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Zero Order and Area Under the Curve Spectrophotometric methods for determination of Cefoperazone in Pharmaceutical Formulation

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Abstract: Simple, fast and reliable spectrophotometric methods were developed for determination of Cefoperazone in bulk and pharmaceutical dosage forms. The solutions of standard and the sample were prepared in methanol. The quantitative determination of the drug was carried out using the zero order derivative values measured at 230 nm and the area under the curve method values measured at 225-235 nm (n=6). Calibration graphs constructed at their wavelengths of determination were linear in the concentration range of Cefoperazone using 5-30 µg/.ml (r^2 = 0.9998 and r^2 = 0.9995) for zero order and area under the curve spectrophotometric method. All the proposed methods have been extensively validated as per ICH guidelines. There was no significant difference between the performance of the proposed methods regarding the mean values and standard deviations. Developed spectrophotometric methods in this study are simple, accurate, precise and sensitive to assay of Cefoperazone in injectables.
Keywords: Cefoperazone, Zero order derivative spectrum, Area under the curve spectrum.

1. Introduction:

Cefoperazone[1-6] is a third generation cephalosporin antibiotic indicated for the treatment of patients infected with susceptible strains of microorganisms. Cefoperazone are indicated for the treatment of the following infections when caused by susceptible organism like respiratory tract infections (upper and lower), urinary peritonitis cholecysitic , cholangits, and other intra-abdominal infections, septicemia, meningitis, skin and soft tissue infections bone and joint infections, pelvic inflammatory diseases, endometritis gonorrhea, and other infections of the genital tract.

Cefoperazone is chemically 7[R{2-(4-ethyl-2,3-dioxopiperazin-1-yl-carboxamide)-2-4hydroxylphenyl}acetamide]-3-[1-methyl-1H-tetrazol-5yl-thiomethyl]]-3-cephem-4caboxylate [3], [4].

The molecular formula of Cefoperazone is $C_{25}H_{27}N_9O_8S_2$.Structure is given in the [Fig. 1].The molecular mass of Cefoperazone is 667.65 g/mol. It is official drug in Indian Pharmacopoeia, British Pharmacopoeia and United state Pharmacopoeia. Freely soluble in water, soluble in methanol and very slightly soluble in alcohol.

Literature survey reveals that, stability-indicating HPLC[7-8], TLC[9], Fluorimetric determination[10], were found and few spectrophotometric methods for the quantitative estimation of Cefoperazone in bulk and pharmaceutical formulations have been developed.

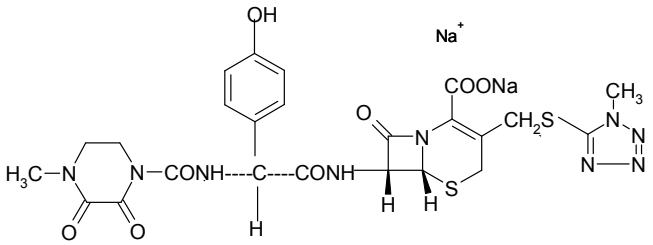

Figure 1. Chemical structure of Cefoperazone

2. Experimental

2.1. Materials and Methods

Cefoperazone was a gift sample by Karnataka Antibiotics and Pharmaceutical Ltd., Bangalore, India and was used without further purification. All chemicals and reagents used were of analytical grade and were purchased from Merck Chemicals, India.

2.2. Instrumentation

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

2.3. Preparation of Standard and Sample Solutions:

Stock solution of 1000 µg/ml of Cefoperazone was prepared in Methanol, for zero order and area under the curve spectrophotometric analysis. The standard solutions were prepared by dilution of the stock solution with Methanol in a concentration range of 5, 10, 15, 20, 25 and 30 µg/ml with Methanol for zero order and area under the curve spectrophotometric methods. Methanol was used as a blank solution.

2.4. Assay Procedure:

An aliquot of powder of Cefoperazone equivalent to the weight of 100 mg tablet was accurately weighed and transferred to volumetric flask and was dissolved in 100 ml of Methanol and made up to the volume with Methanol. The solutions were filtered through a 0.45 µm nylon filter and sonicated for about 15 min and then volume made up with Methanol. This solution was filtered to remove any insoluble matter. The filtrate was collected in a clean flask. Appropriate dilutions were made with Methanol from stock solution for both zero order and area under the curve spectrophotometric methods.

