

Spectrophotometric Determination of an Antimalarial Drug Mefloquine in Bulk and Pharmaceutical Formulations by Iron Phenanthroline Method

Ritika Manoj Makhijani and Mahalaxmi Murugan

Department of Chemistry

VES College of Arts, Science and Commerce, Chembur, Mumbai, India

Abstract: A spectrophotometric method have been developed for determination of an antimalarial drug Mefloquine. The developed method is new, simple, sensitive, precise, accurate and reproducible. At 510 nm, absorbance of orange coloured chromogen is measured, which is produced by oxidation of drug with 1, 10-phenanthroline. Beer's Law is obeyed in the concentration range of 4.0 – 28.0 $\mu\text{g/ml}$ for the developed method. The molar absorptivity and sandell's sensitivity are found to be 2269.87 $\text{L mol}^{-1}\text{cm}^{-1}$ and 0.166 $\mu\text{g/cm}^2$ respectively. Various parameters affecting the stability and development of colour was thoroughly studied and optimized. The method has been successfully applied for determination of mefloquine in both pure and dosage forms. The result obtained by the developed method is found to be in good agreement when compared with the standard methods.

Keywords: Mefloquine hydrochloride, spectrophotometry, 1,10- phenanthroline

I. INTRODUCTION

Mefloquine hydrochloride (Fig-1) is the hydrochloride salt of 4-quinolinemethanol-2- piperidinyl-2,8-bis(trifluoromethyl), hydrochloride. In 1970s, United States Army developed Mefloquine, and in mid 1980s it came into use. 1980s¹⁻³. In the World Health Organization's List of Essential Medicines, mefloquine is considered as the safest and most effective medicines needed in a health system⁴. Mefloquine is an antimalarial drug, which is found to be effective against all forms of malaria, and in endemic areas this is the main drug recommended for malaria chemoprophylaxis.^{5,6} Since malaria is the world's most widespread parasitic infection, ranking among the major health and developmental challenges for poor countries, Mefloquine plays an important role for the control, treatment, and prevention of this disease worldwide.⁷

As per Literature, an HPLC method for the estimation of potentially counterfeit chloroquine, quinine, and mefloquine tablets was reported.⁸ Some papers described the determination of MQ in biological fluids, such as blood, plasma, and urine, by HPLC using UV detection.⁹⁻¹¹ An HPLC method for the quantitative enantioselective analysis of mefloquine stereoisomers was also described.¹² But no simple, sensitive and precise spectrophotometric method is yet reported for this drug in any official literature. So in the present study, a specific, precise, accurate and validated spectrophotometric method has been developed for the estimation of mefloquine hydrochloride in bulk and tablet dosage form.

II. MATERIALS AND METHODS

Instrumentation

All measurements of absorption spectra were made on model LABMAN UV-VIS Spectrophotometer using quartz cells of 1cm path length and wavelength range 320-1000nm was used for absorbance measurement. All chemicals employed in the present study were of analytical grade and purchased from Loba Chemie. Double distilled water prepared by distilling water in a Borosil glass apparatus containing alkaline Potassium Permanganate was used for preparation of standard solution as well as for all experimental work.

Preparation of Standard solution of drug

An accurately weighed 5 mg of mefloquine dissolved in methanol. The final volume is adjusted with methanol to 100ml in standard flask.

Preparation of Reagents

0.005M Fe (III) - Dissolve 0.241g of anhydrous ferric ammonium sulphate in 100cm³ of double distilled water, 0.05M 1,10-phenanthroline - Dissolve 0.991g of the reagent in 100 cm³ of alcohol, 0.02M o-phosphoric acid - Dilute 0.15cm³ of laboratory reagent (AR Grade) of o- phosphoric acid to 100 cm³ with distilled water.

