METHOD DEVELOPMENT AND VALIDATION OF CIPROFIBRATE IN BULK AND TABLET DOSAGE FORM BY UV SPECTROSCOPY.

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ABSTRACT

Ciprofibrate is used for the treatment of hyperlipidemias, in particular those classified as type IIb, type III, and type IV. Ciprofibrate decreases levels of serum triglycerides and very low density lipoprotein (VLDL) cholesterol, and increases high density lipoprotein (HDL) cholesterol. Ciprofibrate is a fibric acid derivatives approved for clinical use. Ciprofibrate is also known as 2-(4-(2,2dichloro cyclopropyl) phenoxy)-2-methylpropanoic acid. The molecular weight is 289.15g/mol, and formula is C13H14Cl12O3.the natural form of ciprofibrate is pale cream solid or a white to light yellow powder. OBJECTIVES: Develop and validate a simple, rapid, accurate, economic and precise UV/VIS method for ciprofibrate in bulk and tablets formulation. METHODOLOGY: Choices of a common solvent were essential so various solvent ranges including Methanol, Distilled Water, Ethanol, dimethyl formamide, phosphate buffer PH 3 were analysed. CONCLUSION: Among different solvents methanol has showed better result, hence methanol was selected as a solvent for the proposed method. Ciprofibrate showed maximum absorbance at 233 nm. The percentage recoveries for Ciprofibrate were found in the range of 99-100 %. Method was quantitatively evaluated in terms of linearity, accuracy, precision, robustness, ruggedness and recovery. The method was simple, convenient and suitable for the determination of ciprofibrate from bulk and tablet dosage.

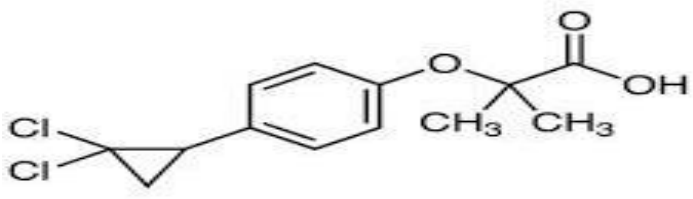
Key words: Ciprofibrate, UV spectroscopy, Tablets.

INTRODUCTION

Ciprofibrate used to lower the level of fats (lipids) in the blood, its lowering effect primarily through the activation of PPAR- ALPHA, leading to increased expression of enzymes and receptor involved in lipid metabolism. This results in reduced level of enzymes and receptor involved in lipid metabolism. This results in reduced level of triglycerides and LDL cholesterol while increasing HDL cholesterol. Literature review related that some spectrophotometric and HPLC methods have been reported for the estimation of ciprofibrate in tablet formulation, raw materials.

Main objective is to develop and validate UV visible method.

STRUCTURE:



VALIDATION:

Establishing documentation evidence, which provides a high degree of assurance that specific process, will consistently produce a product meeting its predetermined specifications and quality attributes.

System Suitability:

It is a checking of a system to ensure system performance before or during the analysis of unknowns. System solubility tests are an integral part of UV methods and they verify the resolution and reproducibility of the system are adequate for the analysis to be performed %RSD.

Accuracy(% Recovery):

For accuracy determination, three different concentrations were prepared separately i.e. 50%, 100%, and 150% for the concentration of absorbance values are recorded for the same.

MATERIALS AND METHODS:

Instrumentation: A Shimadzu UV -1800 240 UV/VISIBLE Spectrophotometer was used having two matched 1 cm matches quartz cell.

Materials: The ciprofibrate drug and cifirate 150mg were gifted by Medrich Limited, Bengalore. The solvents used is methanol.

Methods:

PREPARATION OF STANDARD STOCK SOLUTION:

10 mg of ciprofibrate was accurately weighted and transferred into 10 ml volumetric flask. About 7ml of methanol was added and sonicated to dissolve it completely. Then made volume up to the mark with the same solvent. The concentration of the resultant 1000µg/ml. Further standard stock solution was prepared by diluting it with methanol to get 100µg/ml. Again solution was dilution has made with the same solvent to get a concentration of 10µg/ml. The solution was scanned between 200-400 nm ranges against blank. From the UV spectrum,233nm was selected as absorption maximum for the drug ciprofibrate.

