ORIGINAL ARTICLE

Simple UV Spectrophotometric Method Development for Determination of Meropenem in Bulk Form

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ABSTRACT

The drug Meropenem was analyzed by using UV spectrophotometer. The quantification of the drug was achieved in the wavelength range of 200-400 nm at 298nm. The developed method was applied for rapid analysis of the bulk form. The value of Relative Standard Deviation were found to be within acceptable range of less than 2%. The parameters of validation- linearity, precision, accuracy, specificity, robustness, limit of detection and limit of quantitation were calculated according to International Conference on Harmonization guidelines. The UV spectrophotometric method was performed at 298 nm. The samples were prepared in water followed by the stability studies of meropenem in aqueous solution at 4, 25 and 40 degrees C along with acidic and alkaline conditions. The results were satisfactory with good stability after 24 h at 4 degrees C. The method was validated and demonstrated to be rugged. The limit of quantitation and the limit of detection were established as 0.187 and 0.569 respectively. The developed validated UV spectrophotometric method is potentially valuable for routine laboratory analysis because of its ease, simplicity, rapidness, sensitivity, precision and accuracy.

INTRODUCTION

Meropenem belongs to carbapenem antibiotic which significantly active against the major bacterial pathogens causing meningitis and well penetrated into the cerebrospinal fluid. A Study indicates that meropenem is an efficient and well-tolerated antibiotic for the management of adults with bacterial meningitis. [1]

Meropenem is a carbapenem antibiotic commonly given in the management of hospital acquired infectious disease. Meropenem incases of seriously sick patients with sepsis or septic upset, untimely, suitable and appropriate antibiotic for treatment as the most important intervention available to clinicians. [2–4]

It is the very effective choice against the gram negative and positive bacterias due to its very broad spectrum activity. [5] Pharmacokinetics of meropenem has a short one-hour half-life and show linear relationship of dose-response. [6,7] It shows protein binding (2 to 3%) which is clinically insignificant.[8] While the patients with renal dysfunction increased elimination half-life of meropenem, some level of meropenem clearance also affected by the addition of RRT. [9-13] consequently, particularly dosing must be adjusted especially if patient taken RRT required to improve and increase antibiotic exposure and improves poor clinical outcomes compliance in these patients. [14]

After administration of a standard dose of 1g intravenously Plasma meropenem concentrations reach a peak (Cmax) of approximately 30 mg/L, about 1 hour is elimination half-life, and as the dose increases the area under the plasma concentration-time curve also increases linearly. The volume of

distribution is 21L, demonstrating mainly extracellular distribution. Meropenem partially distributed into the cerebrospinal fluid. The drug elimination done by both metabolism and excretion. Meropenam up to 70% is eliminated in urine, and the rest is reported for passing through an opened β-lactam ring- kind of the compound, ICI 213689.

In patients with renal insufficiency extended the t½ of meropenem and show a good relationship with creatinine clearance. Thus the dose of individual with decreased creatinine clearance adjusted on the basis of creatinine clearance.
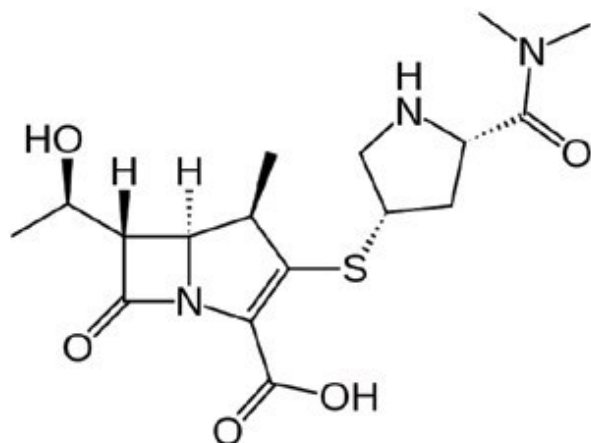

Figure 1. Meropenem

Meropenem (Figure 1) is an antibiotic that is carbapenem of broad-spectrum. It is suitable active and effective against Gram-positive and Gram-negative microorganisms. The modes of action of Meropenem is exerted through penetrating bacterial cells rapidly and causes to cell death via interfering with essential cell wall constituents in the synthesis.[15] To ensure quality, reliability and consistency of the result for all analytical application by Validation, it is a necessary and basic requirement.[8] But in analytical chemistry, in pharmaceutical analysis some special conditions and aspects exist that have to be taken into consideration in comparison. Assessment of (batches and stability investigations etc.) is based on the account of result of different procedures or control tests, thus their performances can harmonize each other and ensure reliability.