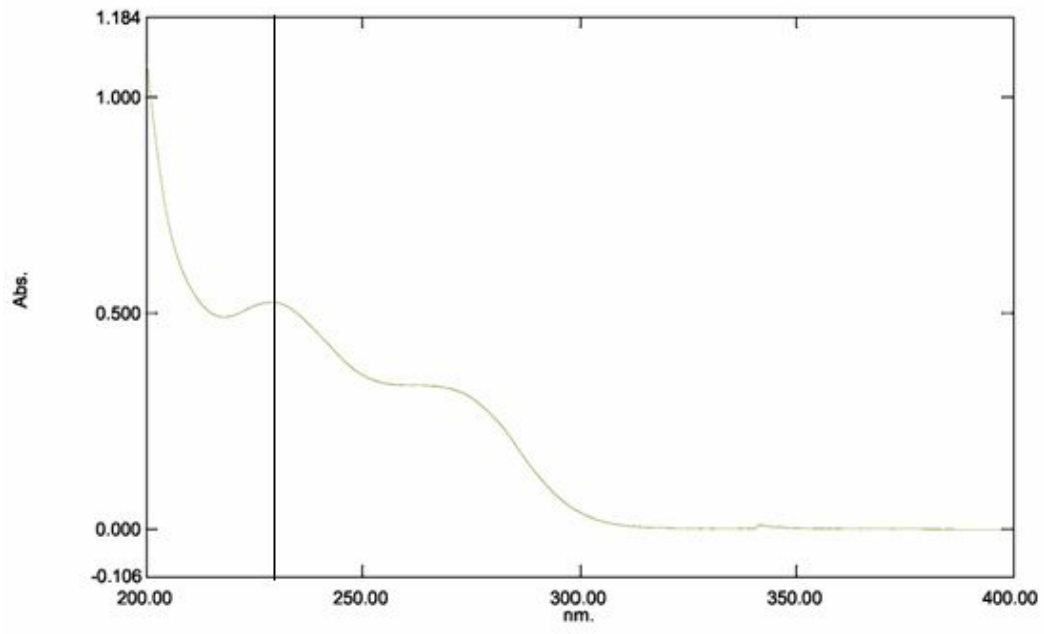

Figure 2. Zero order derivative spectrum of Cefoperazone in Methanol

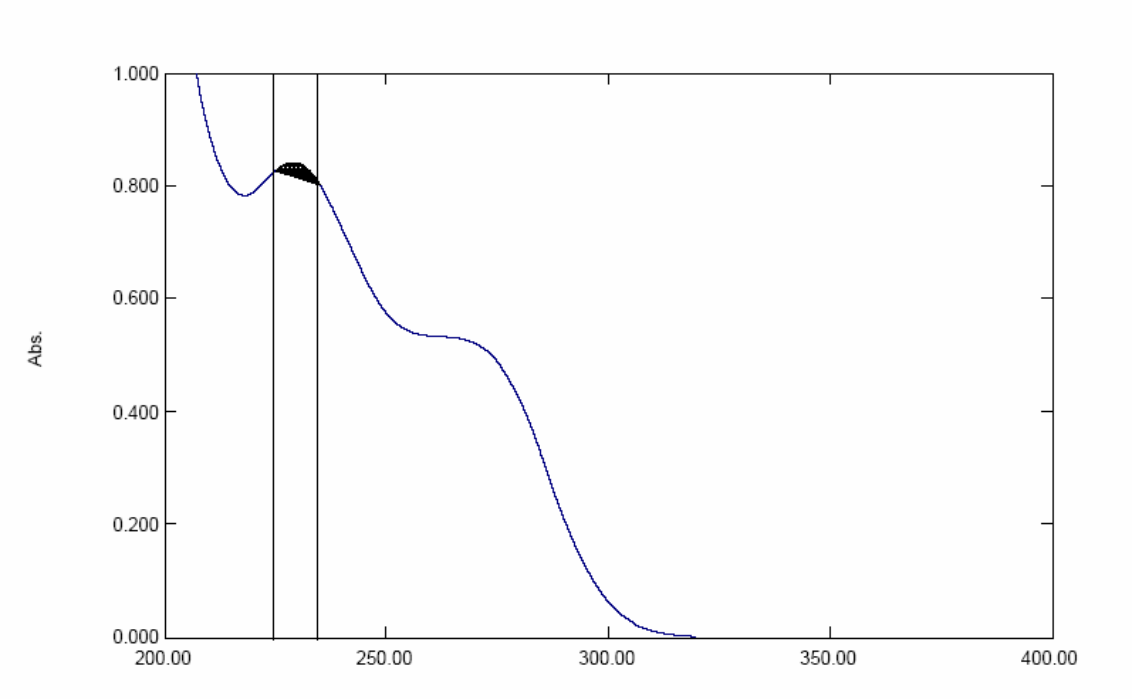

Figure 3. Area under the curve spectrum of Cefoperazone in Methanol

3. Results and Discussion

The zero order and area under the curve spectra for Cefoperazone were recorded at the wavelength of 230 nm and 225-235 nm respectively [Fig. 2 and 3].

3.1. Linearity and Range:

Under the experimental conditions described, the graph obtained for zero order and area under the curve spectra showed linear relationship. Regression analysis was made for the slope, intercept and correlation coefficient values. The regression equations of calibration curves were $y = 0.0346x + 0.0098$ ($r^2 = 0.9998$) at 230 nm for zero order derivative spectrophotometry and $y = 0.007x - 0.0011$ ($r^2 = 0.9995$) at 225-235 nm for area under the curve spectrophotometry. The range was found to be 5-30 µg/ml for both zero order and area under the curve spectrophotometric methods. (Table I).

