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VISIBLE SPECTROSCOPIC DETERMINATION OF FAROPENEM SODIUM IN PHARMACEUTICAL DOSAGE FORM

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Faropenem, Visible Spectrophotometric, Potassium Ferri-Cyanide, 1, 10-Phenanthroline.

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ABSTRACT: Two simple, precise, accurate and economical visible spectrophotometric methods were developed for the determination of faropenem in bulk and in tablet dosage forms have been described. The method A was based on the formation of green color complex with Potassium ferri-cyanide in the presence of Ferric chloride, which show maximum absorbance (λ max) at 745nm.The method B is based on the reduction of ferric ion into ferrous ion by the drug in the presence of Ferric ammonium sulphate-1, 10-phenanthroline to form a highly stable Orange red colourferrion complex measured at 511 nm. Mean assays of method A and B was found to be 99.9% and 99.4 % respectively. LOD and LOQ of method A was found to be 2.22 µg/ml and 7.44 µg/ml respectively and for method B it was 7.88 and 26.11 µg/ml.The results of analysis for both the methods have been validated statistically as per ICH guidelines. The proposed methods were simple, sensitive and economical for the quantitative determination of faropenem and were successfully employed for the estimation in pure and in tablet dosage forms.

INTRODUCTION: Faropenem **(Figure 1)** is chemically (5R, 6S, 8R, 2'R)-2-(2'-tetrahydrofuryl)-6-(1- hydroxyl ethyl)-2-penem-3-carboxylic acid[1]. Faropenem is a novel beta-lactam antibiotic sharing similarities with both the penicillin and cephalosporins[2]. Faropenem is indicated in acute bacterial sinusitis, community acquired pneumonia, acute exacerbations of chronic bronchitis, uncomplicated skin and skin structure infections and urinary tract infections[3].

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It exhibits a broad spectrum of activity that includes Gramnegative, Gram-positive and some anaerobic bacteria[4]. The primary mode of action of Faropenem is consistent with that of other betalactam antibiotics namely binding to penicillinbinding proteins.

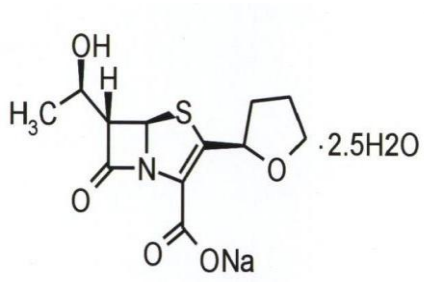

FIG. 1: CHEMICAL STRUCTURE OF FAROPENEM

Literature survey revealed that few analytical methods such as spectrophotometric [5-8], HPLC[9-15] and LC-MS[16-17] methods have been reported. No

colorimetric or visible spectrophotometric method has been reported, hence a new sensitive and efficient visible method was developed and validated as per ICH guidelines[18-19] for the assay of the drug Faropenem in tablet formulations**.**

Experimental:

Instruments:

Electronic Weighing balance - single (pan balance, Model Axis LC/GC), Digital pH meter (Model-Systronics), Sonicator- Ultra Sonicator (Model-Bandelinsonorex), Double Beam UV-Visible spectrophotometer - Schimadzu 1800. UV spectra of standard and sample solutions were recorded in 1cm quartz cells at the wavelength ranges of 200-400 nm.

Chemicals and Reagents:

Faropenem was obtained as a gift sample from Hetero drugs pvt.ltd, Hyderabad, India. sodium acetate, glacial acetic acid, $FeCl_3$ was purchased from Merck, Mumbai. Potassium ferricyanide, ferric ammonium sulphate and 1-10 Phenanthroline was purchased from SD Fine chem, Mumbai. Distilled water was prepared in house. All other chemicals used were AR grade.

Preparations of Buffer and Reagents:

Preparation of Acetate Buffer pH 4.6:

5.4gms of sodium acetate was dissolved in 50ml of distilled water in a 100 ml volumetric flask, 2.4ml of glacial acetic acid was added and diluted upto the mark with water. pHwas adjusted if necessary with orhtophospharic acid.

Preparation of5%$FeCl_3$solution:

5 gms of FeCl3 was dissolved in distilled water and final volume was make up with the same to 100 ml.

Preparation of Potassium Ferricyanide:

100mg of Potassium ferricyanide was dissolved in 100 ml distilled water.

Preparation of Ferric Ammonium Sulphate-1, 10-Phenanthroline:

2 ml of 1 M HCl was added to 0.19 gms of 1-10 Phenanthroline mixed well and 0.16 gms of ferric ammonium sulphate was added and Dilute it to 100 ml with distilled water.

Preparation of standard stock solution:

A standard stock solution of faropenam was prepared by dissolving 100 mg of it in distilled water in a 100 ml volumetric flask, the final volume was made upto the mark with the same to get the final concentration of 1mg/ml.

Preparation of working standard solution:

A working standard solution containing 100µg/ml was prepared by diluting the above stock solution. The fresh working standards were prepared dialy.