Experimental Procedure

Different portions (1.0- 7.0ml, 100 µg/ml) of Standard mefloquine solution is delivered into a series of 25mL standard flask and then 1.0 mL of 5.0 x10⁻³ M of Fe (III) solution, 1.0 mL of 5.0x10⁻² M 1,10 -phenanthroline are added successively. The total volume in each tube is brought to 20 ml with distilled water. The flasks are kept on a boiling water bath for 40 min. The tubes are removed and cooled to room temperature. 1.0 ml of 2.0 x10⁻² M of o- phosphoric acid is added and volume in each flask is made up to the mark with distilled water. The absorbance of the colored complex solution is measured after 5 min against a reagent blank prepared similarly except drug and maximum absorbance is found to be at 510 nm (Fig-2). The amount of the mefloquine drug is computed from the appropriate calibration graph (Fig-3). Effect of concentration of H₃PO₄, 1,10Phenanthroline and time of digestion on the absorbance are studied by keeping other parameter constant.

Analysis of Pharmaceutical Sample

Analysis of pharmaceutical sample Tablets powdered equivalent to 5 mg of the drug is weighed accurately and transferred into 100 ml beaker and shaken with 50 ml methanol by following standard method. The standard solution is filtered into 100ml standard flask and volume is adjusted with methanol. Suitable aliquots of this solution used for the determination of mefloquine contents by procedure describe earlier.

Effect of Concentration of H₃PO₄ on Color Development

After addition of 3.0cm³ of H₃PO₄ absorbance remains constant. Hence 4cm³ of H₃PO₄ is selected for the colour development and further experimental studies. (Fig-4)

Effect of Concentration of 1,10-Phenanthroline

After addition of 3.0cm³ of 1,10phenanthroline absorbance remains constant. Hence 4cm³ of H₃PO₄ is selected for the development of colour and further experimental studies. (Fig-5)

Effect of Heating Time on Absorbance

For colour development 60 minutes are sufficient and hence 60 minutes time is selected for further experimental studies. (Fig-6)

III. RESULTS AND DISCUSSION

In order to test whether the coloured product formed in this method adhere to Beer's Law, the absorbance at maximum wavelength of series of seven concentrations are plotted against concentration of drug in µg/cm³. Beer's Law is obeyed within the limits 4.0 to 28.0 µg/ml of mefloquine, Molar absorptivity and sandell sensitivity are found to be 2269.87 L mol⁻¹cm⁻¹ and 0.166 µg/cm² respectively. Regression analysis of Beer's Law plots at λ_{max} reveals a good correlation. The graph show negligible intercept and described by regression equation $y = 0.0051x + 0.0027$. where Y is the absorbance of 1 cm layer, b is the slope, a is the intercept and C is the concentration of the measured solution in µg/mL) The high molar absorptivity of resulting coloured complex indicates the high sensitivity of method.(Table -1) Mefloquine is analysed from the proposed method and the result obtained are comparable with standard method (Table- 2).

Principle of developed method

Ferric salt when reacts with the Mefloquine it gets converted into ferrous salt upon oxidation and can be easily identified by the usual reagent 1,10-phenanthroline. Coloured complex of Fe (II), is well known as ferroin and is the reduction product.¹³⁻¹⁵ The colored product of the reaction is given in Figure 7.

Regression parameters, Optical characteristics Precision and Accuracy of the proposed method are shown in Table -1

Determination of Pharmaceutical Formulations of Metformin by our proposed method and reference method is shown in Table -2

IV. CONCLUSION

The developed method is simple, sensitive, accurate and reproducible. This method can be successfully applied for the analysis of pharmaceutical formulations in any laboratory.

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Fig. 1 Structure of Mefloquine

