Research Article

AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH

www.ajphr.com
2014, Volume 2, Issue 9
ISSN: 2321–3647(online)

Spectrophotometric Determination of Ferophenem Drug and Commei Pharmaceutical Formulation

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ABSTRACT

Two simple, sensitive selective accurate and economical spectrophotometric methods Method A&B for the determination of feropenem in bulk drug and pharmaceutical formulations (tablets) have been described in the present work. Method - A is based on the formation of red colored ion-association complex between feropenem and methiline blue (MB) exhibiting absorption maximum at 650nm and obeying Beer's law in the concentration range of 4-20µg/ml. The Method - B is based on the formation of Ion-association complex between feropenem and safranine-o(SFO) to yield an yellow colored chromogen exhibiting absorption maximum at 520nm(Method B) and obeying Beer's law in the concentration range of 4-20µg/ml. Statistical analysis of the results has been carried out for the proposed methods revealing high accuracy and good precision. The proposed methods developed by the author could be successfully extended to the commercial pharmaceutical formulations (tablets) containing feropenem.

Keywords: Feropenem, Linearity, Validation

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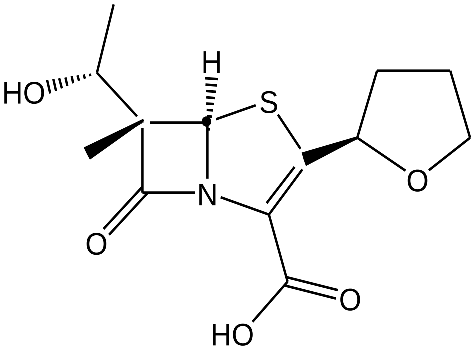
Received 27 July 2014, Accepted 06 August 2014

Please cite this article as: Challa S *et al.*, Spectrophotometric Determination of Ferophenem Dru Commercial Pharmaceutical Formulation.. American Journal of Pharmacy & Health Research 2014.

INTRODUCTION

Feropenem [1-6] is an orally-active beta-lactam antibiotic belonging to the carbapenem group. It is the first orally-active carbapenem antibiotic. The sodium salt feropenem sodium, available under the trade name Farom, has been marketed in India.



(5R,6R)-6-(1-hydroxyethyl)-7-oxo-3-[(2R)-oxolan-2-yl]-4-thia-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid)

MATERIALS AND METHODS:

Apparatus:

All spectral measurements were done on Elico(SL-159), UV – Visible spectrophotometer with 1.0cm matched quartz cells were used for the spectral and absorbance measurements. An Elico LI-120 digital pH meter was used for pH measurements. All spectroscopic measurements were carried out at room temperature (25 ± 2 ◦C).

MB solution (Fluka; 0.2%):

Prepared by dissolving 200mg of methylene blue in 100ml of distilled water and subsequently washed with chloroform to remove chloroform impurities.

Buffer solution P^{H} 9.8(NH_4OH – NH_4Cl):

7gms of NH_4Cl and 6.8ml of liquid Ammonia solutions were mixed and diluted to 100 ml with distilled water and pH was adjusted to 9.8.

SAFRANINE-O solution (Fluka; 0.2%):

Prepared by dissolve in 200mg of safranine-o in 100ml of distilled water.. and subsequently washed with chloroform to remove chloroform impurities.

Preparation of standard solution:

A 1 mg/ml solution was prepared by dissolving 100 mg of pure FPM in 100ml of distilled water and this stock solution was diluted step wise with distilled water to get the working standard solutions of concentration of 25µg/ml

Preparation of Marketed formulations:

In case of marketed formulations, two accurately weighed tablets were crushed to a fine powder and an amount equivalent to 10mg of feropenem was added into different 100mL volumetric flasks and volume was made up with methanol. The samples were filtered through a 0.45µm-membrane filter; different serial dilutions (4 – 20µg/mL) were made from this solution in 25mL volumetric flask. The drug content of this solution was obtained by applying the proposed procedure to aliquot containing different volumes of solution drugs as described above.