Determination of λ max:

Method 1: With Potassium ferricyanide:

In a 10 ml volumetric flask, 1ml of working standard of the drug was taken and 1ml of $FeCl_3$ was added and mixed well. 1ml of potassium ferri cyanide was added and final volume was make up with distilled water. A green colour complex was observed. The resulted solution was scanned for the determination of λmax in the visible range of 400-800 nm.

Method 2: With Ferric ammonium sulphate-1, 10-Phenanthroline:

In a 10 ml volumetric flask, 1ml of working standard drug solution was taken and 1 ml of Ferric ammonium sulphate-1, 10-Phenanthroline solution, 4 ml acetate buffer solution pH 4.5 was added and heated on water bath at 80^{O} C for 10 minutes. The mixture was cooled to room temperature. The final volume was made upto the mark with distilled water. An orange red colour complex was observed. The resulted solution was scanned for the determination of λmax in the visible range of 400-800 nm.

Preparation of sample solution (for Assay of faropenam tablets):

Faropenam Tablets (Farobact; Cipla Pharmaceuticals Ltd,) containing 200mg were successfully analyzed by the proposed methods. 10 tablets of Faropenem were accurately weighed and powdered.

Tablet powder equivalent to 100mg of Faropenem was dissolved in 100 ml of distilled water in a 100ml volumetric flask and filtered. The solution was suitably diluted and analysedemploying the procedures given under the procedure for bulk

samples. None of the excipients usually employed in the formulation of tablets interfered in the analysis of Faropenem by the proposed method. A summary of results of both the methods were shown in **Table 1**.

RESULTS AND DISCUSSION:

Method A:

Faropenem exhibits maximum absorbance (λmax) at 745 nm. Faropenam was found to react with potassium ferri cyanide under the experimental conditions to form a green coloured product exhibiting λmax at 745 nm. The λmax curve was shown in **Figure 2.**

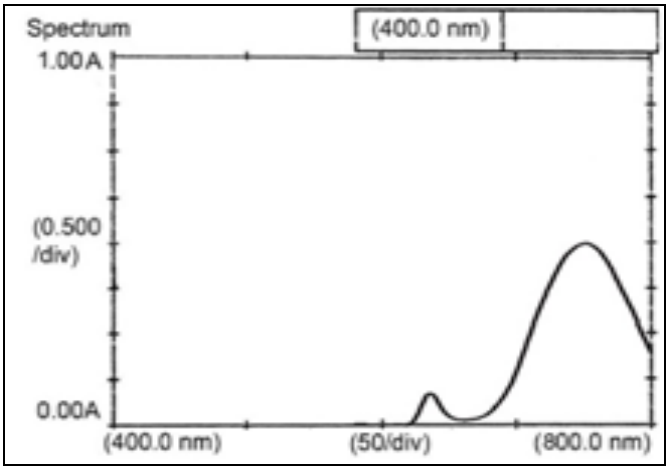

FIGURE 2: λ MAX SPECTRUM OF FAROPENEM (METHOD A)

Method B:

Ferric ammonium sulphate-1, 10-Phenanthroline has been used as a color developing reagent in the spectrophotometric determination of pharmaceutical drug compounds.

In Method B, the ferric ion was reduced by OH group of the drug to ferrous ion, which reacts with 1, 10-phenanthroline and forms Orange red colored ferrion complex which exhibiting λ max at 511 nm. **Figure 3** shows the λmax curve.

The absorbance was found to increase linearly with increasing concentration of faropenam. The effect of pH of buffer was studied by forming the colored product in the presence of various buffers pH the absorbance of the proton transfer product was measured. Acetate buffer pH 4.5 was optimised. The reaction time was determined by following the color development at room temperature.

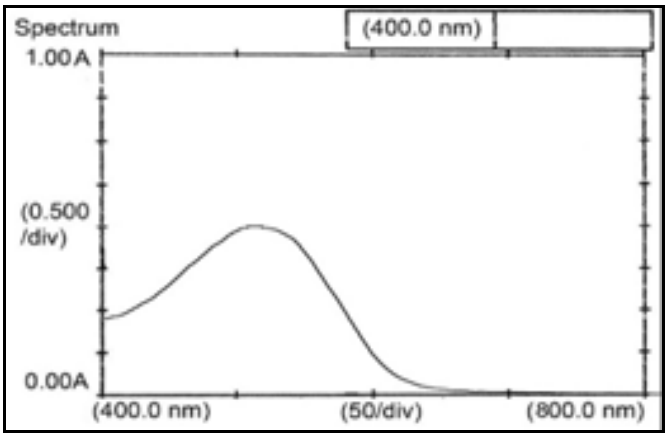

FIGURE 3: λ MAX SPECTRUM OF FAROPENEM (METHOD B)

Validation of the proposed method

Linearity and sensitivity: Calibration curves for Methods A and B in the ranges 8-20 µg/mL and 10-60 µg/mL were linear with correlation coefficients (r2) of 0.9975 and 0.9978 for methods A and B, respectively. The molar absorptivities (ε) at 745 nm and 511 nm for Methods A and B were $1.084X\ 10^{-8}$ and $1.064X10^{-5}$ L/mole/cm, respectively. The sandell's sensitivity values were 0.0232 and 0.0694 for methods A and B respectively. The calibration curves of method A and B were shown in **Figure 4 and 5** respectively.