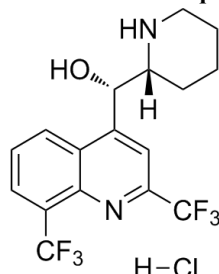


Fig.-2: Absorption spectra of Mefloquine with Fe(III)/1,10-Phenanthroline

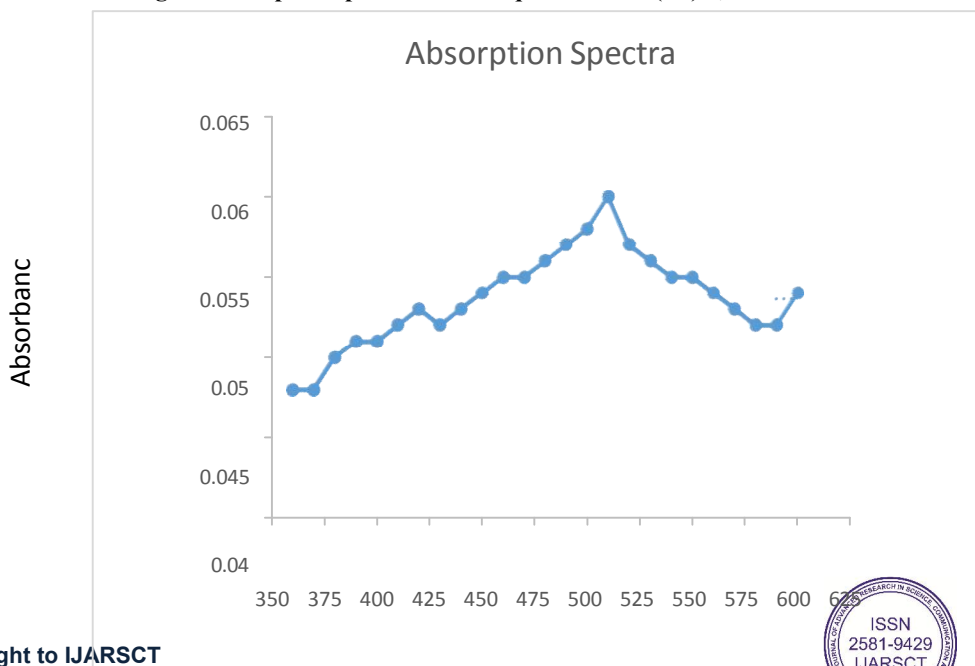


Fig.-3: Calibration curve of Mefloquine with Fe (III)/1,10-Phenanthroline

