

UV-Visible Spectrophotometric Methods For The Estimation Of Cefpodoxime Proxetil In Bulk Drug And Pharmaceutical Dosage Form.

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Abstract: Three simple, sensitive, accurate, and rapid Uv/visible spectrophotometric methods have been developed for the estimation of cefpodoxime proxetil in bulk drug and in pharmaceutical dosage form. Method A involves the determination of cefpodoxime proxetil in bulk drug and pharmaceutical formulations, which shows maximum absorbance at 235 nm in methanol, while method B is based on ion-pair complex between cefpodoxime proxetil and bromocresol purple in acidic medium and the subsequent extraction of the ion pair in chloroform. The yellow colored ion pair complex shows maximum absorption at 415 nm, while method C is based on ion-pair complex between Cefpodoxime Proxetil and bromocresol green in acidic medium and the subsequent extraction of the ion pair in chloroform. The yellow colored ion pair complex shows maximum absorption at 425 nm. Beer's law was obeyed in the concentration range of 5-25 µg/ml in method A, 5-25 µg/ml in method B and 5-25 µg/ml in method C respectively. Results of the analysis were validated statistically and by recovery studies.

Keywords: Cefpodoxime Proxetil, bromocresol green, bromocresol purple.

1. INTRODUCTION:

The cephalosporins are a class of β -lactam antibiotics originally derived from Acremonium, which was previously known as "Cephalosporium".¹ Cefpodoxime Proxetil is a third generation cephalosporin antibiotic indicated for the treatment of patients infected with susceptible strains of microorganisms which include a wide range of gram-positive and gram-negative bacteria. It is commonly used to treat acute otitis media, pharyngitis, and sinusitis.

The therapeutic importance of this compound justifies researcher to establish analytical methods for its determination in bulk and pharmaceutical formulations. Chemically, Cefpodoxime Proxetil is (RS)-1(isopropoxycarbonyloxy) ethyl (+)-(6R,7R)-7-[2-(2-amino-4-thiazolyl)-2-[(Z) methoxyimino]

acetamido]-3-methoxy methyl-8-oxo-5-thia-1-azabi cyclo[4.2.0] oct-2-ene-2-carboxylate. The molecular formula of Cefpodoxime proxetil is $C_{21}H_{27}N_5O_9S_2$ and molecular weight is 557.6 gm/mol.. It is freely soluble in dehydrated alcohol, acetonitrile, methanol and very slightly soluble in water.^[2-7]

Literature survey reveals that, A few analytical methods are found for quantitative estimation of Cefpodoxime Proxetil in bulk drug and pharmaceutical formulation such as the application of ninhydrine and ascorbic acid for the determination of Cefpodoxime Proxetil in pharmaceutical formulations^[8], HPTLC^[9,10], HPLC for the identification of degradation products of Cefpodoxime Proxetil^[11], isomer specific RP-HPLC method^[12] and simultaneous RP-HPLC has been reported for the

estimation of Cefpodoxime Proxetil and clavulanic acid in tablets^[13].

The present work describes one new UV Spectrophotometric method and two new, simple visible spectrophotometric methods involving Cefpodoxime Proxetil with reagents such as bromocresol purple in method B and bromocresol green in method C.

Recovery experiments were performed by adding known amount of drug to the pre-analyzed formulation and reanalyzing the mixture by proposed method. Results were validated statistically and the % recovery was found in the range of 99.6 % to 100.2%. The proposed methods are new, simple, sensitive, accurate, and precise and can be successfully employed in the routine analysis of Cefpodoxime Proxetil in bulk drug and pharmaceutical dosage forms.

2. EXPERIMENTAL

2.1 MATERIALS AND METHODS

The working standard Cefpodoxime Proxetil was obtained as a gift sample from KAPL, Karnataka, India. Cefpodoxime Proxetil DT 100 mg and Cefpodoxime Proxetil DT 200 mg tablets were obtained from Ipca laboratories Ltd Mumbai, India. These are procured from the local market. All the chemicals used were of A.R. grade procured from Qualigens Mumbai, S.D.Fine Chem Ltd, Merck and Spectrochem, Mumbai, India and distilled water (in house production) were used for making the solutions.

