

Spectrophotometric Estimation of Cefprozil Sulphate in Pharmaceutical Formulations

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Three simple, accurate, rapid and sensitive methods (A, B and C) have been developed for estimation of cefprozil sulphate in its pharmaceutical dosage form. The method A is based on reaction of cefprozil with ferric chloride and 1,10-phenanthroline to form a blood red coloured chromogen. The method B is based on reaction of cefprozil with ferric chloride 2,2'-bipyridyl to form blood red coloured chromogen. The method C is based on the reduction of ferric ions of the reagent ferric chloride to ferrous ions by the drug, which further in the presence of potassium ferricyanide produces blue coloured chromogen. These methods exhibit maximum absorption at 510, 520 and 720 nm, respectively and obey the Beer's law in the concentration range of 5-30, 5-50 and 1-10 mcg/mL, respectively. The methods have been statistically evaluated and were found to be precise and accurate. The proposed methods are economical and sensitive for estimation of cefprozil sulphate in bulk drug and in its formulations.

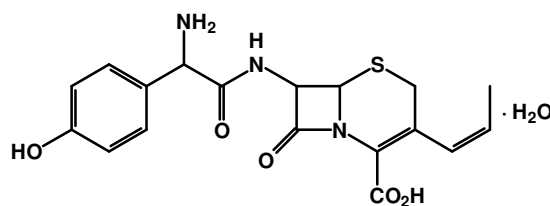
Key Words: UV-Visible spectrophotometry, Cefprozil sulphate, Ferric chloride, 1,10-Phenanthroline, Potassium ferricyanide, 2,2'-bipyridyl.

INTRODUCTION

Cefprozil sulphate¹ is chemically [6R-6 α -7 β (R*)]-7- $[\alpha$ -amino-4-hydroxyphenyl)acetyl]amino]-8-oxo-3(1-propenyl)5-thia-1-azabicyclo-[4.2.0]oct-2-ene-2-carboxylic acid monohydrate. It is a second generation Cephalosporin effective against gram-positive and gram-negative bacteria, including both aerobes and anaerobes. It is indicated for complicated upper and lower urinary tract infections, respiratory tract infections, skin and soft tissue infection and bacteraemia. It is official in Martindale-The Extra Pharmacopoeia². Survey of literature reveals that the drug is determined by

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using HPLC^{3,4} and very few spectrophotometric methods⁵⁻⁷. The present study describes simple, sensitive, accurate, rapid and economical spectrophotometric methods **A**, **B** and **C** for the estimation of cefprozil sulphate in its formulations.



Structure of cefprozil

EXPERIMENTAL

Elico ultraviolet-visible double beam spectrophotometer SL-164 with 1 cm matched quartz cells was used for all spectral measurements.

All the chemicals used were of analytical reagent grade, (i) **1,10-phenanthroline (0.2 M)**: 990 mg of 1,10-phenanthroline was dissolved in 25 mL of distilled water, (ii) **ferric chloride hexahydrate (0.03 M)**: 405 mg of ferric chloride hexahydrate was dissolved in 50 mL of distilled water, (iii) **2,2'-bipyridyl (0.2 M)**: 780 mg 2,2'-bipyridyl was dissolved in 25 mL of distilled water, (iv) **ferric chloride hexahydrate (0.3 % w/v)**: 300 mg of ferric chloride hexahydrate was dissolved in 100 mL of distilled water, (v) **potassium ferri-cyanide (0.2 % w/v)**: 200 mg of potassium ferricyanide was dissolved in 100 mL of distilled water.

Procedure: Standard stock solution was prepared by dissolving 100 mg of cefprozil sulphate in 100 mL of distilled water to get a concentration of 1000 mcg/mL. This was further diluted to get the working standard solutions of 20, 50 and 100 mcg/mL.

Assay procedure

Method A: Aliquots of standard drug solution of cefprozil sulphate 1.0-6.0 mL (50 mcg/mL) were taken and transferred into series of graduated test tubes. To each test tube, 1 mL of ferric chloride hexahydrate (0.03 M) and 1 mL of 1,10-phenanthroline (0.2 M) were added. The test tubes were allowed to stand in water bath at 70 °C for 15 min. The test tubes were then cooled to room temperature and the solutions were made up to 10 mL with distilled water. The absorbance of the red coloured chromogen was measured at 510 nm against reagent blank and a calibration curve was constructed. The absorbance of the sample solution was measured and the amount of cefprozil sulphate was determined by referring to the calibration curve.

