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Validated UV-Visible Spectrophotometric Method for the Estimation of Fenofibrate in Pure and Pharmaceutical Formulation Using MBTH Reagent

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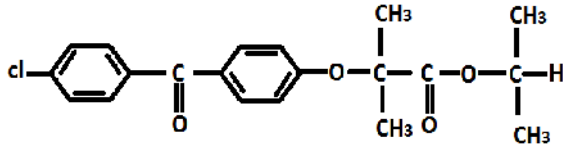
ABSTRACT

A simple, sensitive and reproducible UV visible spectrophotometric method has been developed for the quantitative determination of fenofibrate in bulk drug and pharmaceutical dosage forms using MBTH reagent. The method is based on the measurement of absorbance of fenofibrate in methanol (0.5% MBTH in 0.5% HCl and 1% $FeCl_3$ in 0.5% HCl) at 596 nm. Beer's law is obeyed over the linear range 2-5µg /ml of fenofibrate for the method with apparent molar absorptivity value of 1909.5905 L $mol^{-1}cm^{-1}$. The method was validated in accordance with the current ICH guidelines. The precision results, expressed by reproducibility (RSD ≤ 1.7%) and repeatability (RSD ≤ 1.5%), were satisfactory. The accuracy is also satisfactory (RSD ≤ 0.200532%). The result demonstrated that the proposed method is accurate, precise and reproducible.

Keywords: Fenofibrate, UV visible spectrophotometry, MBTH, molar absorptivity.

INTRODUCTION

Fenofibrate which is chemically propan-2-yl 2-{4-[(4-chlorophenyl) carbonyl] phenoxy}-methyl propanoate. [1] It is mainly used to reduce cholesterol levels in patients at risk of cardiovascular disease. Like other fibrates, it reduces both low-density lipoprotein (LDL) and very low density lipoprotein (VLDL) levels, as well as increasing high density lipoprotein (HDL) levels and reducing triglycerides levels. It also appears to have a beneficial effect on the insulin resistance featured by the metabolic syndrome. [2-4]



(Chemical structure of fenofibrate)

High performance liquid chromatography (HPLC) [5] and thin layer chromatography methods [6] were reported for the estimation of fenofibrate in biological fluid such as plasma, serum and urine but chromatographic techniques are time consuming, costly and time expensive. A survey of literature has not revealed any simple UV-Visible spectrophotometric method for the specific determination of fenofibrate in bulk drugs, formulation and dissolution media of oral formulations. The objective of the present study was to develop simple, precise and accurate analytical method with the better detection range for estimation of fenofibrate UV-Visible range by the addition of MBTH reagent in bulk, pharmaceutical formulation and in vitro studies of oral formulations. The developed method was validated as per ICH guidelines and USP requirement. [7-8]

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MATERIALS AND METHODS

A SHIMADZU model PHARMASPEC-1800 UV-Vis spectrophotometer with 1.0 cm matched cells was used for the electronic spectral measurements. Fenofibrate and all other chemicals used were analytical reagent grade (AR grade). Methanol is used as solvent in all experimental purpose. Fenofibrate pure drug (certified to be 99.76%) was kindly provided by Lupin pharmaceuticals ltd., India. as a gift sample. FINATE-160 (160 mg fenofibrate) were manufactured by FRANCO INDIAN Remedies Pvt. Ltd., India and purchased.

Solutions

An accurately weighed quantity of 10 mg Fenofibrate was transferred in to 100 ml volumetric flask with methanol and sonicated. The volume was made up to the mark with methanol. Aliquots of this standard stock solution (SSS) were transferred to 10 ml volumetric flask (in different concentrations) and to this 2.5ml of 0.5% MBTH and 2.5ml of 1% ferric chloride (both in 0.5% HCl) were added. Then

the solutions are made up to the mark with methanol and kept for 20 minutes to form a blue-green complex and scanned over visible range of 400-800 nm. An overlay spectrum of drug was drawn out and selected the wavelength 596 nm for the analysis at which drug showed maximum absorbance (Fig. 1).

Procedure

For calibration curve; (study of Beer's- Lambert's law)

From SSS 0.2 ml-0.5ml were pipetted out and transferred to 10 ml standard flask and then 2.5 ml of 0.5 % MBTH in 0.5% HCl, 2.5 ml 1% $FeCl_3$ in 0.5% HCl were added to each flask and then the volume is made up with methanol and kept as such for 20 minutes to form a blue-green complex and scanned at 596 nm (Fig. 2 and Table 1). Absorbance plotted against concentration and calibration graph were recorded.

For absorptivity study

From the SSS, a solution of 2µg/ml concentration was prepared. Absorbance of such five of fenofibrate standard solution measured and results of absorptivity study drawn out by A1% 1cm (Table 2).