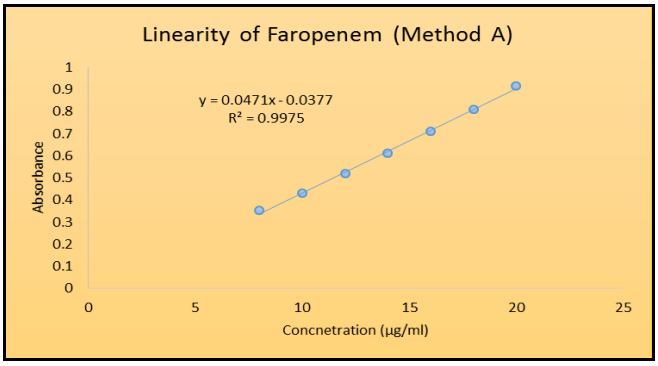

FIGURE 4: CALIBRATION CURVE OF FAROPENEM (METHOD A)

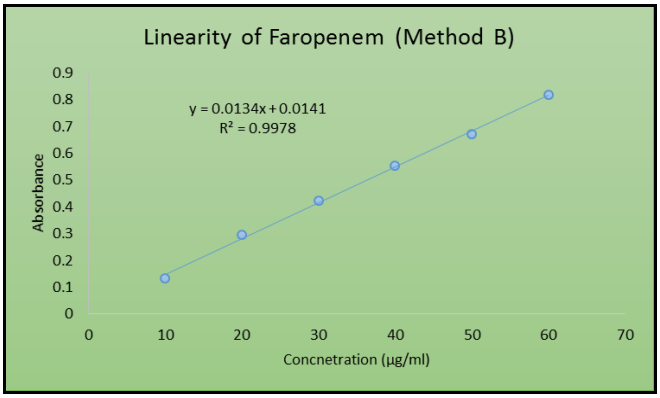

FIGURE 5: CALIBRATION CURVE OF FAROPENEM (METHOD B)

LOD AND LOQ:

The limit of detection (LOD) is defined as the minimum level at which the analyte can be reliably detected for the two methods was calculated using the following equation

LOD= 3.3 X Standard deviation / Slope

In accordance with the formula, the detection limits were found to be 2.229 and 7.88 µg/mL for method A and B, respectively.

The limit of quantification (LOQ) is defined as the lowest concentration that can be measured with acceptable accuracy and precision

LOQ=10 X Standard deviation / Slope

According to this equation, the limit of quantification was found to be 7.44 and 26.11 µg/mL for Method A and B respectively; the summary of validation parameters for the two methods were summarized in **Table 1**.

Accuracy and precision:

The accuracy and precision of the proposed method were determined at three concentration levels of faropenem (within the linear range) by analyzing three replicate analyses on pure drug of each concentration. The percentage relative error as accuracy and percentage relative standard deviations (RSD) as precision for the results did not exceed 2 % for the two methods as shown in **Table 1**, indicating the good reproducibility and repeatability of the two methods. This good level of precision and accuracy was suitable for quality control analysis of faropenem in their pharmaceutical formulation.

Applications of the methods:

The proposed methods were applied to the pharmaceutical formulation containing faropenem. The results are shown in **Table 1**. Indicate the high accuracy of the proposed methods for the determination of the studied drug. The proposed methods have the advantage of being virtually free from interferences by excipients. The percentages were 99.90 ± 0.46 and 99.40 ± 1.67 for method A and B, respectively **(Table 1).**

TABLE 1: SUMMARY OF VALIDATION RESULTS OF METHOD A AND B

Parameters	Results	
	Method –I	**Method-II**
Lamda max (λmax)*	745	511
Beer's law limits (µg/ml)	8-20	10-60
Molar absorptivity(L/mol/cm)	$1.084X\ 10^{-8}$	$1.064X10^{-5}$
Sandell's sensitivity (µg/cm2/0.001absorbance unit)	0.0232	0.0694
Regression equation	Y=0.0455X-0.0132	Y=0.0135X+0.0075
Slope(m)	0.0455	0.0135
Intercept(c)	-0.0132	0.0075
Correlation coefficient (r2)	0.9981	0.9985
Precision (%RSD)**	0.035	0.035
LOD (µg/ml)	2.229	7.88
LOQ (µg/ml)	7.44	26.11
Assay (% Purity)**	99.9	99.4

* Average of 6 replicate samples; ** Average of 3 replicate samples.

CONCLUSION: The development visible spectrophotometric methods for the determination of faropenem in pharmaceutical formulation were simple, sensitive, rapid and accurate. The methods were practical and valuable for routine application in quality control laboratories for analysis of faropenem.

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