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DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF DORIPENAM IN BULK AND PHARMACEUTICAL DOSAGE FORMS

P. Pravalika Reddy*[1], Dr. G. Tulja Rani[2] and T. Devi[3]

Department of Pharmaceutical Analysis.

[1,2,3]Malla Reddy Pharmacy College, Maisammaguda, Dhulapally, Secunderabad-500100.

***Corresponding Author: P. Pravalika Reddy**

Department of Pharmaceutical Analysis. Malla Reddy Pharmacy College, Maisammaguda, Dhulapally, Secunderabad-500100.

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ABSTRACT

In the present work a simple, accurate and cost effective UV Spectrophotometric method has been developed for determination of Doripenem in bulk and pharmaceutical formulations. The optimum conditions for the analysis of drug are established and Doripenem is found to exhibit maximum absorption at 298 nm with water as solvent. The present method is validated as per guidelines of the International Conference on Hormonization (ICH) including parameters like linearity, accuracy, precision, limit of detection and limit of quantification. Drug obeyed Beer's law in concentration range of 10-50µg/ml and the regression equation is found to be Y=0.0239X+0.0105 with correlation coefficient 0.999. From the results it is observed that good correlation exist between drug concentration and absorbance. The percent recovery of Doripenem is found to be 98.3-99.57. The precision is evaluated and relative standard deviation (RSD) is less than 2%, LOD & LOQ are 0.133 & 0.40 respectively. The method is applied to marketed formulation (Doricrit) and Doripenem content is found to be 99.2 with respect to labeled claim. The results suggest that this method can be employed for routine analysis of Doripenem in bulk and commercial pharmaceutical formulations.

KEYWORDS: Doripenem, Spectrophotometric method and Validation.

INTRODUCTION

Doripenem[1] is an ultra broad-specrtum, injectable antibiotic with bactericidal and beta-lactamase resistant activities. It is a beta-lactam antibiotic and belongs to the subgroup of carbapenems. It is particularly active against Pseudomonas aeruginosa. Chemically it is (4R,5S,6S)-6-[(1R)-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.[2]

Doripenem binds to pencillin binding proteins (PBPs) located on the bacterial cell wall, particularly PBPs 2 and 3, thereby inhibiting the final transpeptidation step in the synthesis of peptidoglycan, an essential component of the bacterial cell wall. Inhibition results in a weakening and eventually lysis of the bacterial cell wall. This agent is two- to 16-fold more potent than imipenem and comparable to ertapenem and meropenem. Doripenem can be used for bacterial infections such as complex abdominal infections, pneumonia within the setting of a hospital, and complicated infections of the urinary tract including kidney infections with septicemia.[3] Literature survey reveals few UV spectrophotometric methods[4-5], Capillary electrophoresis[6], HPLC methods.[7] The aim of the present work is to develop a simple accurate, precise and economical spectrophotometric method for the estimation of Doripenem in bulk and pharmaceutical formulation and to validate the developed method as per ICH guidelines.

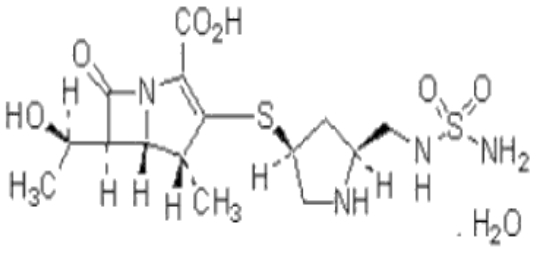

Fig 1: Chemical structure of Doripenem.

MATERIALS AND METHODS

UV Spectrophotometer: Analytical technologies, Model: T 70 series.

Doripenem pure drug was obtained as a gift sample from Aurobindo pvt limited, Hyderabad.

Distilled water, Doricrit is marketed product of Cipla and it is obtained from local pharmacy.

Experimental details

Preparation of standard stock solution

Standard stock solution is prepared by dissolving 100mg of doripenem in 100ml of distilled water. 10ml from above stock solution is transferred to a 100ml volumetric flask and the volume is adjusted to 100ml with the distilled water to give final strength (100µg/ml). The standard solution of doripenem is prepared and scanned from 200-400nm to determine λ_{max}. The absorption maxima was found to be at 298nm.

