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Research Article

SPECTROPHOTOMETRIC ANALYTICAL STUDY FOR THE CHARGE- TRANSFER COMPLEX FORMATION OF CEFEPIME

C.RAMBABU[1], DR. C.A.JYOTHIRMAYEE[2], K. NAGA RAJU[3*]

[1]Professor, Department of Chemistry, A. N. U. PG Centre Nuzvid-521201, [2]Reader and head, PG Department of Chemistry, St. Theresa's College for Women, Eluru-534003, [3*]Assistant professor, Department of pharmaceutical analysis, Sir C. R. R. College of pharmaceutical sciences, Eluru, 534007 Andhra Pradesh, India.

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ABSTRACT

Studies were carried out to develop a simple, rapid and accurate Spectrophotometric method for the analysis of Cefepime (CFP).The method depends on the Charge-Transfer complexation reaction between Cefepime as an electron donor and p-chloranilic acid (P-CA in the method I) and chloranil (CL in method II) as a electron acceptor to form a colored chromogen measured at 525 nm (method I) and 560 nm (method II) .Different variables affecting the reaction were studied and optimized. Under the optimum conditions, linear relationships with good correlation coefficients were found between the absorbance and the concentrations of the studied drug is in the range of 4-120 µg/ml. Beer's law is obeyed in the concentration ranges of 2-40 µg/ml. The accuracy and precision of the methods were satisfactory. The methods were successfully applied to an analysis of Cefepime in their pharmaceutical formulations.

Keywords: Spectrophotometric analytical study, Cefepime, P-Chloranilic acid, Chloranil.

INTRODUCTION

Cefepime[1] is 6R (6L 7β (2)]-1 [7 2-Amino-4-thiazolyl) (methoxy imino) acetyl, amino- 2 –carboxy - 8- oxo-5 thia-1- azabicyclo (4,2,0) oct - 2en - 3yl (methyl)- 1 methyl pyrrolidinium inner salt. Cefepim is semisynthatic fourth generation cephalosporin antibiotic. By reviewing the available colorimetric procedures for the analysis of the cephalosporins , one can easily recognize that most of these methods involve the cleavage of the β-lactam moiety of the cephalosporin structures. . This is mainly used in the treatment of various microbial infections caused by gram+ve and gram-ve microorganisms [2, 4]. Cefepime is official in USP. The USP[3] describe a HPLC method for the estimation of Cefepime formulations. A review of literature revealed that there are U.V Spectrophotometric [5], HPLC[6-12] and Colorimetric method[13] using Folins-Ciocaltue reagent and 1-Chloro-2, 4-dinitrobenzene. Thus the present method aims at developing newer colorimetric method which is rapid accurate, precise, sensitive and reliable.

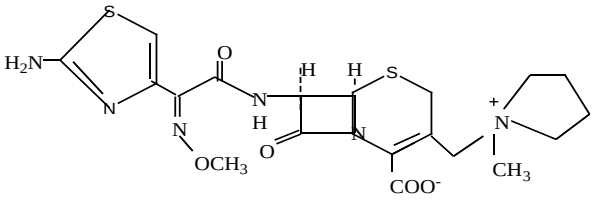

Fig. 1: chemical structure of Cefepime

The methods that are based on charge-transfer complexation are usually rapid and simple to perform. The present work describes an improved direct simple analytical procedure that can be applied at quality-control laboratories for the analysis of cephalosporins. This analytical procedure was based on the reactivity of an intact molecule without cleavage.

MATERIALS AND METHODS

Instrumentation

An Elico, UV – Visible digital spectrophotometer with 1cm matched quartz cells were used for the spectral and absorbance measurements A Systronics 365 digital pH – meter was used for pH measurements.

Preparation of reagents

All the reagents used were of analytical reagent grade and the drug (CFP) solution was prepared in double distilled water.

Preparation of p-chloranilic acid

Weight accurately 100mg of P-Chloranilic acid and dissolved in 20 ml of isopropanol, and make up the volume to 100ml with chloroform.

