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RESEARCH ARTICLE

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF FENOFIBRATE BY UV SPECTROSCOPY

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ABSTRACT

Spectrophotometry offers flexible methods for analyzing drugs in multi-component pharmaceutical formulations when there are a variety of interferences present. For the purpose of estimating the formulation of Fenofibrate, UV-spectrophotometric methods that are simple, sensitive, precise, fast, and accurate have been developed. Using a double beam UV spectrophotometer, the Fenofibrate was scanned in the 200–400 nm wavelength range in spectra measurement mode to estimate the absorption maximum. A sample wavelength of 225 nm was used in a mixed solution containing 1M urea and 0.5M sodium citrate. For Fenofibrate, the range of 5-25 µg/ml was observed, adhering to Beer's limit. The correlation coefficient was determined to be adequate. In accordance with the ICH criteria, validation characteristics for the suggested method were examined, including its accuracy, linearity, precision, limit of detection (LOD), and limit of quantization (LOQ). All parameter's results were found satisfactory. For regular analysis and estimation of Fenofibrate in bulk and dosage form, the suggested approach works well. The outcome proved that the suggested method is exact, accurate, and repeatable.

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INTRODUCTION

Fenofibrate is official drug in Indian Pharmacopoeia. It belongs to the class of fibrates and fibric acids. Propanoate-2-yl-2-{4-[4-chlorophenyl)-carbonyl] phenoxy}-2-methyl propanoate is the IUPAC designation for Fenofibrate. The molecular weight is 360.83 g/mol and the formula is $C_{20}H_{21}ClO_4$. 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). It is administered to patients who pose a risk of cardiovascular problems as a lipid-regulating medication. Triglyceride-rich particles are removed from plasma via lipoprotein lipase activation and a decrease in apoptosis in C-III synthesis, which is how Fenofibrate works. It is used to treat hypertriglyceridemia and hypercholesterolemia either by itself or in conjunction with statins. Lipoprotein lipase activity is inhibited by apoprotein C-III. It lowers the levels of low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL). Additionally, Fenofibrate raises the amount of HDL, or high-density lipoprotein. It is recommended for the management of combined dyslipidemia and hypercholesterolemia. [(1)]

MATERIALS AND METHODS

Chemicals: Sodium citrate, Urea, Fenofibrate (API), Fenofibrate tablets (Stanlip 145mg), Distilled water

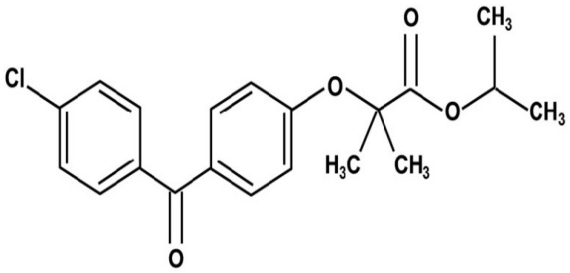

Fig. 1. Structure of Fenofibrate

List of Instruments: UV-Visible Spectrophotometer, Weighing balance, Sonicator, Desiccators, Refrigerator

Preparation of 1M urea solution: The 1M urea solution was prepared by accurately weighing 3g in to a 50ml volumetric flask and the volume was made up to 50ml with distilled water.

Preparation of 0.5M sodium citrate solution: The 0.5M sodium citrate solution was prepared by accurately weighing 6.45g in to a 50ml volumetric flask and the volume was made up to 50ml with distilled water.

Preparation of standard stock solution: A standard stock solution of the analyte was prepared by dissolving an aliquot quantity of standard transferred to a 100mL standard flask

containing 5ml each of 1M urea, and 0.5M sodium citrate as mixed hydrotropic solubilizing agent and warmed for 15 minutes; dissolved the content completely, final volume was made up with distilled water to produce a concentration of 1mg/ml or 1000 µg/ml (Standard stock solution). From stock 10 pipette out and transfer it into 100ml volumetric flask and made up to the mark with distilled water to obtain 100µg/ml (Standard dilution solution-1).[2]

Selection of wavelength: The standard dilution solution-1was transferred into 10ml volumetric flask and diluted to 10ml with distilled water to give concentration of 10 µg/ml and it was used for initial spectral scan in the UV range of 200-400nm to detect maximum wavelength. Fenofibrate shows maximum absorbance at 225nm. [3]

Preparation of sample solution: The Fenofibrate content in its marketed formulation (Stanlip 145mg) was estimated using pre-validated UV Spectrophotometric method. Twenty tablets were accurately weighed and powdered. Powder equivalent to 100mg of fenofibric acid was weighed and transferred to 100mL volumetric flask. The powder was then shaken with 5ml each of mixture of 1M urea, and 0.5M sodium citrate as mixed solubilizing agent and heated for 15 minutes; dissolved the content completely and the final volume was made up with distilled water to produce a concentration of 1mg/ml. The solution was then filtered through a Whattman filter paper. The first few ml of the filtrate was discarded. The remaining filtrate was diluted with distilled water to get the required concentration. Measure the absorbance at 225nm wavelength and % assay was calculated. [3-10]

METHOD DEVELOPMENT

Drug Fenofibrate is insoluble in aqueous solvents. So different solvents have been tried, but the results were not accurate. When the combination of 1 M urea and 0.5 M sodium citrate was used as a solubilizing agent, accurate results were obtained.