2.2 INSTRUMENTATION

For all the methods, Shimadzu model 1700 double beam UV-VIS spectrophotometer with spectral bandwidth of 1.8 nm, wavelength accuracy of 2 nm and a pair of 1 cm matched quartz cells of 10 mm optical path length was used as an instrument for spectral measurements.

2.3. PREPARATION OF STANDARD AND SAMPLE SOLUTIONS:

Preparation of standard stock solution of Cefpodoxime Proxetil:

Pure Cefpodoxime Proxetil powder equivalent to 100 mg was accurately weighed and dissolved in 40 ml of methanol in a 100 ml volumetric flask and the volume was made upto the mark with methanol (1 mg/ml). From this, a standard solution containing 100 µg/ml was prepared with methanol for both the methods.

Preparation of working stock solution of Cefpodoxime Proxetil:

Twenty tablets of Cefpodoxime Proxetil each containing 100 mg were accurately weighed, average

weight was determined and crushed into fine powder. An accurately weighed quantity of powder equivalent to 100 mg of Cefpodoxime Proxetil was transferred into 100 ml volumetric flask and dissolved in 40 ml of methanol and sonicated for 5 mins. The solution was filtered through Whatman filter paper no.41. The residue was washed with 10 ml portions of methanol three times and the total volume of the filtrate was made upto 100 ml with methanol (1 mg/ml). The final concentration was brought to 100µg/ml with methanol.

Method A:

Aliquots of standard solution of Cefpodoxime Proxetil ranging from 0.5-3.0 ml (1 ml = 100 µg) were transferred into a series of 10 ml volumetric flasks. The volume in each flask was made upto 10 ml with methanol and the absorbance's were measured at 235 nm against solvent blank. The obtained absorbance values when plotted against the concentration of Cefpodoxime Proxetil give the calibration graph. The concentration of the unknown sample was determined from the calibration graph (fig 1 & 2) or computed from the regression equation derived from Beer's law data.

Method B

Aliquots of standard solution of Cefpodoxime Proxetil ranging from 0.5 to 2.5 ml (1ml = 100 µg) were transferred into a series of 125 ml separating funnels. To each funnel, 3.0 ml of acid-phthalate buffer (pH 2.2) and 2.0 ml of bromocresol purple reagent was added and the volume of aqueous phase in each flask was brought to 10 ml with distilled water. The flasks were shaken gently for 5 min. Then 10 ml of chloroform was added to each flask. The contents were shaken thoroughly for 5 min and allowed to stand, so as to separate the aqueous and chloroform layers. The yellow colored chloroform layers were collected and absorbance's were measured at 415 nm against the reagent blank. The colored species was stable for 3 hrs. The amount of cefpodoxime Proxetil present in the sample solution was computed from the respective calibration curve (fig 3 & 4).

Method C

Aliquots of standard solution of Cefpodoxime Proxetil ranging from 0.5 to 2.5 ml (1ml = 100 µg) were transferred into a series of 125 ml separating funnels. To each funnel, 3.0 ml of acid-phthalate buffer (pH 2.2) and 3.0 ml of bromocresol green reagent was added and the volume of aqueous phase in each flask was brought to 10 ml with distilled water. The flasks were shaken gently for 5 min. Then 10 ml of chloroform was added to each flask. The contents were shaken thoroughly for 5 min and allowed to stand, so as to separate the aqueous and chloroform

layers. The yellow colored chloroform layers were collected and absorbance's were measured at 425 nm against the reagent blank. The colored species was

stable for than 3 hrs. The amount of Cefpodoxime Proxetil present in the sample solution was computed from the respective calibration curve (fig 5 & 6).

