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NOTE

1,10-Phenanthroline as an Analytical Reagent for the Estimation of Cefepime and Repaglinide

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A simple and sensitive spectrophotometric method has been developed for the estimation of cefepime (CFM) and repaglinide (RGP) in pure as well as in pharmaceutical formulations. This method is based on the oxidation of drug with ferric chloride followed by complexation with 1,10-phenanthroline (1,10-PTL) to form a blood red coloured chromogen exhibiting maximum absorbance at 520 nm (for CFM) or 515 nm (for RPG). Beer's law is obeyed in the concentration range of 1–7.5 μg/mL for CFM and 2.5–15 μg/mL for RPG. The method was extended to pharmaceutical formulations. There was no interference from any common pharmaceutical excipients and diluents.

Key Words: 1,10-Phenanthroline, Cefepime, Repaglinide.

Cefepime (CFM) is an antibacterial agent belonging to the third generation cephalosporins. Chemically, it is 1-(6R,7R)-7-[(2Z)-(amino-4-thiazolyl)(methoxy imino)acetyl] amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl] methyl]-1-methyl-pyrrolidinium. Repaglinide (RPG) is a non-sulfonylurea antidiabetic drug; chemically is 2-ethoxy-4-[2-[[(1S)-3-methyl-1-[2-(1-piperidinyl) phenyl] butyl] amino]-2-oxoethyl] benzoic acid. Literature survey reveals that a few methods have been reported for the determination of CFM[1–3] and RPG[4, 5] which include HPLC and colorimetry. The present method describes the reaction of cefepime or repaglinide with ferric chloride and 1,10-phenanthroline to develop a blood red coloured species, which exhibits absorption maximum at 520 or 515 nm respectively.

Spectral and absorbance measurements were made on Systronics UV-Visible spectrophotometer-117 with 10 nm matched quartz cells.

Preparation of standard and sample solutions

Cefepime: The stock solution (1 mg/mL) of cefepime (CFM) was prepared by dissolving 100 mg of drug in 100 mL of distilled water and it was diluted with distilled water to obtain a concentration of 25 μg/mL.

Formulation (injection) powder equivalent to 100 mg of CFM was accurately weighed and dissolved in 100 mL of distilled water and further diluted with water to obtain a concentration of 25 μg/mL and filtered if necessary.

Repaglinide: The stock solution (1 mg/mL) of repaglinide (RPG) was prepared by dissolving 100 mg of drug in 5 mL of methanol and then made up

to 100 mL with distilled water. This solution was diluted with distilled water to obtain the working standard solution of concentration 50 μg/mL.

An accurately weighed amount of tablet powder of RPG equivalent to 100 mg of the drug was dissolved in 5 mL of methanol and then made up to 100 mL with distilled water. This solution was further diluted with distilled water to obtain a concentration of 50 μg/mL and filtered if necessary.

Assay procedure

Aliquots of standard drug solution ranging from 0.5–2.5 mL (25 μg/mL for CFM or 50 μg/mL for RPG) were transfered to a series of 10 mL graduated test tubes. To each of the test tubes, 0.5 mL of ferric chloride and 2.0 mL of 1,10-phenanthroline (0.2%) (for CFM) or 1.0 mL of 1,10-phenanthroline (0.2%) (for RPG) were added and heated for 10 min in a boiling water bath, cooled and then 1 mL of *o*-phosphoric acid was added. The solutions were made up to volume with distilled water. The absorbance was measured at 520 nm (for CFM) or at 515 nm (for RPG) against a reagent blank. The coloured species was stable for 1 h. The amount of the drug in the sample was computed from the Beer-Lambert plot.

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 Beer's law limits) were calculated and the results are summarized in Table-1.

Regression characteristics like standard deviation of slope (S_b), standard deviation of intercept (S_a), standard error of estimation (S_e), % range of error (0.05 and 0.01 confidence limits) were calculated and are shown in Table-1.

This method depends upon the oxidation of drug with Fe(III) and subsequent coloured complex formation of the resulting Fe(II) ion with 1,10-PTL. 1,10-PTL forms a complex of low tinctorial value with Fe(III) which in turn functions as a better oxidant than Fe(III) itself. The reduction product is a tris-complex of Fe(II), well known as ferroin[6].

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION OF THE PROPOSED METHODS FOR CEFEPIME AND REPAGLINIDE

Parameters	Cefepime	Repaglinide
λ_{max} (nm)	520	515
Beer's law limits (μg mL^{-1})	1–7.5	2.5–15
Molar absorptivity (1 mol^{-1} cm^{-1})	5.157×10^4	2.966×10^4
Sandell's sensitivity (μg cm^{-2}/0.001 absorbance unit)	0.0093	0.01524
Regression equation (Y = a + bC)		
Slope (b)	1.05×10^{-1}	-1.5×10^{-3}
Intercept (a)	2.8×10^{-3}	6.5×10^{-2}
Correlation coefficient (r)	0.9997	0.9999
Relative standard deviation (%)*	0.396	0.727
% Range of error (confidence limits)*		
0.05 level	0.3313	0.6078
0.01 level	0.490	0.899

* Average of eight determinations.

Commercial formulations of CFM and RPG were successfully analyzed by the proposed and reference methods. The values obtained by the proposed and reference methods are presented in Table-2. As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the pre-analyzed formulations. These results are summarized in Table-2. There is no interference in the proposed analytical methods. In conclusion the proposed spectrophotometric methods for the estimation of CFM and RPG are simple, sensitive, accurate and can be used for the routing quality control of these drugs in bulk as well as in pharmaceutical formulations.

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

Name of the dosage form	Labelled amount (mg)	Content of drug found		% Recovery by proposed method*
		Proposed method (mg)	Reported method[R] (mg)	
Cefepime				
Injection I	500	500.12	502.5	100.02
Injection II	500	500.45	500.1	100.09
Repaglinide				
Tablets I	2	1.98	1.99	99.00
Tablets II	2	2.01	2.01	100.50

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

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REFERENCES

1. X. Yan, H. Yan, G. Cao and X. He, *Zhongguo Xinyao Zazhi*, **13**, 47 (2004).
2. V. Evagelo, A. Tsantili-kalkoulidou and M. Koupparis, *J. Pharm. Biomed. Anal.*, **31**, 1119 (2003).
3. M.S. Elazazy, A. Shalaby, M.N. Elboikiny and H.M. Khalil, *Sci. Pharm.*, **71**, 211 (2003).
4. M. Gandhimathi, T.K. Ravi and S.K. Renu, *Anal. Sci.*, **19**, 1675 (2003).
5. K.V.S.R. Krishna Reddy, J. Babu, M. Moses, T. Vijayavithal, S. Eswaraiah, M. Satyanarayan Reddy, P.K. Dubey and K. Vyas, *J. Pharm. Biomed. Anal.*, **32**, 461 (2003).
6. A. Besada, *Anal. Lett.*, **20**, 427 (1980).

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