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Spectrophotometric Estimation of Cefetamet Pivoxil in Pharmaceutical Formulations

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Three new simple, sensitive, selective and economical methods (**A**, **B** and **C**) have been developed for the quantitative estimation of cefetamet pivoxil in bulk and its pharmaceutical formulations. Method **A** is based on the formation of pink coloured chromoges obtained when drug was dizotised with nitrous acid followed by coupling the resulting diazonium salt with diphenylamine exhibiting λ_{max} at 521 nm. Method **B** is based on the redox reaction of drug with Folin-Ciocalteau (FC) reagent exhibiting λ_{max} at 675.5 nm. Method **C** is based on the formation of coloured Schiff base obtained when drug reacted with PDAB (*p*-dimethylaminobenza1dehyde) to form yellow coloured chromogen exhibiting λ_{max} at 411 nm. These methods obeyed Beer's law in the concentration range of 10-50, 5-25 and 20-100 µg/mL, respectively. The results of analysis for the 3 methods have been validated statistically and by recovery studies. The results are comparable with those obtained with UV spectrophotometeric method in double distilled water at λ_{max} 234 nm.

Key Words: Cefetamet piovxil, Diphenylamine, Folin-Ciocalteau, Spectrophotometry, *p*-Dimethylaminobenzaldehyde.

INTRODUCTION

Cefetamet pivoxil is chemically (z)-7-[2-(2-aminothizol-4-yl)-2-methoxyimino acetamido]-3-methyl-3-cephem-4-carboxylic acid (Fig. 1)[1,2]. It is a 3rd-generation cephalosporin antibiotic characterized by a broad antibacterial spectrum and a resistance to β-lactamase producing organisms in addition to its antimicrobial activity (*Streptococii*, *staphylococci*, *pneumococci*, *etc.*[3]). Cephalosporins are distributed widely into tissues and body fluids, including pleural, pericardial and synovial fluids. However, while the earlier cephalosporins failed to penetrate the central nervous

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systems, the 3rd-generation cephalosporins enter the central nervous system and reach therapeutic concentrations, there sufficient for treatment pharyngitis. These characteristics are of considerable clinical and hence, analytical interest[4]. Several analytical procedures are available in the literature for the analysis of cefetamet pivoxil, *via* high performance liquid chromatographic[5,6], RP-HPLC[7], liquid chromatographic[8] and liquid chromatographic-tandem mass spectrophotometric[9] methods.

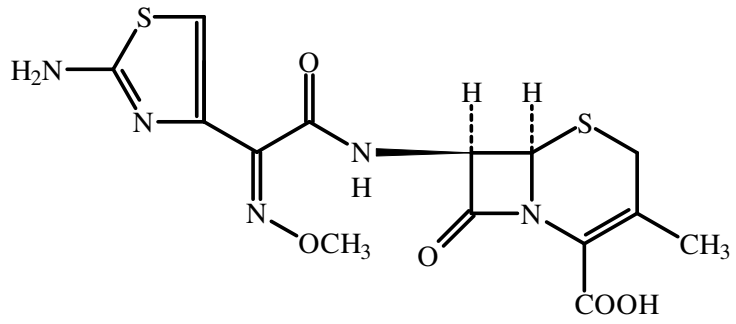

Fig. 1. Cefetamet pivoxil

EXPERIMENTAL

Analytical grade chemicals were used. All spectral measurement were made on Elico SL 164 Double Beam, UV-visible spectrophotometer.

Standard and sample solutions: Cefetamet pivoxil (pure or formulation) (*ca.* 100 mg) was accurately weighed and dissolved in 20 mL of double distilled water, transferred to standard 100 mL volumetric flask, the final volume made upto the mark with double distilled water. The final concentration was brought to 100 µg/mL with double distilled water.

Assay

Method A: Aliquots of cefetamet pivoxil ranging from 1-5 mL (1 mL = 100 µg) were transferred in to a series of 10 mL, volumetric flasks. To each of the above aliquots, conc. HCl (0.2 mL) and 1 mL aqueous solution of sodium nitrite (0.1 % w/v) were added and set aside for 15 min at room temperature. Aqueous solution (1.0 mL) of ammonium sulfamate (0.5 % w/v) and 1.0 mL alcoholic solution of diphenylamine (0.25 % w/v) were added to the solution and diluted with distilled water. The absorbance of pink coloured species was measured of 521 nm, against reagent blank, the coloured species was stable for more than 2 h. The amount of cefetamet pivoxil in the sample was computed from calibration curve.