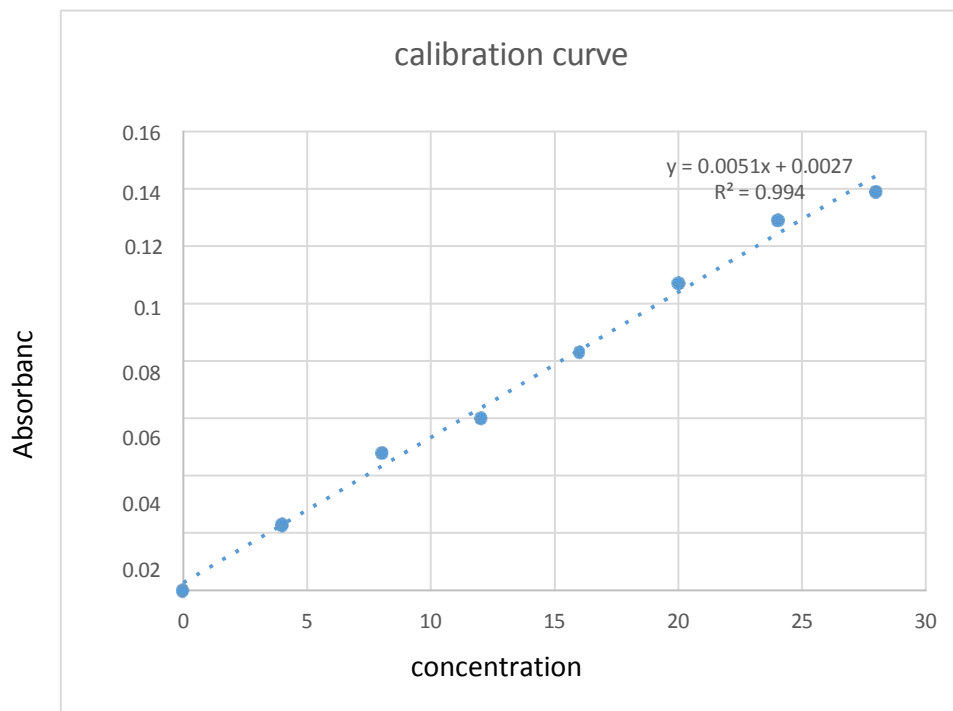


Fig.4 Effect of concentration of H₃PO₄ on colour development

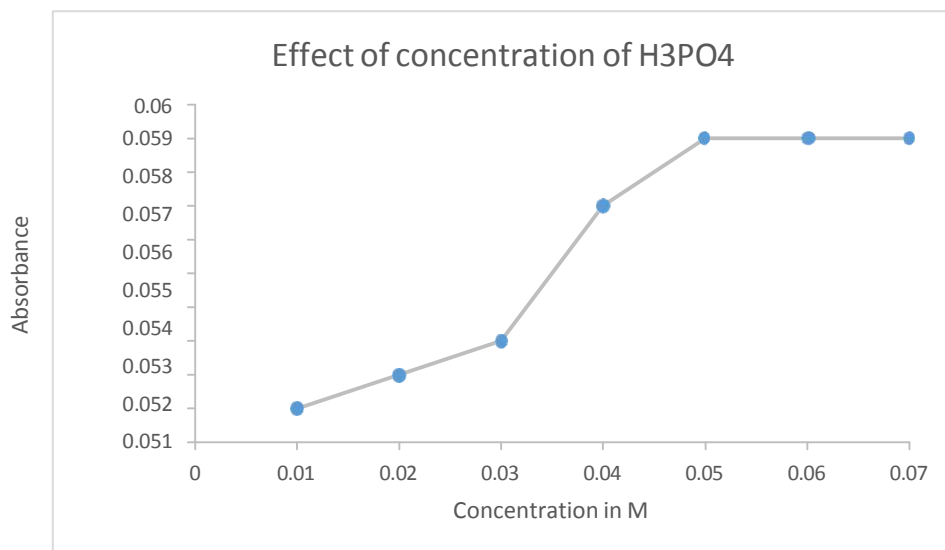


Fig.5 Effect of concentration of 1,10-Phenanthroline on absorbance of developed system