Table I: Stastical data for the calibration graphs for determination of Cefoperazone by Proposed methods

Parameters	Zero order derivative	Area Under the Curve
Linearity range (µg/ml)*	5-30	5-30
$r^2 \pm$ S.D*	0.9998	0.9995

*n=6

Table II: Results of Intra and Inter Day Precision

Parameters	Intra Day Precision		Inter Day Precision	
	S.D*	% RSD*	S.D*	% RSD*
Zero derivative	0.2903	0.2901	0.2569	0.2571
Area under the curve	0.1940	0.1941	0.7083	0.7019

*n=6

Table III: Data of recovery studies

Level of % recovery	Mean Recovery*	Standard Deviation*	% RSD
Zero order derivative spectrophotometric method			
80%	100.013%	0.01398	0.01397
100%	100.011 %	0.00866	0.00865
120%	100.016 %	0.01143	0.01143
Area under the curve spectrophotometric method			
80%	100.02%	0.02037	0.02037
100%	100.00%	0.01527	0.01527
120%	100.01%	0.00946	0.00946

*n =6

Table IV: Assay results for the determination of Cefoperazone in pharmaceutical formulation

Parameters	Injectable brand name	Drug Content (mg)	% Found
Zero order derivative[a]	Kephazon 100 mg	100.01	100.01
Area under the curve[a]	Kephazon 100 mg	100.02	100.02

*n=6

Table V: Summary of validation parameters

Parameter	Zero derivative method	First derivative method
Wavelength (nm)	230	225-235
Linearity range (µg/ml)	5-30	5-30
Correlation coefficient	0.9998	0.9995
Slope(m)	0.0346	0.002
Intercept(c)	0.0098	0.006
Limit of detection (µg/ml)	0.4007	0.952
Limit of quantitation (µg/ml)	1.2145	2.886

3.2. Precision:

To determine the precision of the method, Cefoperazone solutions at a concentration of 15 µg/ml were analyzed each six times for both zero order and area under the curve spectrophotometric methods. Solutions for the standard curves were prepared fresh everyday (Table II).

3.3. Sensitivity:

The limit of detection (LOD) and limit of quantification (LOQ) were calculated by using the equations LOD = 3 x σ / S and LOQ = 10 x σ /S, where σ is the standard deviation of intercept, S is the slope. The LOD and LOQ were found to be 0.4007 µg/ml and 1.2145 µg/ml respectively for zero order derivative and The LOD and LOQ were found to be 0.2160 µg/ml and 0.6546 µg/ml for area under the curve methods respectively.

3.4. Recovery:

To study the accuracy of the proposed methods, and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition method. This study was performed by addition of known amounts of Cefoperazone to reanalyzed solutions of commercial injectables (Table III).

3.5. Analysis of the Marketed Formulation:

There was no interference from the excipients commonly present in the injectables. The drug content was found to be 100.006% and 100.01% zero order and area under the curve spectrophotometric methods respectively. It may therefore be inferred that degradation of Cefoperazone had not occurred in the marketed formulations that were analyzed by this method. The low % R.S.D. value indicated the suitability of this method for routine analysis of Cefoperazone in pharmaceutical dosage form (Table

IV). The summary of the validation parameters is depicted in (Table V).

4. Conclusion

No UV or Area Under Curve spectrophotometric methods have been described for the determination of Cefoperazone. Therefore simple, fast and reliable derivative spectrophotometric methods were developed for the routine determination of Cefoperazone. The developed methods can be concluded as accurate, sensitive and precise and can be easily applied to the pharmaceutical formulation.

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References

1. Trevor AJ., Katzung BG., Katzung and Trevor's pharmacology. 8th ed New York, Mc graw Hil., 2009,363-8.
2. ONeil MJ., The Merk Index- an encyclopedia of chemicals, Drugs and Biologicals. 13th edNew Jersey, Merk and co., 329.
3. Sweetmann SC., Martindale – The Complete Drug Reference, 33rd ed London (UK), Pharmaceutical Press., 2002, 168.
4. British Pharmacopoeia, Her Majesty's stationery office, London, Ph Eur Monograph 1204; 2005 vol-1, 368.
5. Indian Pharmacopoeia, Indian ministry of health & family welfare, The Indian pharmacopoeia commission Ghaziabad., 2010 vol-2, 1014-6.
6. The United States Pharmacopoeia, 22nd NF, Rockville MD: United States Pharmacopoeial Convention., 2004, 365-6.
7. Lalitha N., Puranik SB., Pai PNS., A Stability-Indicating HPLC Method for Cefoperazone. Eurasian J Anal Chem 2009, 4(1), 110-8.
8. Tsou TL., Huang YC., Lee CW., Lee AR., Wang HJ., Simultaneous determination of Ampicillin, Cefoperazone and Sulbactam in pharmaceutical formulations by HPLC with beta-cyclodextrin stationary phase. J Sep Sci 2007, 30, 2407-413.
9. Nabi SA., Laiq IA., Selective Separation and Determination of Cephalosporins by TLC on Stannic Oxide Layers. Acta Chromatographica 2004, 14, 92-100.
10. Bebwy L., Kelani K., Fattah LA., Fluorimetric determination of some antibiotics in raw material and dosage forms through ternary complex formation with terbium (Tb^{3+}). J Pharm Biomed Anal 2003, 32(6), 1129-225.

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