METHODOLOGY

Materials : Active of meropenem and distilled water was used as the solvent for all dilution in which meropenem showed complete dissolution. Other materials used included Glass wares- volumetric flask, stirrer, beakers, pipette and measuring cylinder.

Instruments : Weighing Balance used for weighing the drug was 'Electronic Balance' (ATL 3000G/0.001G) and 'Ultraviolet-Visible Spectrophotometer' (Schimadzu UV-1800 240V) was used for the measuring absorbance of Meropenem dilutions.

Selection of wavelength: The detection of Meropenem was done by using UV spectrophotometer in the range of 200-400nm. The maximum absorbance was received at 298nm which was selected as the detection wavelength for the drug.

Standard stock solution: The standard stock solution of Meropenem was prepared by 50 mg of drug dissolved in DI water to prepare the final volume in 250 ml of volumetric flask. This provided a solution of 40μg/ml of meropenem working stock solutions.

RESULTS

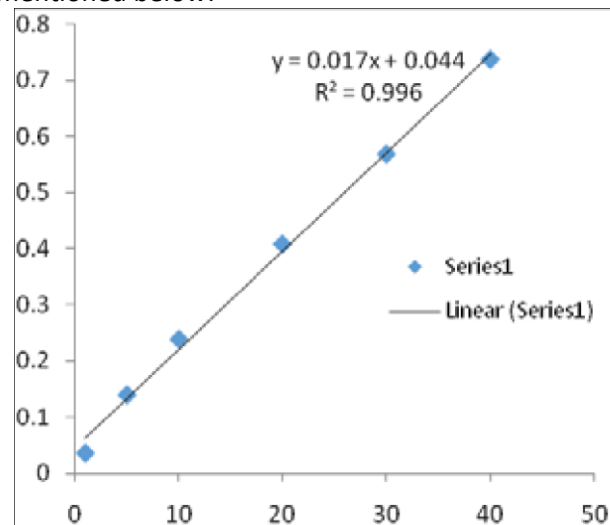**Method validation:** The basic tools for the method validated for a drug as per ICH Guidelines are mentioned below:
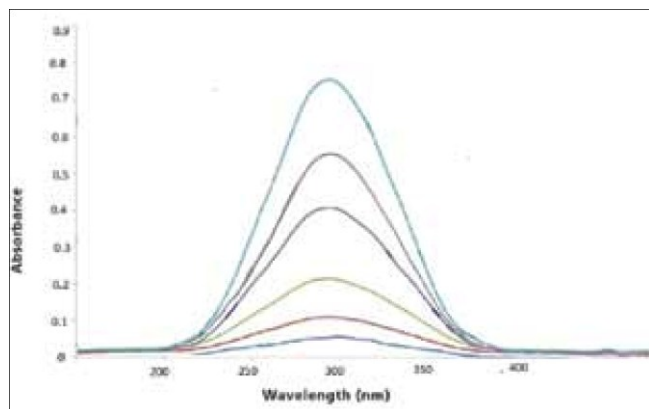

Figure 2. LINEARITY OF MEROPENEM

Fig 3: UV SPECTRUM

Linearity: The precise volume of the 'standard stock solution of meropenem' were taken in 6 separate volumetric flasks of 50ml. The stock solution was further diluted up to obtain ultimate concentration of 1, 5, 10, 20, 30 and 40µg/ml of meropenem. Later the absorbance versus concentrations values were plotted to construct the calibration curves and to calculate the regression equation for meropenem Fig 2. The results are shown in **table I.**

Table I: Regression equation of meropenem

Drug	Regression equation	r2
Meropenem	y = 0.017x + 0.044	0.996

Precision: The response of the Meropenem aliquots were estimated six times at the wavelength of 298nm for the repeatability studies and their results are represented in terms of RSD values. Intermediate Precision comprised of both the intraday and interday precision check, these studies were executed by estimating the comparable responses three times on the same day and as well as on different days. The results are demonstrated in terms of % relative standard deviation shown in table II.

