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NOTE

Spectrophotometric Determination of Ezetimibe and Cefepime

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A simple, sensitive spectrophotometric methods has been developed for the estimation of ezetimibe and cefepime in pure as well as in pharmaceutical formulations. This method is based on the formation of diazo coupling product with N-1-napthyl-ethylene diamine dihydrochloride in the presence nitrous acid, which exhibits maximum absorbance at 555 and 570 nm for ezetimibe and cefepime, respectively. Beer's law is obeyed at the concentration range of 2.5-12.5 μg/mL for ezetimibe and 25-125 μg/mL for cefepime, respectively.

Key Words: Spectrophotometric, Ezetimibe, Cefepime.

Ezetimibe (EZM)[1] is a cholesterol reducing agent. Chemically, it is 2-azetidinone, 1-(4-fluorophenyl)-3-[(3S)–3-(4-fluorophenyl)-3-hydroxy propyl]-4-(4-hydroxy phenyl)-(3R,4S). Cefepime (CFM)[2] is an antibacterial agent belongs to the third generation cephalosporins. Chemically, it is 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-pyrrolidinium. Literature survey reveals that no colorimetric method has been reported for ezetimibe and a few methods have been reported for the determination of cefepime[3-5] which include HPLC and colormetry.

Spectral and absorbance measurements were made on Systronics UV-visible spectrophotometer-117 with 10 mm matched quartz cells. All the chemicals used were of analytical grade. Hydrochloric acid (5 N), sodium nitrite (0.1%), ammonium sulphamate (0.5%) and N-1-naphthyl-ethylene diamine dihydrochloride (0.1%) were prepared.

Preparation of standard solutions: Accurately weighed 100 mg of EZM was dissolved in 10 mL of sodium hydroxide (0.1 N) and then diluted stepwise with distilled water to obtain working standard solution of 50 μg/mL. The stock solution of cefepime (1 mg/mL) was prepared by dissolving 100 mg of drug in 100 mL of distilled water and then diluted with distilled water to obtain a concentration of 500 μg/mL.

Preparation of sample solutuions: Accurately weighed amount of tablet powder of ezetimibe equivalent to 100 mg was dissolved in 10 mL of NaOH (0.1 N), diluted to 100 mL with distilled water and filtered. This solution was further diluted with distilled water so as to obtain a concentration of 50 μg/mL. Formulation (injection) powder equivalent to 100 mg of cefepime was accurately weighed and dissolved in 100 mL of distilled water and it was further diluted with water to obtain a concnetration of 500 μg/mL and filtered if necessary.

Assay procedure for ezetimibe: Aliquots of solution 0.5 to 2.5 mL (50 μg/mL) were transferred into a series of 10 mL volumetric flasks, 0.5 mL of hydrochloric acid and 1.0 mL of sodium nitrite were added and shaken for 2 min to complete diazotization. Then, 0.5 mL of ammonium sulphamate was added and shaken for 1 min. N-1-Naphthylethylene diamine dihydrochloride (2.0 mL) was added and made up to the volume with distilled water. The absorbance was measured at 555 nm against a reagent blank. The amount of ezetimibe present in the sample solution was computed from its calibration curve.

Assay procedure for cefepime: Aliquots of solution 0.5 to 2.5 mL (500 μg/mL) were transferred into a series of 10 mL volumetric flasks, 2.0 mL of HCl and 1.0 mL of sodium nitrite were added and shaken for 2 min to complete diazotization. Ammonium sulphamate (0.5 mL) was added and shaken for 1 min followed by the addition of 0.5 mL of ammonium sulphamate and shaken for 1 min. N-1-Napthylethylene diamine dihydrochloride (0.5 mL) was added and made upto the volume with distilled water. The absorbance was measured at 570 nm against a reagent blank. The amount of cefepime present in the sample solution was computed from its calibration curve.

The optical characteristic 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) were calculated and the results are summarized in Table-1. Regression characteristics like slope, intercept, % range of error (0.05 and 0.01 confidence limits) were calculated (Table-1).

Commercial formulations of ezetimibe and cefepime were successfully analyzed by the proposed and reference methods[R], values obtained by the proposed and reference methods (Table-2). Adding a fixed amount of the drug to the pre-analyzed formulations performed accuracy and recovery experiments (Table-2). There is no interference in the proposed analytical methods. In conclusion the proposed spectrophotometric method for the estimation of ezetimibe and cefepime are simple, sensitive, accurate and can be used for the routine quality control of these drugs in bulk as well as in pharmaceutical formulations.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION OF THE PROPOSED METHOD

PARAMETER		TMZ	GMC
λ_{max} (nm)		555	570
Beer's law limits (μg/mL)		2.5-12.5	2-125
Molar absorptivity (L mol^{-1} cm^{-1})		2.1×10^4	2.0×10^3
Sandell's sensitivity (μg cm^{-2}/0.001 absorbance unit)		0.018	0.238
Regression equation (Y = a + bC)	Slope (b)	0.0528	0.004
	Intercept (a)	-0.018	-0.068
Correlation coefficient (r)		0.9999	0.9998
Relative standard deviation (%)*		0.360	0.700
% Range of error (Confidence limits)*	0.05 level	0.301	0.585
	0.01 level	0.445	0.865

*Average of eight determinations

TABLE-2
ASSAY AND RECOVERY OF EZETIMIBE AND CEFEPIME IN DOSAGE FORMS

Name of the dosage form	Labeled amount (mg)	Content of drug found		% Recovery by proposed method*
		Proposed method (mg)	Reference method[R] (mg)	
Tablets I	10	10.02	10.03	100.20
Tablets II	10	10.03	9.98	100.00
Cefepime				
Injection I	500	500.22	502.50	100.04
Injection II	500	500.35	500.35	100.07

*R Reference was UV method developed in the laboratory.
**Recovery amount was the average of five determinations.

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