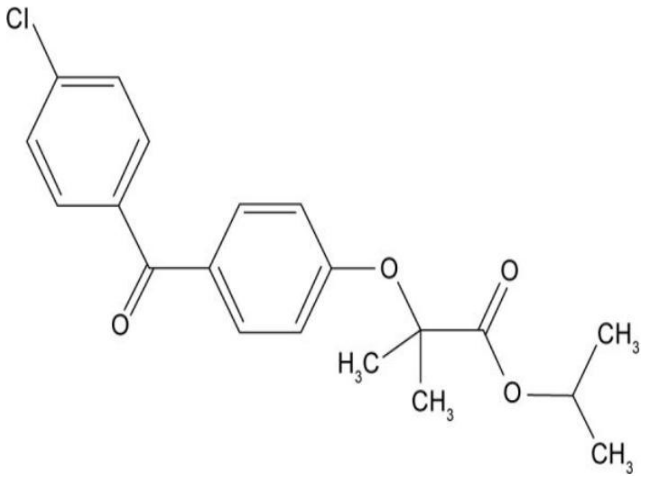

Figure 1: Molecular structure of fenofibrate

It is used alone or in combination with statins in the treatment of hypercholesterolemia and hypertriglyceridemia. A survey of literature showed few UV spectrophotometric, few HPLC, UPLC methods and few HPTLC methods are available for estimation of fenofibrate in pharmaceutical preparation and in biological fluids. The aim of the present research work is to develop a simple, accurate, sensitive, precise and rapid UV-Spectrophotometric method for the determination of fenofibrate in bulk and its tablets[5,6].

MATERIALS AND METHODS

Instrumentation

A SHIMADZU model PHARMASPEC-1800 UV-Vis spectrophotometer with 1.0 cm matched cells was used for the electronic spectral measurements.

Chemicals

Fenofibrate and all other chemicals used were analytical reagent grade (AR grade). DMF (Dimethyl formamide) is used as solvent in all experimental purpose.

Pharmaceutical formulation

Fenofibrate tablets Lipicard-160 (160 mg) was purchased from local market for analysis.

Determination of working wavelength (λ_{max})

The solutions of fenofibrate were scanned in UV range 400 to 200 nm in 10 mm quartz cell against blank solution separately. The overlain spectra show λ_{max} for fenofibrate at 290 nm.

Preparation of standard stock solution[7,8]

10 mg quantity of fenofibrate weighed accurately and transferred in100ml volumetric flask. Sufficient quantity of DMF is added to the flask to dissolve the drug and then diluted up to 100 ml with same solvent, so as to obtain concentration of 100µg/ml. These stock solutions are used for preparation of subsequent dilutions for calibration curve.

Construction of standard calibration curve

The drug, five working standard solutions are prepared by pipette out the aliquots from standard stock solutions of fenofibrate in 10ml volumetric flask and diluted up to10ml by solvent DMF get working solutions of concentration 2 to 10µg/ml. These series of different concentrations of fenofibrate were scanned at 290 nm and absorbance was recorded. The standard calibration curve was constructed by plotting concentrations versus absorbance over the range of 2 to10 µg/ml. The correlation coefficient was found to be as 0.999 for obtained calibration curve of fenofibrate.

Preparation of stock solution of marketed formulation

Twenty tablets of Lipicard-160 containing 160mg of fenofibrate were weighed and finely powdered. Average weight per tablet is calculated. A quantity of tablet powder equivalent to 10mg fenofibrate was weighed accurately and transferred to a 100 ml of volumetric flask. Powder is dissolved in DMF solvent, and this solution contain 10 mg fenofibrate. Then add 15mg of fenofibrate to the above solution and the final volume up to 100 ml mark was made with same solvent. Now, this stock solution contains10mg of fenofibrate. The prepared test stock solution was filtered through the Whatman filter paper. From this stock solution further dilutions were made. The resulting solution was analyzed at λ_{max} of the drug against solvent blank.

Analytical method validation[9-11]

According to the ICH guidelines:

Linearity

Appropriate dilutions of prepared stock solutions of fenofibrate and atorvastatin were analyzed at the irrespective wavelength maxims. During the analysis, Beer's limit was obeyed by both fenofibrate and atorvastatin for simultaneous equation method and absorbance ratio method. The Beer-Lambert's concentration range is 0 to 30 ug/mL for both the drug.

Precision (Repeatability)

Inter-day precision and intra-day precision was evaluated by using marketed tablet powder equivalent to 100% of label claim amount of fenofibrate. It is expressed in terms of SD and % RSD. SD and % RSD was obtained by repeating assay off our replicates of single sample concentration three times on the same day and on different days.

Accuracy

Accuracy of the methods is determined by recovery studies. It is performed by standard addition method. Known amount of standard fenofibrate was added in the pre-analyzed tablet powder in 80%, 100% and 120% of label claim and concentration was determined.

Limit of detection (LOD) and limit of quantitation (LOQ)

LOD and LOQ for fenofibrate were calculated on the basis of standard deviation of slopeandy-intercept. Itis calculated as following equations:

$$\mathbf{LOD = 3.3 \times \sigma/S}$$

$$\mathbf{LOQ = 10 \times \sigma/S}$$

Where, σ = Standard deviation of the response, and

S = Slope of the calibration curve.

RESULTS AND DISCUSSION

The Beer-Lambert's concentration range is 2-10 µg/mL for fenofibrate at 290 nm. The coefficient of correlation for fenofibrate at 290 nm and is 0.999. Fenofibrate shows good regression value at their respective wavelength (λ_{max}). From recovery study it is revealed that any small change in the concentration of fenofibrate in the solution can be detected accurately by this method. Percentage estimation of fenofibrate in selected tablet dosage form was found to be 98.85% with standard deviation less than 2.