Method B: Aliquots of standard drug solution of cefprozil sulphate 0.5-5.0 mL (100 mcg/mL) were taken and transferred into series of graduated test tubes. To each test tube 1 mL of ferric chloride hexahydrate (0.03 M) and 1 mL of 2,2'-bipyridyl (0.2 M) were added. The test tubes were allowed to stand in water bath at 70 °C for 15 min. The test tubes were then cooled to room temperature and the solutions were made upto 10 mL with distilled water. The absorbance of the red coloured chromogen was measured at 520 nm against reagent blank and a calibration curve was constructed. The absorbance of the sample solution was measured and the amount of cefprozil sulphate was determined by referring to the calibration curve.

Method C: Aliquots of standard drug solution of cefprozil sulphate 0.5-5.0 mL (20 mcg/mL) were taken and transferred into series of graduated test tubes. To each test tube 1 mL of ferric chloride hexahydrate (0.3 % w/v) and 0.5 mL of potassium ferricyanide (0.2 % w/v) were added and thoroughly shaken and set aside for 5 min. The volume in each test tube was made upto 10 mL with distilled water. The absorbances of the solutions were measured at 720 nm against reagent blank, within 0.5 h and the calibration curve was plotted. Similarly, the absorbance of the sample solution was measured and the amount of cefprozil sulphate was determined by referring to the calibration curve.

The methods were extended for the determination of cefprozil sulphate in tablets (Cefzil, Aurobindo) was chosen. Twenty tablets of cefprozil sulphate were accurately weighed and powdered. Tablet powder equivalent to 100 mg of cefprozil sulphate was dissolved in 50 mL of distilled water, sonicated for 15 min, filtered and washed with distilled water. The filtrate and washings were combined and the final volume was made to 100 mL with distilled water. The solution was suitably diluted and analyzed as given under the assay procedure for bulk samples.

Recovery studies: To ensure the accuracy and reproducibility of the results obtained, adding known amounts of pure drug to the previously analyzed formulated samples and these samples were reanalyzed by the proposed method and also performed recovery experiments.

RESULTS AND DISCUSSION

In the present study, the method **A** and **B** are based on the reduction of ferric chloride to ferrous form by the drug, which forms complex with 1,10-phenanthroline and 2,2'-bipyridyl to yield blood red coloured chromogen. The coloured chromogen were stable for more than 3 h and exhibited maximum absorption at 510 and 520 nm, respectively. In the method **C**, the estimation is based on the reduction of ferric ions to ferrous ions by the drug, which further in the presence of potassium ferricyanide produces blue coloured chromogen having a maximum absorbance at 720 nm. The blue coloured chromogen was stable for 0.5 h at room temperature.

The conditions required for the formation of coloured complexes were optimized. Statistical analysis was carried out and the results of which were satisfactory. The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in Table-1.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION DATA

Parameters	Method A	Method B	Method C
λ_{\max} (nm)	510	520	720
Beer's law limits mcg/mL	5-30	5-50	1-10
Molar absorptivity (L/mol cm)	1.31×10^4	6.96×10^5	1.95×10^4
Sandell's sensitivity (micrograms/cm ² /0.001 absorbance unit)	0.092	0.124	0.1004
Regression equation* (Y)			
Slope (m)	0.0310	0.0170	0.0100
Intercept (c)	0.0114	0.0155	0.0122
Correlation coefficient (r)	0.9989	0.9999	0.9998
Precision (relative standard deviation %)	0.1650	0.2480	0.5620
Standard error of mean	0.0040	0.0213	0.0345
% Range of error (confidence limits)			
0.05 level	0.1339	0.1350	0.9200
0.01 level	0.1347	0.1310	0.7700

*Y = mx + c, where X is the concentration in micrograms/mL and Y is absorbance unit.

The regression analysis using the method of least squares was made for slope (m), intercept (c) and correlation obtained from different concentrations and the results summarized in Table-1.

The reproducibility and precision of the methods are very good as shown by the low values of coefficient of variance (CV). Recovery studies were close to 100 % that indicates the accuracy and precision of the proposed methods and also indicates non-interferences from the formulation excipients. All the validated parameters are summarized in Table-2.

TABLE-2
ASSAY OF CEFPROZIL SULPHATE IN
PHARMACEUTICAL FORMULATION

Sample no.	Labeled amount (tablet) (mg)	%Obtained* by proposed method (mg)			%Recovery** by the proposed method		
		A	B	C	A	B	C
1	500	498.3	499.2	500.5	98.8	99.9	100.2
2	500	499.8	500.3	501.6	100.1	99.6	100.5

*Average of three determinations; **After spiking the sample.

In conclusion, the proposed methods are simple, sensitive, accurate and economical for the routine estimation of cefprozil sulphate in bulk and in its formulations.

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