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NOTE

Spectrophotometric Determination of Cefepime and Ezetamibe

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A simple and sensitive visible spectrophotometric method has been developed for the estimation of cefepime and ezetamibe (EZM) in pure as well as in pharmaceutical formulations. This method is based on the formation of oxidative-coupling product with 3-methyl-2-benzothiazolinone hydrazone in the presence of ceric ammonium sulphate, which exhibits maximum absorbance at 640 nm and 555 nm for cefepime and ezetamibe respectively. Beer's law is obeyed at the concentration range of 10–40 μg/mL for cefepime and 5–25 μg/mL for ezetamibe. The method has been statistically evaluated and is found to be precise and accurate.

Key Words: Spectrophotometric determination, Cefepime, Ezetamibe.

Cefepime (CFM) is III generation cephelosporin and is chemically pyrrolidinium, 1-[[6R,7R)-7-[(2Z)-(2-amino-4-thiazolyl) (methoxyimino) acetyl] amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-en-3-yl] methyl]-1-methyl-. Ezetamibe (EZM)[4] is a cholesterol reducing agent. Chemically EZM is 2-azetidinone, 1-(4-fluorophenyl)-3-[(3s)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)-. A few methods[1–3] have been reported for CFM. Literature survey reveals that no methods are reported for the estimation of EZM. The present method describes the reaction of cefepime or ezetamibe with 3-methyl-2-benzothiazolinone hydrazone (MBTH) reagent in the presence of an oxidizing agent like ceric ammonium sulphate (CAS) to develop a coloured species, which exhibits absorption maximum at 640 nm or 555 nm respectively.

All the chemicals used were of analytical grade. Spectral and absorbance measurements were made on Systronics UV-Visible spectrophotometer-117 with 10 mm matched quartz cells.

MBTH (0.2%): 200 mg of MBTH was dissolved in 100 mL of distilled water.

CAS: Required amount of CAS was dissolved in 100 mL of 0.72 M sulphuric acid to get 0.5% and 1.0% solutions.

Preparation of standard and sample solutions

100 mg of CFM was dissolved in 100 mL of distilled water. The stock solution

was further diluted with distilled water to get a working standard solution of 200 µg/mL. Accurately weighed injection powder of CFM equivalent to 100 mg of the drug was dissolved in 100 mL of distilled water and filtered. This solution was further diluted with water to get 200 µg/mL of working standard solution.

100 mg of EZM was dissolved in 10 mL of sodium hydroxide (0.1 N) and made up to 100 mL with distilled water. The stock solution was further diluted with distilled water to get working standard solution of 100 µg/mL. Ten tablets of EZM were accurately weighed and finely powdered. The powder equivalent to 100 mg of the drug was dissolved in 10 mL of sodium hydroxide (0.1 N), made up to 100 mL with distilled water and filtered. The solution was further diluted with water to get 100 µg/mL working standard solution.

Assay procedure: Aliquot volumes of standard CFM solution ranging from 0.5 to 2.0 mL (200 µg/mL) or EZM solution ranging from 0.5 to 2.5 mL (100 µg/mL) were transferred to a series of 10 mL volumetric flasks. To each of the flasks, 1.0 mL of MBTH and 1.5 mL of 0.5% ceric ammonium sulphate for CFM or 1.5 mL of MBTH and 1.5 mL of 1.0% ceric ammonium sulphate for EZM were added and kept aside for 5 min at room temperature. The solutions were made up to volume with distilled water. The absorbance of the coloured species formed was measured at 640 nm or 555 nm respectively against a reagent blank. The amount of the drug present in the sample was computed from the Beer-Lambert plot.

The reaction of MBTH with CFM or EZM in the presence of ceric ion proceeds *via* oxidative coupling reaction. Under the reaction conditions, MBTH on oxidation loses two electrons and one proton, forming the electrophilic intermediate, which is the active coupling species. The intermediate reacts with amine (CFM)[5] or phenol (EZM)[6-7] by electrophilic attack on the most nucleophilic site on the aromatic ring of the amine or phenol (*i.e.*, *para* or *ortho* position if *para* position to amino or phenolic hydroxyl group is substituted) and the resulting intermediate is spontaneously oxidized with CAS to form the coloured species having maximum colour sensitivity, stability and minimum blank colour. The experimental conditions were optimized by studying the effect of MBTH concentration, CAS concentration and sequence of addition.

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), regression equation, correlation coefficients, % range of error (0.05 and 0.01 confidence limits) are calculated and shown in Table-1.

Pharmaceutical formulations of CFM and EZM were successfully analyzed by the proposed method. The results obtained by the proposed method and reported method are presented in Table-2. To evaluate validity and reproducibility of the method, known amounts of pure drug were added to previously analyzed samples and the mixtures were analyzed by the proposed method. There is no interference of other ingredients present in formulations. These results indicate that the method is simple, rapid with reasonable precision and accuracy and is applicable to various formulations of cefepime and ezetamibe.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION OF THE PROPOSED METHODS FOR CFM and EZM

Parameter	CFM	EZM
λ_{max} (nm)	640	555
Beer's law limits (μg/mL)	10–40	5–25
Sandell's sensitivity (μg cm^{-2}/0.001 absorbance unit)	0.0470	0.0330
Molar absorptivity (l mol^{-1} cm^{-1})	1.0×10^4	1.22×10^4
Regression equation (Y = a + bC)	—	—
Slope (b)	0.0200	0.0300
Intercept (a)	0.0100	0.0020
Correlation coefficient (r)	0.9993	0.9998
Relative standard deviation (%)*	0.2223	0.6849
Range of error (confidence limits)*	—	—
0.05 level	0.1858	0.5727
0.01 level	0.2750	0.8473

*Average of eight determinations.

TABLE- 2
ASSAY AND RECOVERY OF CFM and EZM IN DOSAGE FORMS

Name of the dosage form	Labelled amount	Content of drug found		% Recovery by proposed methods†
		Proposed method (mg)	Reported method[R] (mg)	
Cefepime:				
Injection I	500	499	500.12	99.8
Injection II	500	501	500.45	100.2
Ezetamibe:				
Tablet I	10	10.12	10.05	101.2
Tablet II	10	10.04	10.02	100.4

†Recovery amount is the average of five determinations.

[R]Reference was UV method developed in the laboratory.

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