Estimation of fenofibrate in tablet formulation sample

Ten tablets were weighed accurately and powdered. Powder equivalent to 10 mg (label claim -160 mg) was taken and transferred to 100 ml volumetric flask and dissolved in methanol, sonicated for 10 minutes, filtered and further diluted to get final concentration 100µg/ml of fenofibrate (label claim basis). From the above solution 0.2 ml-0.5ml were pipetted out and transferred to 10 ml standard flask and then 2.5 ml of 0.5 % MBTH in 0.5% HCl, 2.5 ml 1% $FeCl_3$ in 0.5% HCl were added to each flask and then the volume is made up with methanol and kept as such for 20 minutes to form a blue-green complex and scanned at 596 nm (Table 3).

Table 1: Caliberation Curve

S. No	Concentration (µg/ml)	Absorbance
1.	2	0.208
2.	3	0.310
3.	4	0.419
4.	5	0.502

Table 2: Absorptivity (1%, 1cm) values of Fenofibrate at 596 nm

S. No	Conc. (g/100ml)	Abs.	A(1%, 1cm)
1.	0.0002002	0.382	1908.0919
2.	0.0002005	0.386	1905.1870
3.	0.0002003	0.378	1906.1692
4.	0.0002009	0.389	1907.2867
5.	0.0002004	0.379	1909.2175
	Mean		1907.19046
	±SD		1.53876
	%RSD		0.080682

Table 3: Estimation of Fenofibrate in tablet formulation

S. No.	Wt. Of tablet powder taken mg(label claim 160mg)	Abs. at 596 nm	Amount of drug per tablet (mg)	% Purity
1.	0.045	0.382	0.1598	99.91
2.	0.0451	0.385	0.1607	100.47
3.	0.0442	0.380	0.1618	101.18
4.	0.0446	0.384	0.1621	101.33
5.	0.044	0.381	0.1630	101.91
	Mean			100.96
	± SD			0.7794
	% RSD			0.7719

RESULT AND DISCUSSION

The method was accurate, simple, rapid, reliable, sensitive and reproducible. The wavelength 596nm was selected which showed good linearity between the concentrations.

Validation of analytical data

The method was validated in accordance with the current ICH guidelines. The study of Beer's- Lambert's law was checked by preparing standard solution at four different concentration and the linearity of the calibration graphs and conformity of the UV-VIS measurement of the proposed methods to Beer's law were proven by the values of the correlation coefficient of the absorptivity study. The linear range of concentration for the analysis of fenofibrate was found to be 2-5µg/ml for UV-VIS spectrophotometric method.

The utility of this method was verified by analysis of recovery of the assay in the marketed tablet sample. The tablet sample (label claim- 160mg) fenofibrate was prepared and processed according to the proposed method.

Recoveries were determined by standard addition method (SAM). The mean % recoveries of fenofibrate by UV-VIS method were found to be 99.36% (Table 4). [9]

The reproducibility and repeatability of the developed method were established by study of precision for fenofibrate determined by 5 replicate analyses on the tablet formulation. [10] The % RSD was found to be 1.7% and 1.5% respectively for UV-VIS spectroscopic methods (Table 5, 6 & 7).

Correlation coefficient for UV -VIS Spectrophotometric

Table 4: Determination of accuracy by percentage recovery method

Drug	Level of addition	Amount of pure drug added (µg/ml)	Amount of pure drug recovered (mg)	% recovery
Fenofibrate	50%	0.005	0.01497	99.48
	75%	0.007	0.01743	99.13
	100%	0.010	0.01995	99.47
		Mean		99.36
		±SD		0.199249
		%RSD		0.200532

Table 5: Reproducibility

S. No	Conc. (µg/ml)	Abs. at 596 nm
1.	**2**	**0.211**
2.	**2**	**0.202**
3.	**2**	**0.204**
4.	**2**	**0.207**
5.	**2**	**0.203**
	Mean	**0.2054**
	±SD	**0.0036469**
	%RSD	**1.7**

Table 6: Repeatability

S. No	Conc.(µg/ml)	Abs. at 596 nm
1.	**2**	**0.203**
2.	**2**	**0.202**
3.	**2**	**0.201**
4.	**2**	**0.208**
5.	**2**	**0.200**
	Mean	**0.2028**
	±SD	**0.0031144**
	%RSD	**1.5**

Table 7: Validation Parameters

S. No	Parameter	Result
1.	Absorption maxima (nm)	596
2.	Linearity range (µg /ml)	2-5
3.	Slope	0.101
4.	Intercept	0.003
5.	Correlation coefficient (r2)	0.998
6.	Molar absorptivity	1907.19046
7.	Accuracy (% recovery)	99.36
8.	Precision	
	a)Reproducibility	%RSD 1.7
	b)Repeatability	%RSD 1.5