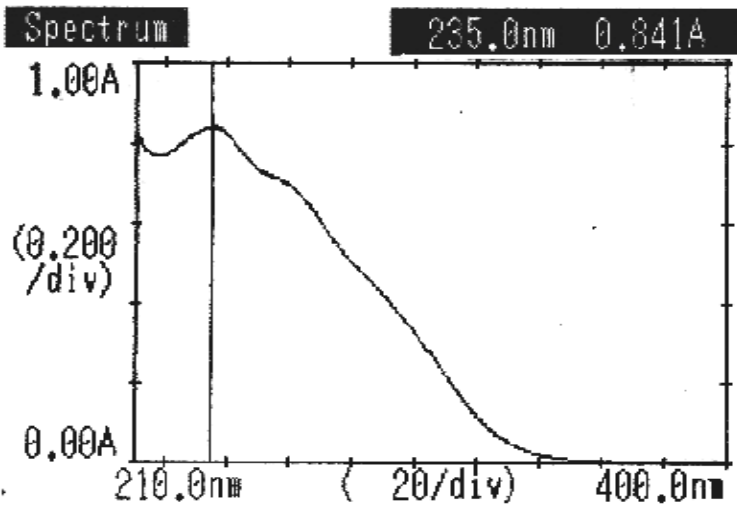


Fig.1: Absorption Spectrum of Cefpodoxime Proxetil in Methanol.

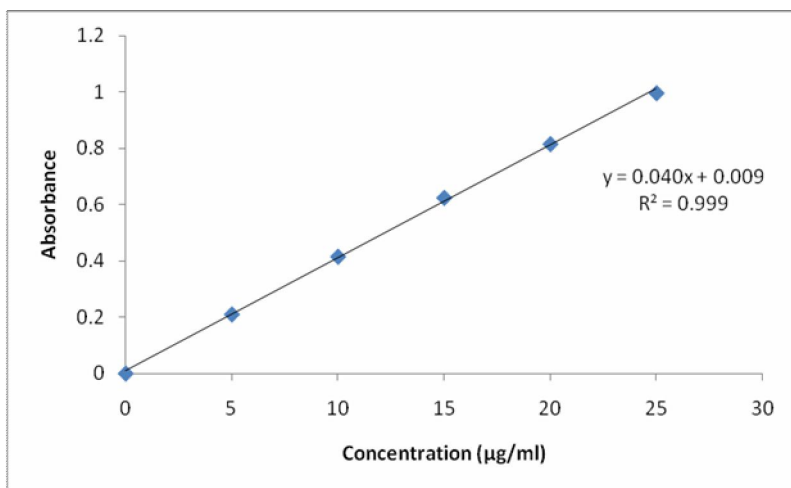


Fig. 2: Calibration curve of Cefpodoxime Proxetil in Methanol.

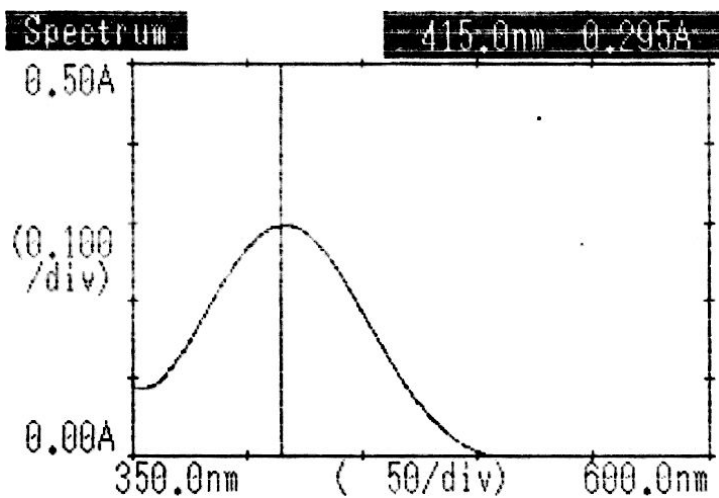


Fig. 3: Absorption Spectrum of Cefpodoxime Proxetil with Bromocresol Purple.