$$\%\ \text{Assay} = \frac{\text{Sample absorbenc}}{\text{Standard absorbenc}} \times \frac{\text{Wt.of Std}}{\text{Dilution of std}} \times \frac{\text{Wt.of Sample}}{\text{Dilution of Sample}} \times \frac{\text{Purity}}{100} \times \frac{\text{Wt.of Tablet}}{\text{Lable claim}} \times 100$$

Table 1. Assay of Fenofibrate tablet formulation

	Amount of tablet(mg)		%Label claim	% RSD
Fenofibrate	Labeled	Found		
	145	144.5	99.65	0.99

VALIDATION

Linearity: The serial dilutions were prepared from the standard stock solution to get a respective concentration of 5-25µg/mL absorbance of all the solution was measured at 225 nm. Calibration curve was plotted by taking absorbance on x-axis and concentration on y-axis. [10-15]

Precision: Precision of the method was determined by repeatability (intraday precision) and intermediate precision (interday precision) for standard solution (15µg/ml) by six replicate measurements from the homogenous solution absorbance were absorbed and % RSD was calculated. [3-5]

LOD and LOQ: The detection limit of an individual's analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantified as an exact value. Quantification limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. [1-5]

Accuracy: Accuracy was determined by standard addition method. To the sample solution, a known amount of standard solution was added at three different levels i.e., 80%, 100%, 120% of triplicate and the solution were analysed and % recovery was calculated. [5-10]

Robustness: Robustness of this method was determined by analysing the Fenofibrate standard solution of 15µg/mL at different max (i.e. ±1) of actual max. Absorbance was measured. [3-5]

RESULTS AND DISCUSSION

Linearity: The linearity concentration lies for Fenofibrate lies in between 5-25 µg/ml. linearity data and Calibration curve, correlation coefficient, intercept and slope were calculated for Fenofibrate and results were shown in Table-1and Fig 2.

Table 2. Linearity of Fenofibrate at 225 nm & Statistical data

S.No	Concentration (µg/ml)	Absorbance	Fenofibrate	
1	5	0.031	λmax	225nm
2	10	0.057	Linearity	5-25 µg/ml
3	15	0.082	Slope	0.0053
4	20	0.109	r^2	0.999
5	25	0.135	intercept	0.0028

Precision: A variation of results within the same day (intraday), variation of results between days (inter day) was analyzed. Intra and inter day precision was determined by analyzing Fenofibrate for six times at 225 nm. The precision data was shown in Table.3.

Tabl 3. Precision data of Fenofibrate

S.No	Concentration (µg/mL)	Intraday absorbance	Interday Absorbance
1	15	0.071	0.088
2	15	0.072	0.087
3	15	0.069	0.086
4	15	0.071	0.084
5	15	0.069	0.088
6	15	0.070	0.085
Mean		0.070	0.0863
Stdev		0.00121	0.00163
%RSD		1.7	1.8

Table 4. LOD and LOQ data

Parameters	Fenofibrate
LOD	0.82 µg/ml
LOQ	2.5 µg/ml

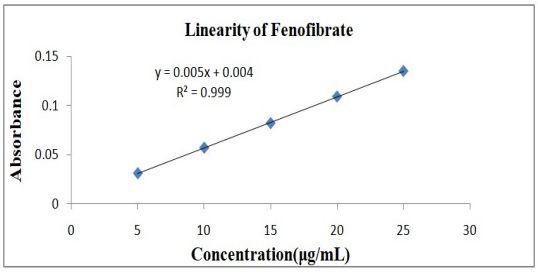

Fig. 2. Calibration curve of Fenofibrate

Limit of detection: LOD for Fenofibrate by the proposed method was determined on the response and slope of the regression coefficient.

Limit of quantization: Limit of quantization for Fenofibrate by the proposed method was determined on the response and slope of the regression coefficient.

$LOQ = 10 \times \sigma / S$

LOD and LOQ was calculated and shown in Table: 4.

Table 5. Accuracy data of Fenofibrate

Sample (%level)	Amount Taken	Amount added	Amount recovered	% Recovery	Average
80	15 15 15	12 12 12	26.8 27.2 26.8	98.8 % 101.3 % 98.8 %	99.6 %
100	15 15 15	15 15 15	30.2 29.8 30	101.4 % 98.9 % 100.2 %	100.1 %
120	15 15 15	18 18 18	32.6 33 32.8	97.8 % 100.3 % 99 %	99%

Accuracy: Accuracy is the closeness of the test results obtained by the method to the true value. The recovery technique was performed to judge the accuracy of the proposed method. For this, known quantities of the Fenofibrate solution were mixed with definite amounts of pre-analyzed formulations. The total amount of Fenofibrate was determined by using the proposed method and the amount of added drug was calculated by the difference. Recovery studies were carried out by spiking the samples solution with standard solution 80%, 100%, and 120% for three replicates data was shown in Table-5.

Robustness: The solutions were prepared and analyzed with change in the analytical conditions like different laboratory conditions and different analyst's .Robustness data was shown in Table: 5.

Table 5. Robustness data of Fenofibrate

S.No	Wavelength	Test Absorbance	Standard Absorbance	% Assay
1	224nm	0.094	0.093	101 %
2	225nm	0.091	0.090	101.1 %
3	226nm	0.093	0.094	98.9 %

CONCLUSION

By the above experimental results and parameters it was concluded that, this developed UV- Spectroscopy method for the estimation of Fenofibrate was found to be simple, precise, accurate, robust, economic and rapid makes this method more acceptable and cost effective and it can be effectively applied for routine analysis in research institutions and quality control department.

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