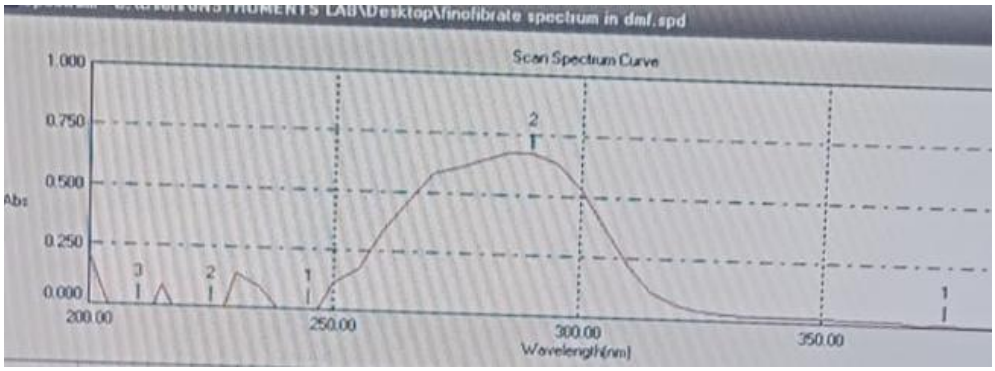

Figure 2: Maximum wavelength of fenofibrate

Table 1: Linearity of fenofibrate

Concentration (µg/ml)	Absorbance
2	0.186
4	0.376
6	0.559
8	0.731
10	0.928

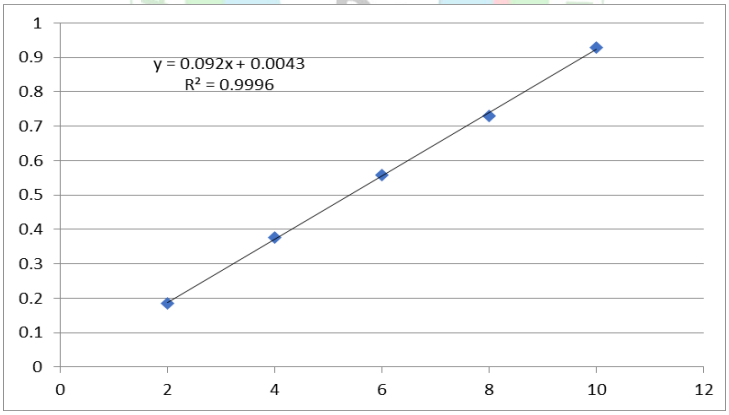

Figure 3: Linearity graph

Table 2: Precision

S. No.	Conc. (µg/ml)	Absorbance (intraday)	Absorbance (interday)
1	10	0.987	0.992
2	10	0.989	0.989
3	10	0.986	0.991
4	10	0.988	0.988
5	10	0.984	0.991
6	10	0.988	0.988
Mean		**0.987**	**0.99**
Std. dev.		**0.0007**	**0.00282**
% RSD		**0.07**	**0.284**

Table 3: Results for accuracy

S. No.	Level of adding	Amount added (µg/ml)	Amount recovered(µg/ml)	Percentage recovery
1	80	1.2	1.16	96.66
2	100	1.5	1.48	98.66
3	120	1.8	1.79	99.44

Table 4: Results for robustness

S. No.	Wavelength	Absorbance
1.	288	0.981
2.	290	0.997
3.	292	0.986

Table 5: Results for ruggedness study

S. No.	Analyst	%RSD
1	Analyst-1	0.944
2	Analyst-2	0.951

Table 6: Assay of tablets

Drug	Labelled amount	Mean	SD	% Assay	% RSD
Fenofibrate	160mg	98.97	0.070	98.92	0.070

Table 7: LOD and LOQ of fenofibrate

LOD	0.243 µg/ml
LOQ	0.738 µg/ml

The reliability and validity of the proposed method is assessed by recovery studies. Result of recovery study was found to be within the prescribed limit and results. No interference in result observed in the result due to tablet excipients. The limit of detection (LOD) and limit of quantitation (LOQ) values for fenofibrate are 0.243 µg/ml and 0.738 µg/ml respectively. Low value of LOD and LOQ indicate that the method has good sensitivity.

Precision of method was determined by repeatability and intermediate precision study by intra-day and inter-day precision. The % RSD was calculated for fenofibrate % RSD value not more than 2.0% indicate good repeatability and intermediate precision. An intermediate precision is a study of variation with in laboratory in different days.

CONCLUSION

The proposed UV spectrophotometric method is simple, useful, rapid, reliable and provide acceptable accuracy, linearity, precision and reproducibility. This method can be adopted for routine analysis of fenofibrate in pure form and pharmaceutical tablet dosage form. Validation parameters complies the applied spectrophotometric methods of analysis and were found to be simple, sensitive, accurate and satisfactory capable for determination of fenofibrate in tablet formulation with reproducible specific results. The linear concentration range of preordain elaborated method were observed wider. Thus, proposed UV-VIS spectrophotometric method is applicable for the quality control and routine analysis and may also proposed for determination from biological fluid other solid dosage form containing same drugs.

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Author contributions

All authors contributed to experimental work, data collection, drafting or revising the article, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Competing interest statement

All authors declare that there is no conflict of interests regarding publication of this paper.

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