Accuracy: The accuracy of the method was carried at three different levels i.e. 80%, 100% and 120% through standard additions. The recovery percentages of Meropenem were calculated. This was followed by estimation of the 'mean percentage recovery'. Values obtained in recovery studies are shown in **table III.**

Table II. Inter day and intraday precision of Meropenem

Drug	Conc. ppm	Inter-day %STD	%RSD	Intra-day %STD	%RSD
Meropenem	1	0.0001	0.3322	0.0005	1.66
	5	0.0005	0.4499	0.001	1.24
	10	0.0011	0.5464	0.004	1.69
	20	0.0055	1.393	0.0005	0.141
	30	0.0075	1.0434	0.005	0.978
	40	0.002	0.2935	0.002	0.341

Table III. Percentage Recovery

Drugs	Conc ppm	%STD	% RSD
Meropenem	80%	0.001	0.204
	100%	0.0005	0.141
	120%	0.001	0.306

LOD and LOQ

Limit of detection (LOD)

The limit of detection (LOD) is calculated by the following formula: $3.3\sigma/S$ which was found to be 0.18785167 **Limit of quantitation (LOQ)**

Limit of quantitation (LOQ) is calculated by the following formula: $10\sigma/S$ which was found to be 0.56924747

Where, 'σ' refers to (RSD) relative standard deviation of the response and 's' is the slope of the analytic by forming calibration curve.

Stability Studies

The samples of Meropenem were also submitted to stability testing under following conditions

Thermal Stress

For this conditions samples were kept at three different temperatures 4, 25 and 40 OC followed by absorbance determination at 298nm.

Chemical Degradation:

The degradation effect was evaluated after the addition of 0.1 N NaOH and on the addition of 0.1 N HCl and absorbance was determined at a maximum of 298nm.

The solution from the primary solution was taken and place it in UV light for 2hrs. The absorbance at the same wavelength 298nm was then measured after 2hrs.

The results of stability testing are presented in **table IV.**

Table IV. Degradation Studies	
Degradation Parameters	**Absorbance**
Thermal Degradation	
Stored at 4°C	3.274
Stored at ambient temperature (25°C)	3.156
Stored at 40°C	3.109
Photo degradation	
UV Light (2hrs)	3.372
Acidic Degradation	
0.1 N HCl	0.186
Alkaline Degradation	
0.1 N NaOH	0.342

DISCUSSION

The results for all parameters of validation (Accuracy, precision, linearity, quantitation limit and detection limit) were found under defined limits.

Linearity range for the drug is over 1, 5, 10, 20, 30 and 40µg/ml at selected wavelength of 298nm (Figure 3). The coefficient of correlation for meropenem at 298nm is 0.996. Meropenem represented good regression values at the respective wavelengths of 298nm. The projected method also revealed accurate measurements despite that minor alteration in the concentration of Meropenem. The reliability and validity of projected method is proved by recovery studies. Precision is assessed by studying the repeatability. Moreover, Result of repeatability shows intraday precision and the precision under the same operating conditions over a small interval of time. Both inter-day and intraday precision study was performed and value of % RSD found to be NMT 2.0% which indicated good repeatability and intermediate precision. The forced degradation studies presented low degradation value in acidic medium and high degradation values under all conditions of stress.

CONCLUSION

The projected method of UV spectrophotometer is precise, simple, accurate, economic and rapid. It has also been validated in terms of accuracy, precision, linearity and reproducibility. Therefore, proposed method can be proficiently used for evaluation of Meropenem in bulk form.

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