ISSN : 0974-7419 Volume 12 Issue 12

Trade Science Inc.

Analytical CHEMISTRY

An Indian Journal

Full Paper

ACAIJ, 12(12) 2013 [458-460]

IR quantification of Doripenem in pharmaceutical dosage form

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ABSTRACT

Simple and sensitive Infrared Spectrophotometric method has been developed for the estimation of Doripenem in pharmaceutical formulation; Beer's concentration range was found to be 1mg-5mg. The correlation coefficient for the method was found to be 0.998 and the developed method was analyzed for specificity, limit of detection (LOD), limit of quantification (LOQ), linearity of response, precision and accuracy; thus the proposed method could be adopted for routine analysis of bulk drug and its formulation.

KEYWORDS

Infrared spectroscopy (IR);
Beer's law;
Limit of detection (LOD);
Limit of quantification (LOQ).

INTRODUCTION

Doripenem[5] is chemically (4R, 5S, 6S)-6-(1-hydroxyethyl)-4-methyl-7-oxo-3- [(3S,5S)-5[(sulfamoylamino)methyl]pyrrolidin-3-yl]sulfanyl-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid. It is a beta-lactam ultra-broad spectrum injectable antibiotic and belongs to the subgroup of carbapenems. In comparison to other carbapenems, it has equal or greater activity than meropenem and imipenem against *β-lactam–nonsusceptible Enterobacteriaceae*, including strains with extended spectrum *β-lactamases* (ESBLs). Doripenem was found to be the most active carbapenem against *Pseudomonas aeruginosa*. Several analytical methods have been reported for the determination of Doripenem raw material. Literature survey revealed that few sophisticated analytical methods have been reported for the estimation of Doripenem. The present work aims to devise a novel method by Infrared spectrophotometry (IR) which has not been reported till date.

MATERIALS AND METHOD

All the chemicals used throughout the experiment were of highest purity of (IR grade).

1. Potassium bromide (KBr)
2. Internal standard: potassium thiocyanate (KCNS)
3. Bulk material: sample of Doripenem was gifted from orchid pharmaceutical Limited.
4. Dosage form : Doripenem was purchased from local market.

EXPERIMENTAL METHODS[1]

Instrumentation

All spectral measurements were made on ABB-IR instrument (model no. MB 3000) with KBr press (model no. M15).

Calibration of the standard

Potassium thiocyanate was used as an internal standard which was preground, dried, and then reground

with dry KBr to make a concentration of about 0.2% by weight of thiocyanate. The final mixture was stored over phosphorus pentoxide. Five different concentration of standard and KBr-KCNS were prepared by mixing known weights of the standard substance with a known weight of the KBr-KCNS mixture and then grinding by using agate mortar & pestle. A standard calibration curve was constructed using absorbance and concentration.

TABLE 1 : Ratio for preparing discs.

KBr/KCNS (in mg)	50	50	50	50	50	50
Standard (in mg)	0.0	1	2	3	4	5

The discs were prepared by using KBr press and the infrared spectrum was recorded in absorbance mode; the calibration curve was obtained by plotting the amplitude of the IR absorption at 2060 cm^{-1} (prominent band) against the concentration of the substance.

TABLE 2 : Optical parameters of Doripenem by IR – spectroscopy.

S. No	Parameters	Infrared spectroscopy quantification method
1	Beer's law limit(mg)	0.5-2.5
2	Regression equation (y= mx+c)	15.69x+0.016
3	Slope(m)	28.624
4	Intercept (c)	1.785
5	Correlation coefficient	0.998
6	LOD (µg/mL)	0.370
7	LOQ (µg/mL)	1.122

TABLE 3 : Assay result for Doripenem.

S. No	Method	Label claim	Amount found by proposed method(mg)	% label claim	SD	SE	(95%) CI	% RSD
1	Infrared spectroscopy quantification method	500mg	497.190	99.43	0.80033	0.462	0.3400	0.8077

***Each value is a mean of 3 determinations**

TABLE 4 : Recovery studies.