METHOD VALIDATION OF UV SPECTROSCOPY

The method was developed and validated according to the analytical procedure as per the ICH guidelines for validation of analytical procedures in order to determine linearity, accuracy, precision, robustness, ruggedness, LOD, LOQ.

- **Linearity:**

The analytical method should be linear i-e, should be a direct relationship between the concentration of the analyte (s) and the signal produced

Linearity is usually evaluated by analysing sample containing the analyte at5 different concentration level. the correlation coefficient, Y-intercept, slope of the regression line and residual sum of square should be calculated.

- **Accuracy:**

Accuracy is the closeness of the test result to the true or theoretical value accuracy is assessed by using minimum of a determination over a minimum of 3 concentration levels

Accuracy is then reported as a percentage recovery of the theoretical amount of analyte in the sample together with confidence interval.

- **Precision:**

a.) Inter-day precision:

It was done by analysing the solution by same analyte on alternate day till 5th day result indicate that the solution is stable up to 1day. Thereafter degradation may have taken place leading lower percent label claim.

b.) Intra-day precision:
It was done by analysing the solution by same analyst within a day result indicates that the solution is stable up to 1day thereafter degradation may have taken place in the solution.

- **Limit Of Quantitation (LOQ):**

LOQ is the lowest amount of an analyte that can be quantitated with suitable accuracy and precision.

- **Limit of Detection (LOD):**

LOD is the lowest amount of an analyte that can be detection but not necessary quantitation

- **Robustness:**

The robustness of the proposed assessed method was with changes in the analytical wavelength (270±1nm). Robustness was carried out at two different concentration levels (2 and 20µgmL-1) the results was expressed as standard deviation and relative standard deviation and are compiled the results revealed that the slight changes in the analytical wavelength did not adversely influence the absorbance intensity and indicate acceptable robustness of the proposed method.

- **Ruggedness:**

Ruggedness of the proposed method was evaluated by comparison of the absorbance of reaction that have been measured by two different analyte. In the same laboratory. Ruggedness carried out at two different concentration level (2and 20µg/ml-1). The results are expressed as standard deviation and relative standard deviation.

RESULTS AND DISCUSION

Solubility studies

The solubility of drug in different solvents were studied. Since, the drug is polar in nature, different polar solvents like Methanol, Ethanol, Phosphate Buffer with pH, Dimethyl formamide and water were studied. From the solubility studies, it was found that the drug Ciprofibrate is freely soluble in Methanol. The results are given in Table.

S.no	Solvents used	Parts of solvent required for parts of solute (in ml)	Descriptive
1	Methanol	1-10	Freely soluble
2	Phosphate buffer PH 3	10-30	Soluble
3	Ethanol	30-100	Sparingly soluble
4	Dimethyl formamide	30-100	Sparingly soluble
5	Water	100-1000	Slightly soluble

TABLE 1: SOLUBILITY STUDIES

IDENTIFICATION OF DRUG

MELTING POINT:

Instrument	Drug name	Standard values	Observed value
Melting point apparatus-laboratory setup	Ciprofibrate	174-177ºc	176ºc