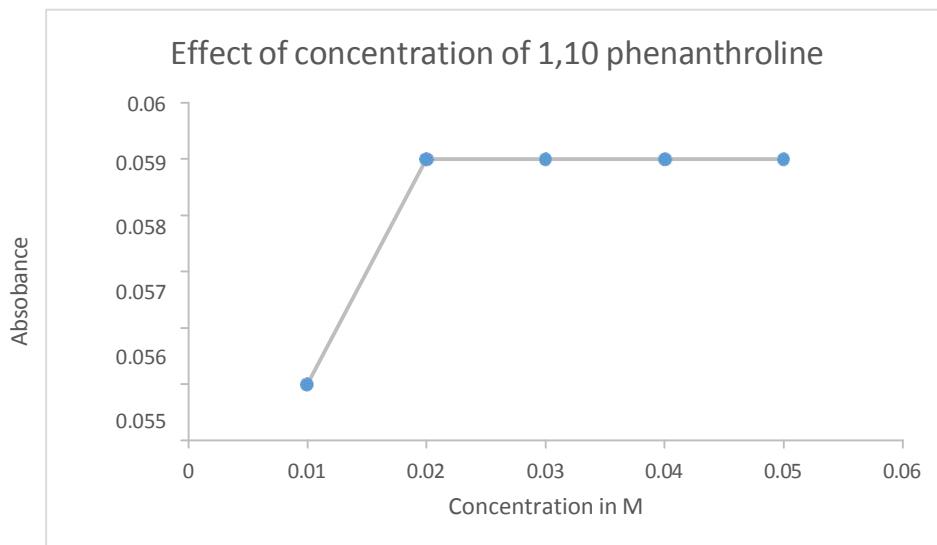


Fig.6 Effect of heating time on absorbance

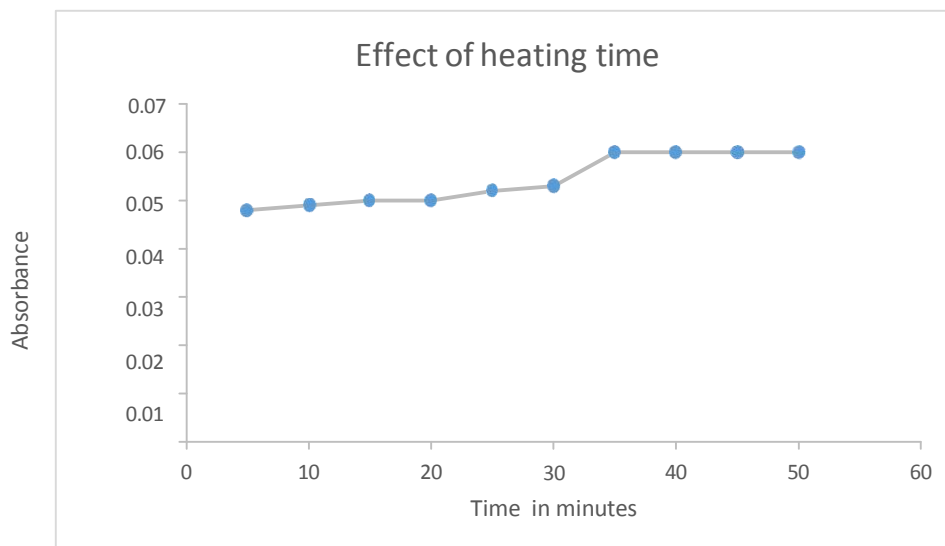


Fig.7 Coloured development reaction

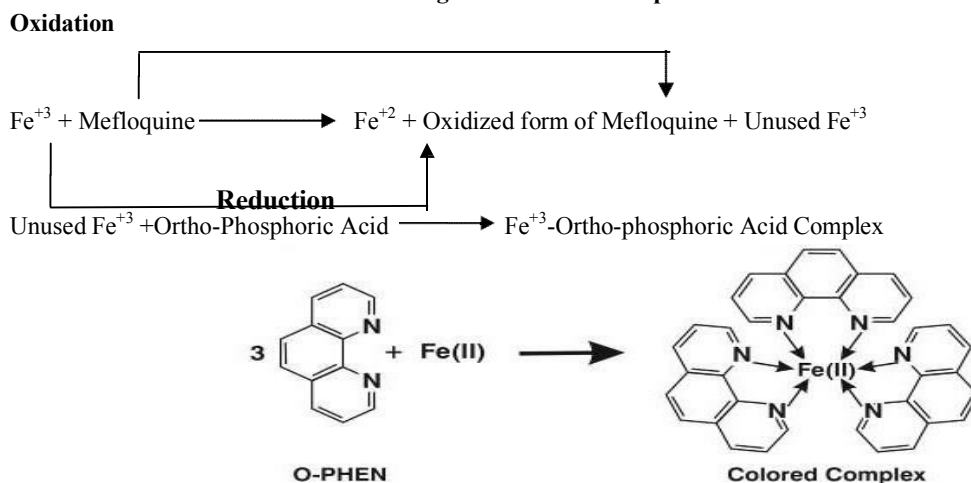


Table-1 Regression parameters, Optical characteristics Precision and Accuracy of the proposed method.

Parameter	Method
λ_{max} Maximum Wavelength	510 nm
Beer's Law Limits $\mu\text{g}/\text{cm}^3$	4-28
Sandell's Sensitivity ($\mu\text{g}/\text{cm}^2 / 0.0001$ Absorbance)	0.166
Molar Absorptivity $\text{Lt.mole}^{-1}.\text{cm}^{-1}$	2269.8
Slope (b) ^a	0.0051
Intercept (a) ^a	0.0027
S.D on intercept (S _a)	0.0089
Correlation Coefficient (r)	0.994
Standard Deviation (S)	0.0369
%Relative Standard Deviation	39.126
Limit of Detection (LOD) $\mu\text{g}/\text{cm}^3$	5.762
Limit of Quantification (LOQ) $\mu\text{g}/\text{cm}^3$	17.462

^aRegression equation is given as $Y = a + bC$, Where Y is the absorbance and C is the concentration in $\mu\text{g}/\text{cm}^3$ and b is %Relative standard deviation which is calculated for ten determinations.

Table-2 Determination of Pharmaceutical Formulations of Metformin

Drug	Manufacturing company	Labelled amount(mg)	*Amount found by Proposed Method	*Amount found by Reference Method
Mefloquine tablet	Abbott Healthcare Pvt. Ltd.	500	499.69	499.87

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