Method B: Aliquots of cefetamet pivoxil ranging from 0.5-2.5 mL (1 mL = 100 µg) were transferred into a series of 10 mL, volumetric flasks, to each 1.5 mL Folin-Ciocalteau reagent (20 % v/v in distilled water) was added and allow to stand for 10 min. Then 1 mL aqueous solution of sodium hydroxide (1 N) was added, the final volume made upto 10 mL, with distilled water. The absorbance of the resultant blue coloured species formed was measured of 675.5 nm, which remains stable for 2 h after final dilution. The amount of cefetamet pivoxil in the sample was computed from calibration curve.

Method C: Aliquots of cefetamet pivoxil ranging from 1.0-5.0 mL (1 mL = 200 µg) were transferred into a series of 10 mL volumetric flasks. To each 2.0 mL alcoholic *p*-dimethylaminobenzaldehyde (0.5 % w/v) was added and heated at 60-70ºC for 25 min. After cooling, the volume was brought upto 10 mL with ethanol and the absorbance of the yellow coloured species formed was measured at 411 nm against reagent blank, which remains stable more than 10 h after final dilution. The amount of cefetamet pivoxil in the sample was computed from calibration curve.

The results of the above methods are compared with the results obtained with UV spectrophotometeric method. In UV method, solution of cefetamet pivoxil in distilled water either pure or formulation (100 µg/mL), was prepared. Aliquots of cefetamet pivoxil ranging from (0.5-2.5 mL) (1 mL = 100 µg) were transferred into series of 10 mL volumetric flasks. The volume was made upto mark with distilled water and the absorbance of the solution was measured of 234 nm against solvent blank. The amount of cefetamet pivoxil was computed from its calibration curve.

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, absorption maxima, molar absorptivity, Sandell's sensitivity, percent relative standard deviation (calculated from the eight measurements containing three-fourth of the amount of the upper Beer's law limits of cefetamet pivoxil) and per cent range of error (0.05 and 0.01 confidence limits) were calculated for the three methods and the results are summarized in Table-1. The optimum conditions for colour development for method **A**, **B** and **C** have been established by varying the parameters one at a time and keeping the other parameters fixed and observing the effects of product on the absorbane of the coloured species and it was incorporated in the procedures. The values obtained for the determination of cefetamet pivoxil in different tablet samples T_1, T_2 and T_3 by proposed methods are presented in Table-2.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

	Method A	Method B	Method C
λ_{max} (nm)	521	675.5	411
Beer's law limits (μg/mL) (C)	10-50	5-25	20-100
Molar absorptivity (L mol^{-1} cm^{-1})	2.6790×10^{3}	1.2095×10^{4}	6.5074×10^{3}
Sandell's sensitivity (μg/cm^2 0.001 absorption units)	0.030	0.025	0.055
Regression equation (Y = a + bc)*			
Slope (b)	9.6952×10^{-2}	2.9514×10^{-2}	1.0059×10^{-2}
Intercept (a)	-8.4095×10^{-2}	1.3892×10^{-2}	0.3131×10^{-2}
Correlation coefficient (r)	0.9980	0.9999	0.9999
RSD (%)	0.7430	0.7443	0.3467
Range errors**			
Confidence limits with 0.05 level	± 0.0012	± 0.0028	± 0.0077
Confidence limits with 0.01 level	± 0.0018	± 0.0041	± 0.0026

*Y is the absorbance and C is the concentration in μg/mL
**For eight measurements

TABLE-2
EVALUATION OF CEFTAZIDIME IN PHARMACEUTICAL PREPARATIONS

Sample no.	Labelled amount (mg)	Amount obtained (mg) proposed method*			Reference method	Percentage recover**		
		A	**B**	**C**	UV	**A**	**B**	**C**
T_1	100	99.62	99.15	99.62	99.89	99.69 ± 0.64	100.30 ± 0.77	99.51 ± 0.42
T_2	100	99.65	99.26	99.79	99.74	99.63 ± 0.52	99.73 ± 0.48	99.69 ± 0.35
T_3	100	99.84	99.54	99.84	99.93	99.71 ± 0.34	99.64 ± 0.51	99.71 ± 0.41

*Average of eight measurements.
**Mean and standard deviation of eight determinations.

To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceuticals preparation and the mixtures were analyzed by the proposed methods. The per cent recoveries are given in Table-2. These studies revealed that the common excipients and other additions such as lactose, starch, gelatin, talc and magnesium stearate, that are usually present in tablet dosage forms did not interfere at their regularly added levels.

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