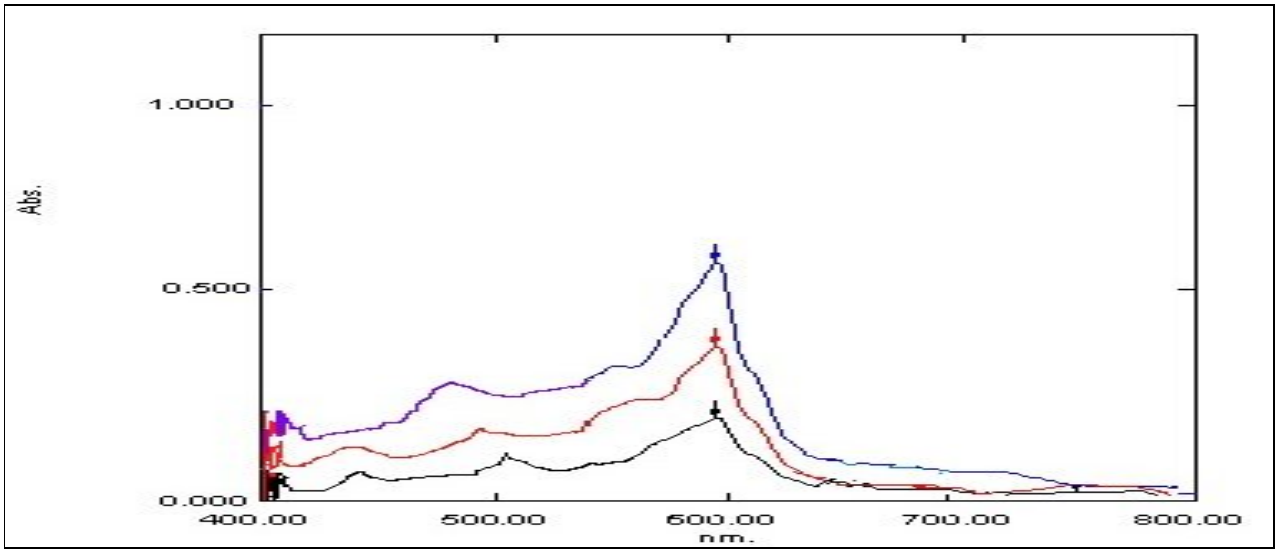

Fig. 1: Overlay spectra of Fenbofibrate

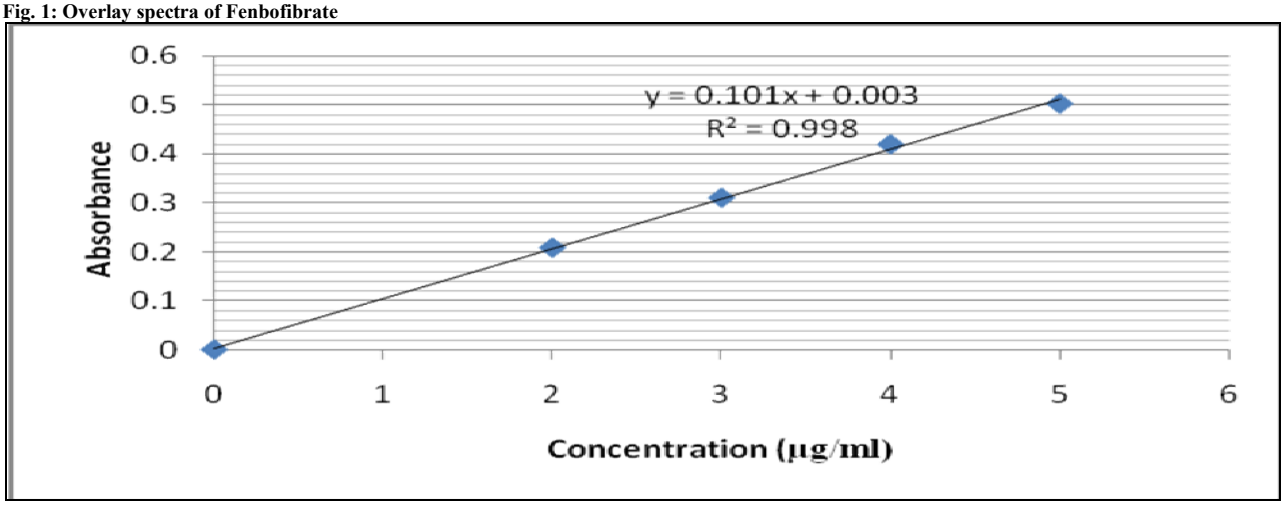

Fig. 2: Plot of Beer's Lambert's law for Fenofibrate at 596 nm

method was found to be 0.998 of fenofibrate was found to be linear.

Ruggedness of the proposed method was carried out for 3 different analysts. The result did not show any considerable statistical difference suggesting that the method developed was rugged.

The stability study was carried out and dug was found to be stable between 20 to 35 minutes.

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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