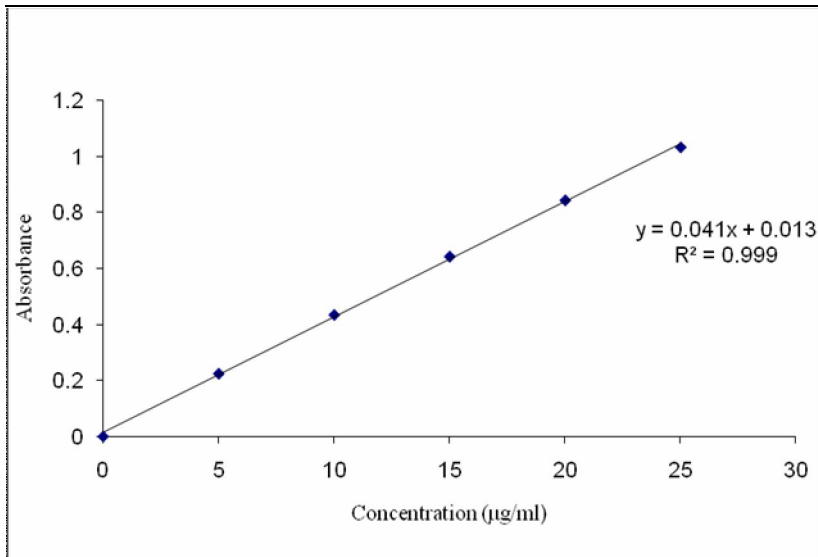


Fig. 4: Calibration curve of Cefpodoxime Proxetil with Bromocresol Purple.

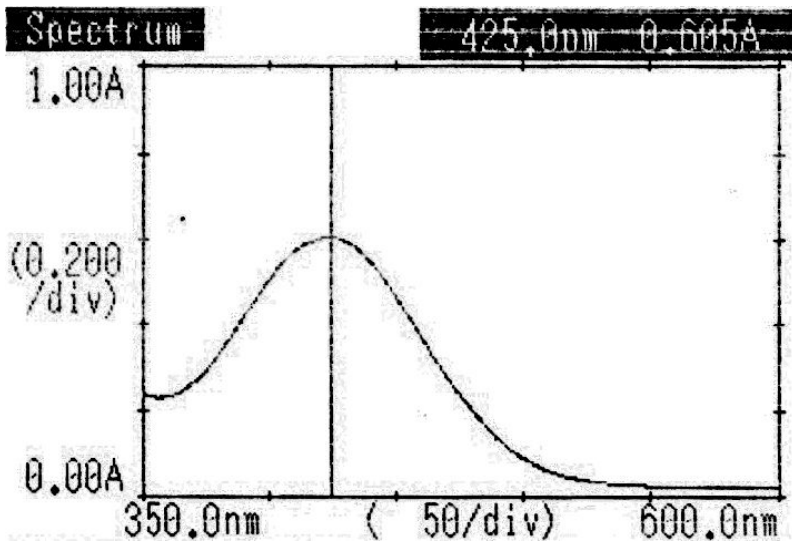


Fig. 5: Absorption Spectrum of Cefpodoxime Proxetil with Bromocresol Green.