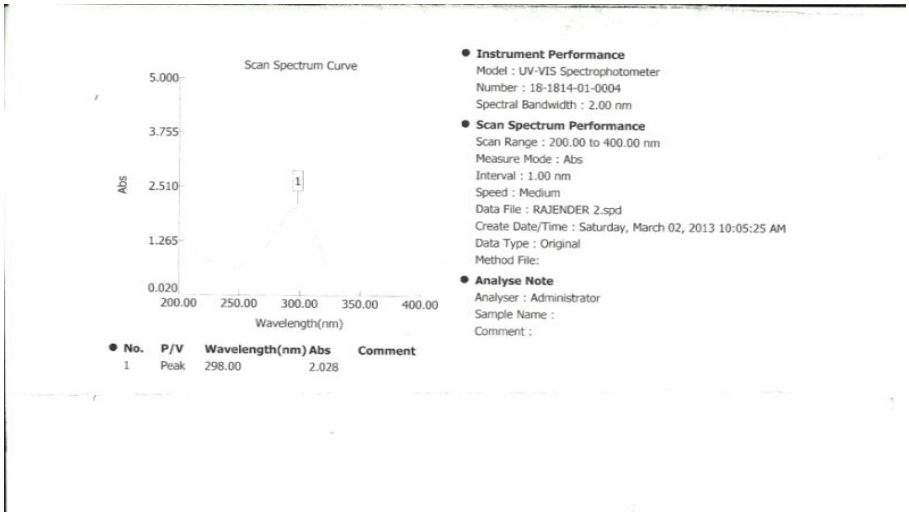

Fig 2: Absorption maxima.

Method

From the above working standard solution a series of standard solution are prepared by pipetting 1, 2, 3 and 5ml into 5 different 10ml volumetric flasks. The volume was made up to 10 ml with distilled water and the absorbance is measured against blank at 298nm.

Application of proposed method for formulation

From the Doripenem Powder for injection (Doricrit), a quantity of powder equivalent to 10mg of drug is taken and transferred to a 100ml volumetric flask. The sample was first dissolved in water (25ml) and sonicated for about 10-15min, finally up the volume is made up to the mark with water. The solution is filtered and final dilution of the sample (20µg/ml) is prepared and the absorbance is measured against blank at 298nm.

Validation of the method

The proposed method is validated as per ICH guidelines.[7-9] The method is validated in terms of linearity, accuracy and precision.

Linearity

A series of standards with 10µg/ml, 20µg/ml, 30µg/ml, 40g/ml and 50µg/ml respectively are prepared. The absorbance of all the standards are measured at 298nm against blank. The calibration curve is plotted by taking absorbance on Y axis and concentration in µg/ml on X-axis.

Table 1: Linearity Data

S. No	Concentration (µg/ml)	Absorbance
1	10	0.253
2	20	0.474
3	30	0.704
4	40	0.941
5	50	1.189

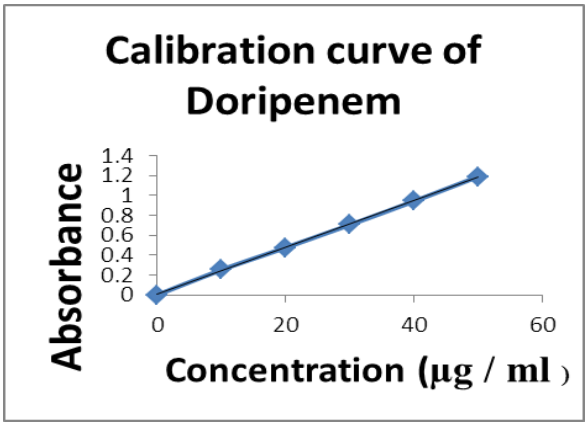

Fig 3: Calibration curve of Doripenem.

Accuracy

To the reanalyzed sample solutions, a known amount of standard stock solution is added at different levels i.e. 80%, 100% and 120%. The solutions are reanalyzed by proposed method as per ICH guidelines and statistically analyzed.

Table 2: Recovery studies.

Sample	Concentration(µg/ml)		% Recovery of pure drug	Statistical analysis	
	Pure drug	Formulation			
80%	16	20	99.55	Mean	99.52
80%	16	20	99.50	SD	0.0521
80%	16	20	99.52	%RSD	0.052
100%	20	20	99.21	Mean	99.57
100%	20	20	100.0	SD	0.398
100%	20	20	99.51	%RSD	0.399
120%	24	20	98.46	Mean	98.3
120%	24	20	98.27	SD	0.109
120%	24	20	98.27	%RSD	0.110

The results of recovery studies showed that the % amount found was between 98.3% to 99.57%.