Preparation of Chloranil

Take 100ml of chloranil, and dissolved in 100ml of 1, 4-dioxane.

Chloroform is used as it is.

Preparation of drug solution

Stock solution of CFP(1mg/ml) was prepared by dissolving 100mg of CFP initially in 50ml distilled water followed by basification with 0.1M sodium hydroxide and extraction into chloroform (3x25 ml) followed by dilution to 100ml with chloroform. And from this stock solution was diluted step wise with distilled water to get the working standard solutions of concentration of 50µg/ml.

Procedures

Method I: Into a series of 10ml graduated tubes containing aliquots of standard drug solution ranging from 1.0-6.0ml (1mg/ ml), 2.0ml of P-Chloranilic acid was added and kept aside for 5 minutes. Then the volume of the contents were made up to 10ml with chloroform and read at 525 nm against a reagent blank. The amount of the drug was computed from the calibration curve. The color was found to be stable for 30 minutes.

Method II: Into a series of 10ml graduated tubes containing aliquots of standard drug solution ranging from 1.0 to 6.0 ml (1mg/ ml), 2ml of chloranil followed by chloroform was added for bringing the volume to 7ml.The final volume was brought to 20ml with dimethyl formamide and the absorbance was measured against a reagent blank at 560nm. The amount of drug was computed from the calibration curve. The colour was found to be stable for one hour.

RESULTS AND DISCUSSION

The optimum conditions for colour development for methods I and II have been established by varying the parameters one at a time and keeping the other parameters fixed and observing the effects of products on the absorbance of the colored species. Beer's law limits, molar absorbivity, Sandal's sensitivity, % range of error and %

relative standard deviation are summarized in Table I. The regression analysis using the method of least squares was made for the slope (b), intercept (a) and correlation coefficient (r)obtained from different concentrations are given in Table I The results showed that these methods have reasonable precision.

Table 1: Optical regression characteristics, precision and accuracy of the proposed methods for Cefepime

Parameter	Method - I	Method - II
λmax(nm)	525nm	560nm
Beer's law limits (μg.ml^{-1})	20-120	20-120
Molar absorbivity (lit . mole^{-1},cm^{-1})	1.406 x 10^4	9.83x10^3
Sandell's sensitivity (μg.cm^{-2}/0.001 abs.unit)	0.1189	0.1489
Regression equation (y*=a+bx) slope (b)	0.0609	0.0394
Intercept (a)	6.6 x 10^{-3}	1.2 x 10^{-3}
Correlation Co-efficient (r)	0.9998	0.9997
% R.S.D.	0.9852	1.012
% Range of error** (confidence limits) 0.05 level	1.035	1.062
0.01 level	1.623	1.666

*Y = a+ bx where x is the concentration of Cefepime in μg/ml and Y is the absorbance at the respective λmax.

**Average of six determinations considered.

To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical dosage forms and the mixtures were analyzed by the proposed methods. The percentage recoveries are given in Table - 2. The interference studies revealed that the common excipients and other additives that are usually present in the injection dosage forms did not interfere at their regularly added levels.

Table 2: Assay of Cefepime in Pharmaceutical formulation

Formulation	Labeled amount in mg	Amount found by proposed Method M_I	Amount found by proposed Method M_{II}	% Recovery* proposed by methods M_I	% Recovery* proposed by methods M_{II}
Injection-I	500	499.18	500.16	99.84	100.03
Injection-II	500	500.84	499.28	100.17	99.86
Injection-III	500	500.25	499.08	100.05	99.82
Injection-IV	500	499.32	500.22	99.87	100.04

R. Reference was UV method developed in the laboratory.

*Recovery amount is the average of six determinations.

CONCLUSION

In conclusion, the proposed methods are found to be simple, selective, and accurate and can be used in the estimation of Cefepime in pure and pharmaceutical dosage forms in a routine manner.

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