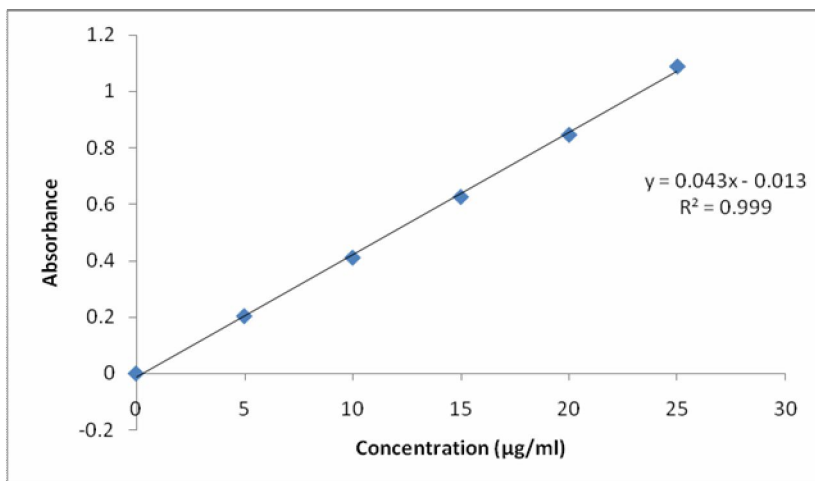


Fig. 6: Calibration curve of Cefpodoxime Proxetil with Bromocresol Green.

Table 1: OPTICAL CHARACTERISTICS AND PRECISION FOR CEFPODOXIME PROXETIL

Parameter	UV Method	BCP	BCG
λ_{\max} (nm)	235	415	425
Beer's law limits ($\mu\text{g/ml}$)(C)	5-25	5-25	5-25
Molar absorptivity ($\text{L mol}^{-1} \text{cm}^{-1}$)	1.8066×10^4	2.3502×10^4	2.3234×10^4
Sandell's sensitivity 0.001 absorbance unit	$\mu\text{g/ml} -$ 0.03086	0.02372	0.024
Regression equation (Y*)			
Slope (b)	0.040	0.041	0.043
Intercept (a)	0.009	0.013	0.013
Correlation coefficient(r^2)	0.999	0.999	0.999
% RSD	0.8092	1.3641	0.8503
Range of errors**			
Confidence limits with 0.05 level	0.0045	0.0050	0.0052
Confidence limits with 0.01 level	0.0067	0.0074	0.0078
LOD ($\mu\text{g} / \text{ml}$)	0.1353	1.03	0.4115
LOQ ($\mu\text{g} / \text{ml}$)	0.3542	3.133	1.24

*Y= bC + a where C is the concentration of cefpodoxime proxetil in $\mu\text{g/ml}$ and Y is the absorbance at the respective λ_{\max}

** For five measurements

Table 2: EVALUATION OF CEFPODOXIME PROXETIL IN PHARMACEUTICAL FORMULATIONS

Sample (Tablet)	Labeled Amount (mg)	Amount Obtained by UV Method*	Percentage Recovery**
T ₁	100	100.1± 0.29	99.9±0.36
T ₂	200	200.1± 0.72	99.8± 0.69

*Average of three determinations

** Mean and standard deviation of three determinations
(100 mg and 200 mg of cefpodoxime proxetil was added and recovered)

Table 3: EVALUATION OF CEFPODOXIME PROXETIL IN PHARMACEUTICAL FORMULATIONS

Sample (Tablet)	Labeled Amount (mg)	Amount Obtained* (mg)		Percentage Recovery**
		Proposed Method BCP	Reference Method UV	
T ₁	100	100.02± 0.019	101.0± 0.29	100.3± 0.45
T ₂	200	199.97± 0.037	200.9± 0.72	99.75± 0.87

*Average of three determinations

** Mean and standard deviation of three determinations (100 mg and 200 mg of cefpodoxime proxetil was added and recovered)

Table 4: EVALUATION OF CEFPODOXIME PROXETIL IN PHARMACEUTICAL FORMULATIONS

Sample (Tablet)	Labeled Amount (mg)	Amount Obtained* (mg)		Percentage Recovery**
		Proposed Method BCG	Reference Method UV	
T ₁	100	99.92± 0.023	101.0± 0.29	100.1± 0.36
T ₂	200	199.96± 0.032	200.9± 0.72	99.6± 0.57

*Average of three determinations

** Mean and standard deviation of three determinations (100 mg and 200 mg of cefpodoxime proxetil was added and recovered)

3. RESULT AND DICUSSION

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity, Sandell's sensitivity and percent relative standard deviation were calculated and the results are summarized in Table 1. The optimum conditions for color development have been established by varying the parameters one at a time and keeping the other parameters fixed and observing the effect of product on the absorbance of the colored species. Then it was incorporated in the procedure.