PROPOSED PROCEDURE FOR METHOD A & B:

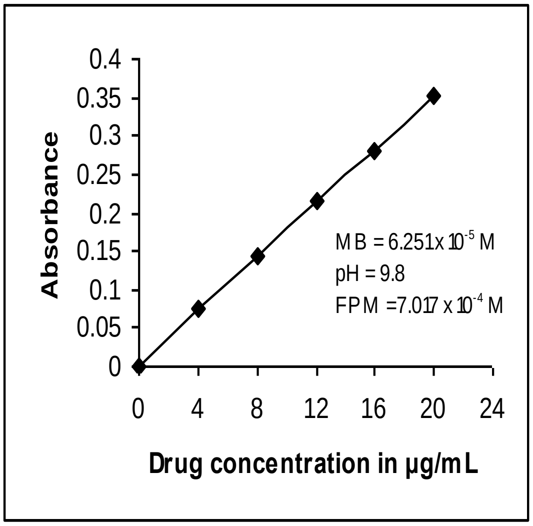
Aliquots of standard drug solution 1.0 - 5.0 ml for method M_{1a}& M_{1b} (100 µg/ml) and 1.0ml of P^H 9.8buffer solution were placed separately in a series of 125ml separating funnels. A volume of 0.5ml of MB (for method M_{1a}), 1.0ml of Safranin o (for method M_{1b}) was added respectively. The total volume of aqueous phase in each funnel was adjusted to 10.0ml with distilled water. Then 10ml of chloroform was added in each separating funnel and the contents were shaken for 2 min and allowed to separate. The organic layer was collected through cotton plug and the absorbance was measured immediate at 650 nm (for method (M_{1a}) and 520nm (for method M_{1b}) against reagent blank. Both the colored species were stable for 2 hours. The amount of drug in a sample was obtained from the Beer's Lambert plot.

RESULTS AND DISCUSSION

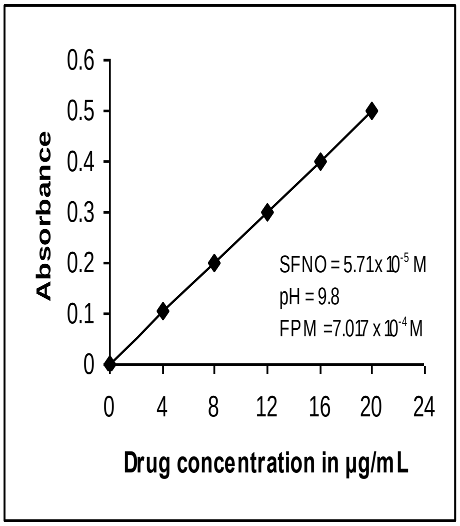
In the present investigation the presence of carboxyl group (acidic), in dihydrothiazine in FPM is responsible for color formation an ion association complex with basic dyes (Methylene blue(method A) and Safranin O(method B), which is extractable into chloroform from aqueous phase. The carboxylate anion (negative charge) of FPM is expected to attract the oppositely charged part of the dye (positive charge methylene blue and Saffranin O) and behave as single unit being held together by electrostatic attraction.

Linearity and Range

The linearity of the method was determined at five concentration levels ranging from 4µg ml to 20µg.mL for ferophenem. The calibration curve was constructed by plotting response factor against various concentrations of feropenem. The slope and intercept value for calibration curve of feropenem was Y=0.01732x+0.0049 (R^2=0.9999) for Method A(MB) and Y=0.0249x+0.003 (R^2=0.9999) for Method B(SAFRANINE O) respectively. The results showed an excellent correlation exists between response factor and concentration of drugs within the concentration range indicated above (Table 1) for Method A(MB) and Method B(SAFRANIN O). The calibration curve is shown in Figure.1

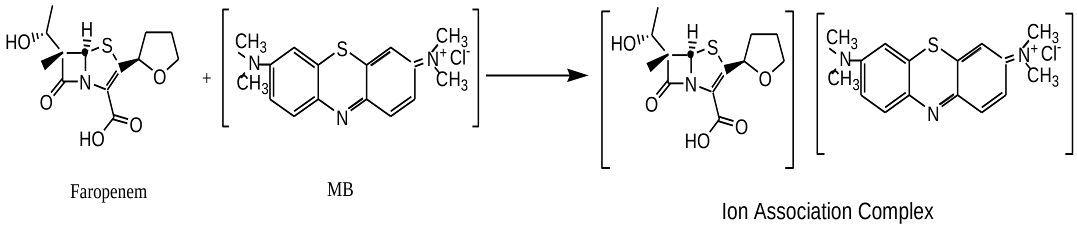


Beer's Law plot of FPM with MB (M_{1a})

