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NOTE

Spectrophotometric Determination of Cefixime Trihydrate

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Two simple, sensitive and selective methods have been developed for the determination of cefixime in pure and pharmaceutical preparations. Method A is based on the formation of green coloured chromogen by oxidative coupling reaction with 3-methyl-2-bezothiazolinone hydrazone (MBTH) and ferric chloride having absorption maximum at 620 nm, whereas method B is based on the reduction and complex formation with ferric chloride and 1,10-phenanthroline which exhibit maximum absorption at 510 nm. These methods obey Beer's law in the concentration range of 1 to 15 μg/mL and 0.2 to 6 μg/mL respectively. The methods are statistically evaluated for accuracy and precision.

Cefixime trihydrate (CXT) is chemically 7-[[(2)-(2-amino-4-thiazolyl) glyoxyl amido]-8-oxo-3-vinyl-5-thia-1-azabicyclo-[4.2.0]-oct-2-ene-2-carboxylic acid, 7-[O-(carboxymethyl) oxime]-trihydrate. It is a semisynthetic cephalosporin antibiotic which is useful in the treatment of bronchitis, gonorrhoea, urinary tract infections, pharyngitis and tonsillitis. Literature survey revealed very few analytical methods which include HPLC[1] and spectrophotometry[2, 3]. The present work deals with the determination of the drug in dosage form using 3-methyl-2-benzothiazolinone hydrazone (MBTH) and ferric chloride (method A) and 1,10-phenanthroline and ferric chloride (method B), which forms coloured chromogens having maximum absorbance at 620 nm and 510 nm respectively.

The standard and sample (powdered tablets) solutions of CXT were prepared by dissolving equivalent amount 100 mg of CXT in distilled water. The above stock solution was further diluted with distilled water to get a working standard solution of 50 μg/mL for method A and 20 μg/mL for method B.

All the chemicals used were of analytical grade. Ferric chloride (0.5% and 0.9%), 1,10-phenanthroline (0.01 M), MBTH (0.2%) were prepared in distilled water.

All spectral measurements were made on Systronics UV-visible spectrophotometer model 117 with 10 nm matched quartz cells.

Assay Procedure

Method A: Aliquots of the drug solution ranging from 0.5–2.5 mL

(1 mL = 50 μg) were transferred into a series of 10 mL volumetric flasks. To each flask 2 mL of $FeCl_3$ (0.5%) and 2 mL of MBTH (0.2%) were added, shaken well and made up to mark with distilled water. It was stable for 3 h. The absorbance was measured at 620 nm against reagent blank. The amount of the CXT present in the sample solution was computed from its calibration curve.

Method B: To a series of 10 mL graduated test tubes, standard drug solution ranging from 0.5–3.0 (1 mL = 20 μg), 0.5 mL of $FeCl_3$ (0.9%) and 1.5 mL of 1,10-phenanthroline (0.01 M) were added. The tubes were heated on a boiling water bath for 10 min, cooled and the solution was made up to mark with distilled water; it was stable for 2 h. The absorbance was measured at 510 nm against reagent blank. The amount of the drug present in the sample solution was computed from its calibration curve.

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, per cent relative standard deviation (calculated from the eight measurements containing 3/4th of the amount of the upper Beer's law limits of CXT) and % range of error (0.05 to 0.01 confidence limits) are summarized in Table-1. Regression analyses using the method of least squares was made for the slope (a), intercept (I), and correlation coefficient (r) obtained from different concentrations are given in Table-1.

. TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

Parameters	Method A	Method B
Beer's law limit (μg/mL)	1–15	0.2–6
Sandell's sensitivity (μg/cm^2/0.001 absorbance unit)	0.01614	0.00766
Molar extinction coefficient (1 mole^{-1}·cm^{-1})	2.7629×10^4	5.9173×10^5
%Relative standard deviation	0.4711	0.9337
%Range of error		
0.05 confidence limits	± 0.3939	± 0.7807
0.01 confidence limits	± 0.5828	± 1.1551
Correlation coefficient	0.9953	0.9994
Regression equation (A*)		
Slope (a)	0.0571	0.1281
Intercept (I)	0.0055	0.0064

A* = I + aC, where C is concentration in μg/mL and A is absorbance unit.

The proposed methods have been extended to commercial formulations and the results obtained by the proposed and reported methods are presented in Table-2. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the pre-analyzed pharmaceutical preparations and the mixtures were analyzed by proposed methods and the per cent recoveries are given in Table-2. Interference studies revealed that the common excipients

and other additives usually present in the dosage form did not interfere in the proposed methods.

TABLE-2
ESTIMATION OF CEFIXIME TRIHYDRATE IN PHARMACEUTICAL FORMULATIONS

Sample	Labelled amount (mg)	Amount obtained (mg)			Per cent recovery of the proposed method**	
		Reported method*	Proposed method			
			A	B	A	B
1	100	99.8	99.7	99.5	99.7	99.5
2	100	100.2	99.8	100.5	99.8	100.5
3	100	100.8	100.6	99.8	100.6	99.8

*UV method developed in our laboratory.
**Average of six determinations

In method A, MBTH loses two electrons and one proton on oxidation, forming the electrophilic intermediate which couples with CXT to form green coloured complex. The blood red coloured complex resulting from CXT with 1,10–phenanthroline and ferric chloride in method B may be due to the fact that each of the two nitrogen atoms in 1,10-phenanthroline has an unshared pair of electrons that can be shared with Fe(II) ion [formed by reaction of CXT with Fe(III)]. Three such molecules of 1,10-phenanthroline attach themselves to the metallic ion to form ferroin complex. The results indicate that the proposed methods are simple, sensitive, precise, reproducible and accurate and can be used for the routine determination of CXT in bulk as well as in pharmaceutical preparations.

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