The value obtained for the determination of Cefpodoxime Proxetil in different tablet samples T₁ and T₂ by proposed method are presented in Table 2.

To test the accuracy and reproducibility of the proposed methods, recovery experiments were carried out by adding known amount of the drug to the pre-analyzed formulation and reanalyzing the mixture by proposed methods. The results of the same are shown in Table 2, 3 & 4.

The Molar absorptivity and Sandell's sensitivity values show the sensitivity of both the methods. The precision is confirmed by % CV (coefficient of variance) values, which are found to be less than 2%,. The analysis results of marketed

formulations (tablets) are in good agreement with the labeled claim. The reproducibility, repeatability, and accuracy of these methods were found to be good, which is evidenced by low standard deviation. The percent recovery obtained (99.9± 0.36- 99.8± 0.69 for method A, 100.3± 0.45-99.75± 0.87 for method B and 100.1±0.36-99.6± 0.57 for method C) indicates non-interference from the common excipients used in the formulations.

4. CONCLUSION

Thus these methods developed in the present investigation are simple, sensitive, accurate, and precise and can be successfully applied for the routine estimation of Cefpodoxime Proxetil in bulk and pharmaceutical dosage forms.

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REFERENCES:

1. Satoshkar RS, Bhandarkar SD, Ainapure SS. Pharmacology and pharmacotherapeutics. 15th ed. Mumbai: Popular Prakashan; 1996.
2. O' Neil MJ, editor. The Merck Index – an Encyclopedia of Chemicals, Drugs and Biologicals. New Jersey: Merck & Co; 2001.
3. British pharmacopoeia. The Department of Health. Vol I. London: The Stationary office; 2009.
4. The United States Pharmacopoeia. XIX Revision. Rockville MD: United States Pharmacopoeial Convention; 1974.
5. <http://www.patient.co.uk/showdoc/30002196> [cited 2009 Dec 5].
6. <http://www.netdoctor.co.uk/medicines/100002389.html> [cited 2009 Dec 5].
7. <http://www.drugs.com/cons/Cefpodoxime.html> [cited 2009 Dec 5].
8. Subbayamma AV, Rambabu C. Application of ninhydrin and ascorbic acid for the determination of Cefpodoxime Proxetil in pharmaceutical formulations. Oriental Journal of Chemistry An International Research Journal of Pure and Applied Chemistry 2008;24(2):REGN No. 38570/84.
9. Abhijit AD, Mangal SN. HPTLC Determination of Cefpodoxime Proxetil in Formulations. Journal of Chromatographia 2007;66(11-12):905-908.
10. Darji BH, Shah NJ, Patel AT, Patel NM. Development and validation of a HPTLC method for the estimation of Cefpodoxime Proxetil. Indian Journal of Pharmaceutical Sciences 2007;69(2):331-333.
11. Naoto F, Takao K, Koichi S, Hiroyuki N. Application of high-performance liquid chromatography hyphenated techniques for identification of degradation products of Cefpodoxime Proxetil. Journal of Chromatography A;1129(2): 153-159.
12. Vasu KK, Vinod KA and Arvind KB. Development and validation of isomer specific RP-HPLC method for quantification of Cefpodoxime Proxetil. J Chromatogr B Analyt Technol Biomed Life Science 2006; 835(1-2):16-20.
13. Malathi S, Dubey RN, Venkatnarayanan R. Simultaneous RP-HPLC estimation of Cefpodoxime Proxetil and clavulanic acid in tablets. Indian journal of pharmaceutical sciences 2009;71(1):102-105.