TABLE 2: MELTING POINT

IR SPECTROSCOPIC METHOD

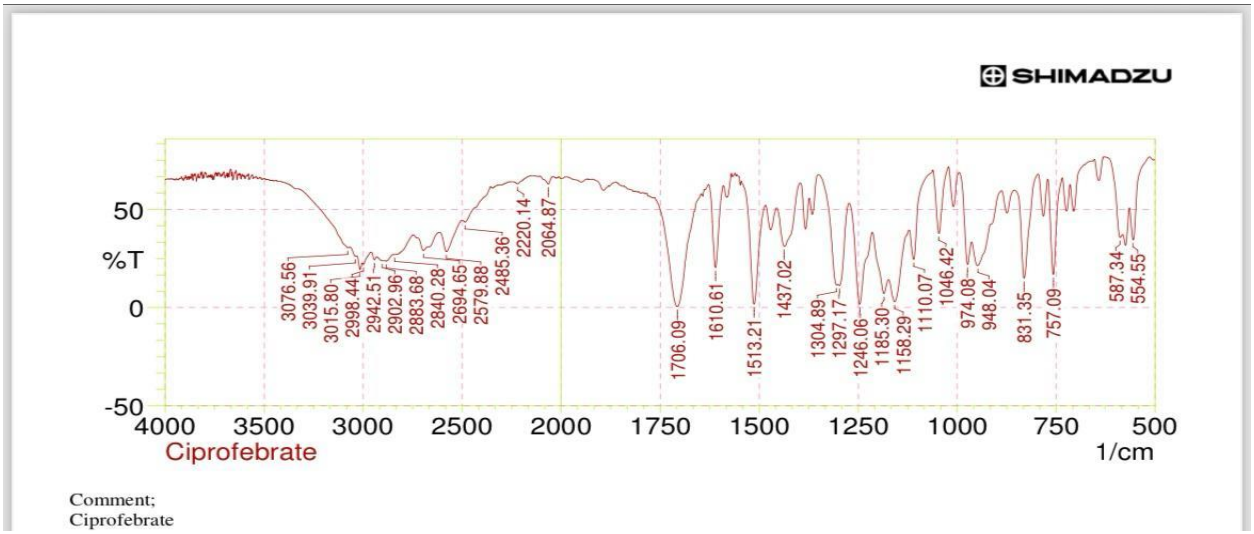


FIGURE 1- IR SPECTRUM

TABLE 3: INTERPRETATION OF IR SPECTRUM OF CIPROFIBRTE

S.NO	Frequency	Mode	Functional group
1	1706.09	C=O stretch	Ketone group
2	831.35, 757.09	C-Cl stretch	Alkyl halides
3	1304.89	C-O stretch	Ether
4	2902.96	C-H stretch	Alkane
5	3076.59	O-H stretch	Carboxylic acid
6	1437.02	C-C stretch	Aromatic group

METHOD DEVELOPMENT OF UV SPECTROSCOPY:

S.NO	Wavelength in nm	Absorbance at 233 nm
1	225	0.650
2	226	0.669
3	227	0.684
3	228	0.712
5	229	0.757
6	230	0.764
7	231	0.778
8	232	0.812
9	**233**	**0.860**
10	234	0.854
11	235	0.845