Precision

Precision is the method to check degree of repeatability of results. 20 µg/ml solution of Doripenem was analysed. The % R.S.D. value is found to be less than 2, so the method developed was precise.

Limit of detection (LOD) and limit of quantification (LOQ)

LOD and LOQ decide about the sensitivity of the method.LOD and LOQ were calculated by LOD=3δ/s and LOQ=10δ/s, respectively, where δ is the standard deviation and s is slope of calibration.

Application of proposed method for pharmaceutical formulation

The spectrum was recorded at 298 nm. The concentrations of the drug were calculated from linear regression equation. The % amount is found to be 99.2.

Table 4: Analysis of formulation.

Dosage form	Label claim (mg/vial)	Conc (µg/ml)	Amount found	% Recovery	Statistical analysis	
Doricrit	500	20	19.84	99.2	Mean	99.2
			19.86	99.3	SD	0.1
			19.82	99.1	% RSD	0.1

RESULTS AND DISCUSSION

The absorption maxima of Doripenem in water is found to be 298 nm. The regression equation is found to be Y=0.0239X+0.0105. The Correlation coefficient is 0.999 which shows that the linear relationship exists between concentration and absorbance. The percent recovery of Doripenem is found to be 98.3-99.57 which suggests this method is accurate. The % Relative standard deviation (RSD) is found to be less than 2% which shows that the method is precise, LOD & LOQ values shows that the method is sensitive. The method is applied to marketed formulation (Doricrit) and Doripenem content is found to be 99.2 with respect to labeled claim. All the results are presented in below table.

Table 5: Optical characteristics.

Parameter	Value
Absorption maximum (nm)	298nm
Beer's law limit (µg/ml)	10-50 µg/ml
Correlation coefficient (R^2)	0.999
Regression equation Y= mX+c	Y=0.0239X+0.0105
Intercept(c)	0.0105
Slope(m)	0.02339
Sandell's sensitivity (µg/cm^2×0.001 absorbance unit)	0.0421
Molar absorptivity (1/mol/cm)	1.0416×10^4
Limit of detection(µg/ml)	0.133
Limit of quantification (µg/ml)	0.40
Precision	(%RSD) 0.0166

CONCLUSION

The developed UV spectroscopic method is simple, sensitive, cost effective with good precision and accuracy. The findings of the work suggest that the method can be applied for quantitative estimation of doripenem in bulk and pharmaceutical dosage forms. Hence this method can be used in the routine work of quality control aspects.

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REFERENCES

1. The United States Pharmacopeia (USP 30), National Formulary (NF25), The United States Pharmacopeial Convention, Inc., Rockville 2007, The United States.
2. http://www.drugbank.ca/drugs/DB06211.
3. http://www.medilexicon.com/drugs/doribax.php.
4. J. Cielecka-Piontek, The UV-derivative spectrophotometry for the determination of doripenem in the presence of its degradation products**,** Spectrochimica; Acta Part A: Molecular and Biomolecular Spectroscopy**,** 1 October 2010; 77(2): 554–557.
5. Andreas S. L. Mendez, Characterization of the antibiotic doripenem using physicochemical methods – chromatography, spectrophotometry, spectroscopy and thermal analysis; Quim. Nova, 2011; 34(9): 1634-1638.
6. Michalska K, Determination of Doripenem and related substances in medicinal product using capillary electrophoresis; J Sep Sci., Feb, 2011; 34(4): 475-82.
7. Jose Kurien, P. Jayasekhar, Stability Indicating HPLC Determination of Doripenem in Pharmaceutical Dosage Forms, Int. J. Pharm. Sci. Rev. Res., Sep – Oct 2013; 22(2): 08: 41-45.
8. Ikeda K, Ikawa K, Morikawa N, Kameda K, Urakawa N, Ohge H, Sueda T, Quantification of Doripenem in human plasma and peritoneal fluid by HPLC with ultraviolet detection, J. Chromatography. B, 2008; 867: 20-25.
9. ICH Guidance on analytical method validation, International convention on quality for the pharmaceutical industry, Toronto, Canada, 2002; 8-10.
10. ICH, Q1B, Stability testing: photo stability testing of new drug substances and Products; International Conference on Harmonization, IFPMA, Geneva, Switzerland, 1996; 3-4.
11. International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceutical for Human Use Validation of analytical procedures: text and methodology Q2 (R1), November, 2005; 1–13.