S.No	Method	Label claim	Amount of drug added (%)	Amount of drug recovered (%)	% Recovery
1	Infrared quantification method	500mg	50	49.8	99.6
			100	99.2	99.2

***Each value is a mean of 3 determinations**

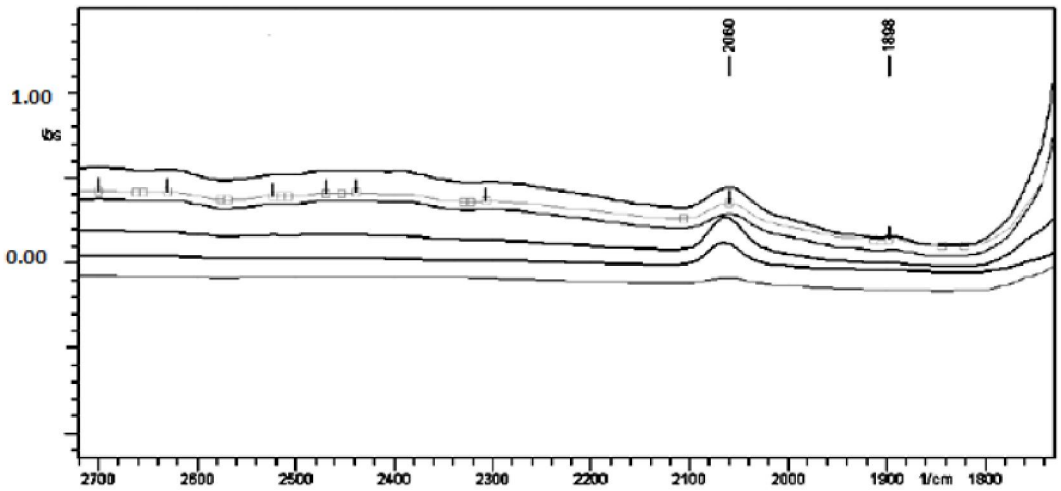

Figure 1 : IR spectra of standard Doripenem with internal standard KBr/KCNS).

ASSAY[1]

Average content of Doripenem vials were determined and homogenized to fine powder. Accurately weighed quantity powder equivalent to 1mg of Doripenem was mixed with the KBr/KCNS mixture and then homogenised by using agate mortar& pestle. The final powder was transferred to KBr press to form a disc and the infrared spectrum in absorbance mode

was recorded. The sample peak area was interpolated on the respective linearity chart of the Doripenem and the concentration was determined.

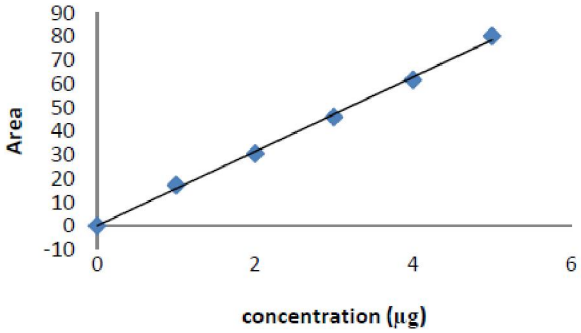

Figure 2 : Calibration curve of Doripenem versus peak area.

RECOVERY STUDIES

The recovery studies were carried out on spiked samples by adding predetermined amount of standard drugs to the respective sample. About 50 and 100% of standard drugs were added to the sample and the absorbance was measured. The percentage recovery was calculated. The recovery study was performed at two levels to confirm the precision and accuracy of the above said method.

RESULTS AND DISCUSSIONS

Doripenem was found to obey Beer's law in the concentration range of 0.5mg-2.0mg; showed good linearity as indicated by correlation coefficient value of to 0.998. The optical parameters of Doripenem are presented in TABLE 2. The percentage of the drug in the formulation was calculated and presented in TABLE 3.

The results of the analysis showed that the amount of drug present in the formulation was in good agreement with the label claim of the formulation. The accuracy of the proposed method was determined by recovery study. The recovery studies were carried out on spiked samples at two levels 50%, 100%. The percentages recovered were found to be in the range of 99-100% represented in TABLE.3 which showed that the excipients in the formulation did not interfere with the analysis. The IR quantification process does not involve prior extraction and is independent of drug materials solubility.

CONCLUSION

The percentage recovery of the method lies between 99-100 %. The correlation coefficient for the method was found to be 0.998 and the recovery studies indicates that there is no interference of other ingredients present in the formulation. Thus the method is simple, precise, accurate, less time consuming and could be used for routine analysis. Without prior treatment of analyte.

ACKNOWLEDGEMENT

The authors are thankful to the Department of Pharmaceutical Chemistry, College of Pharmacy, Madras Medical College for rendering full support to carry out the study.

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