TABLE 4: LAMBDA MAX PROFILE OF CIPROFIBRATE

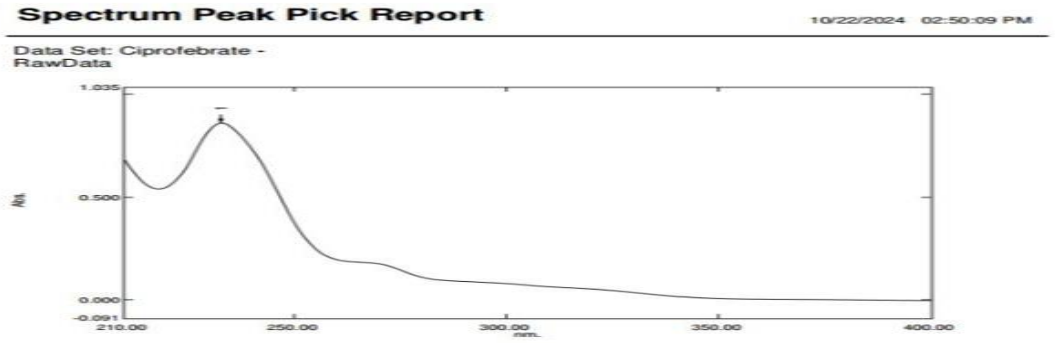


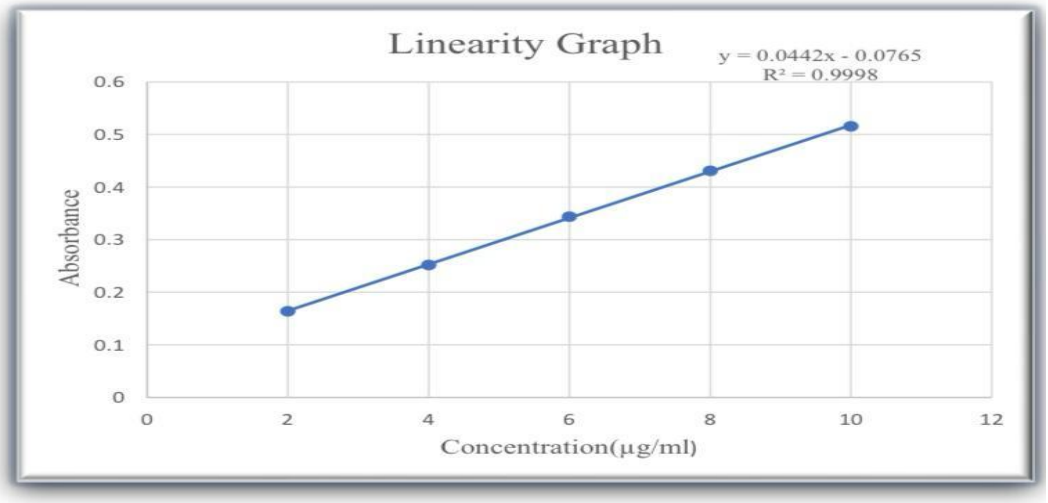
FIGURE 2: ABSORPTION SPECTRA OF CIPROFIBRATE

DETERMINATION OF PERCENTAGE PURITY:

S.NO	Standard absorbance	Sample absorbance	Percentage purity (%)	Average % purity	SD	%RSD
1	0.860	0.875	99.82	99.438	0.0106	0.01066
2	0.859	0.873	99.37			
3	0.858	0.870	99.59			
4	0.860	0.874	99.36			
5	0.861	0.877	99.05			

TABLE 5: %PURITY

FIGURE 3: CALIBRATION CURVE



Recovery study of ciprofibrate by UV method

S.no	% Conc	Average Absorbance	Amount added (mg)	Amount found (mg)	% recovery	Mean recovery	SD	%RSD
1	50%	0.859	4.99	5.1	97.84%	90.80	1.03	1.049
2	100%	0.860	9.99	10.0	99.9%			
3	150%	0.862	14.9	15.1	99.67%			

TABLE 6: % RECOVERY

S.no	Conc µg/ml	Absorption	Average absorption	Correlative coefficient	LOD	LOQ	Slope	Intercept
1	0.5	0.845	0.852	0.9999	0.042022	0.127338	0.8688	0.0046
2	0.75	0.847						
3	1	0.850						
4	1.25	0.858						
5	1.50	0.860						

TABLE 7: LINEARITY

SE of intercept = 0.004948

SD of intercept = 0.011063

LOD =0.042022

LOQ =0.127338

Slope =0.8688

Intercept =0.0046

PRECISION:

A.) Interday precision:

S.no	**Absorbance**	**Average**	**SD**	**% RSD**
1	0.861	0.8436	0.01472	0.174475
2	0.859			
3	0.843			
4	0.831			
5	0.824			

TABLE 8: INTERDAY PRECISION

B.) Intraday precision:

S.no	**Absorbance**	**Average**	**SD**	**% RSD**
1	0.842	0.8516	0.00578	0.67904
2	0.849			
3	0.853			
4	0.855			
5	0.859			

TABLE 9: INTRADAY PRECISION

RUGGEDNESS:

S.NO	Analysts	Conc(µg/ml)	Absorbance	SD	%RSD
1	Analysts -1	10µg/ml 10µg/ml 10µg/ml 10µg/ml 10µg/ml	0.836 0.837 0.833 0.840 0.849	0.005477	0.652828
2	Analysts -2	10µg/ml 10µg/ml 10µg/ml 10µg/ml 10µg/ml	0.858 0.849 0.837 0.847 0.854	0.007127	0.839507

TABLE 10: RUGGEDNESS

ROBUSTNESS:

S.no	**Wavelength**	**Absorbance**
1	233	0.858
2	235	0.845
3	237	0.842

TABLE 11: ROBUSTNESS

CONCLUSION:

The method were found to be rapid, economical, accurate and precise for the determination of ciprofibrate in bulk drug in tablet by UV-Spectrophotometer methods produce comparable results can be used for precise and accurate analysis of ciprofibrate in its pure and tablet dosage form. The values of % recovery was close to 100% indicating reproducibility and accuracy of the proposed method successfully employed as a quality control tool for the analysis of ciprofibrate in its tablet dosage form and in bulk drug.

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