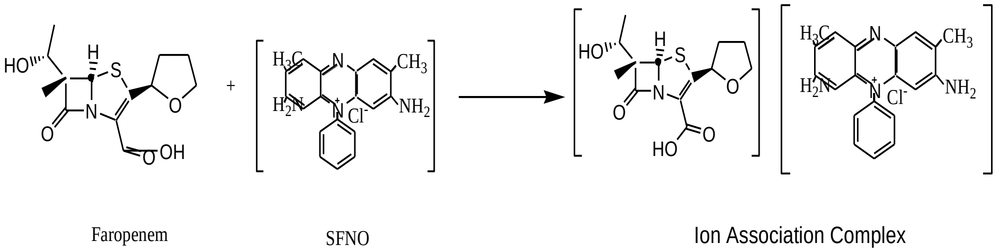


Beer's Law plot of FPM with SFNO (

Method (M_{1a})



Method (M_{1b})



Sensitivity (LOD and LOQ):

The limit of detection (LOD) is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from back-ground levels. The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy, precision and variability. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve The values of LOD and LOQ for Method A(MB) and Method B(SAFRANINE O) are given in Table 1**.**

Table – 1 Statistical Analysis of Calibration Graphs and Analytical Data In the Determination of the Feropenem using the Proposed Methods

Parameter	**M_{1a}**	**M_{1b}**
λ_{max} (nm)	650	520
Beer's law limits (µg/ml)	4.0 - 20.0	4.0 – 20.0
Molar absorptivity (1 $mol^{-1}.cm^{-1}$)	5.024×10^3	7.161×10^3
Sandell's sensitivity (µg.cm^{-2}/0.001 absorbance unit)	3.932×10^{-2}	5.124×10^{-2}
Optimum photometric range (µg/ml)	6.5 – 16.0	12.5 – 25.0
Regression equation (Y=a+bc) slope (b)	0.01732	0.0249
Intercept (a)	0.0049	0.003
Correlation coefficient (r)	0.9999	0.9999
Relative standard deviation (%)*	0.2825	0.4549
0.05 level	0.2965	0.4775
0.01 level	0.4150	0.7489

* Average of six determinations considered

Precision and Accuracy:

The precision of the method was demonstrated by intraday variation studies. In the intraday studies, six repeated injections of standard and sample solutions were made and the response factor of drug peaks and percentage RSD were calculated. The accuracy of the method was determined by recovery experiments. The recovery studies were carried out six times and the percentage recovery and standard deviation of the percentage recovery were calculated and presented in (**Table.1**).

Analysis of pharmaceutical preparations:

Commercially available feropenem tablets were subjected to analysis by the proposed methods along with a reference method. Comparison of the results obtained with the proposed methods [Method A(MB) and Method B(SAFRANIN O)] and UV methods for dosage forms (**Table - 2**) of feropenem confirm the suitability of these methods for commercial pharmaceutical formulations.

Table 2: Estimation of Feropenem in Pharmaceutical Formulations

Sample	**Labelled amount (mg)**	**Amount obtained (mg) Proposed methods***		**UV method**	**%Recovery of Proposed methods***	
		Method-A	**Method-B**		**Method-A**	**Method-B**
Tablet - 1	200	199.64	199.89	59.98	99.98	99.94

Average of six determinations

CONCLUSION

The proposed methods developed by the author made use of simple reagents, which most ordinary analytical laboratories can afford. Moreover the proposed methods are also sensitive and selective and can be used for the routine analysis of the cited drug in their available dosage forms. The methods are also suitable and valid for application in laboratories lacking liquid chromatographic instruments.

ACKNOWLEDGEMENTS

The authors on thankful to M/S Hetero Drugs Limit, Hyderabad for gift sample and prof., Department of Chemistry, Acharya Nagarjuna University, Guntur. For providing additional laboratory facilities

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