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Research Article

SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF CHLOROQUINE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

Simple, Sensitive, Precise, Accurate and Cost-effective Difference spectrophotometric method for the determination of Chloroquine in bulk and tablet dosage form has been described. The ultraviolet spectra of a Chloroquine containing , amine as functional group is dependent on the state of ionization of the functional group & consequently on the pH of the solution. The proposed method is based on the principle that, Chloroquine exhibits different spectral characteristics in alkaline medium (0.1 M Sodium hydroxide) & acid medium (0.1 M Hydrochloricacid) ,difference in absorptivity (ΔA) is directly related to concentration. **ΔA = abc** Chloroquine in acidic medium is scanned over UV region by taking basic drug solution as blank. From the absorbance values, Two wave lengths are selected one at 285 nm(positive peak) and another at 345 nm(negative peak). The sum of the absolute values at these wavelengths is called amplitude. The amplitude is proportional to the amount of drug. Factors affecting selection of optimum pH,choice of wave lengths for maximum accuracy and precession are discussed. Beer's law is obeyed in the concentration range of 50-250 µg/ml with correlation coefficient of 0.999. The developed method has been successfully applied to pharmaceutical formulations without any interference from common excipients.

Keywords: Acidic medium (0.1 M Hydrochloric acid), Basic medium (0.1 M Sodium hydroxide), Chloroquine (CQ).

INTRODUCTION

Chloroquine (CQ)

Chloroquine, chemically,7-chloro-4-(4-diethylamino-1-methylbutylamino) quinoline, was originally synthesised in 1934 in Germany as Resochin. As the diphosphate and renamed chloroquine. It was extensively studied in America. It is soluble in water; but very slightly soluble in ethanol. It is practically insoluble in chloroform. The structural formula of chloroquine phosphate is as given in Figure I.

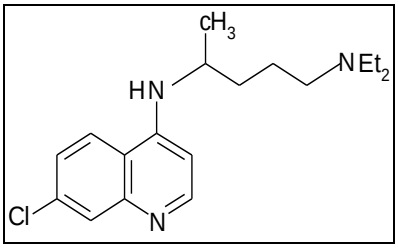

Figure I: Chloroquine

Uses

1. Chloroquine is the drug of choice for clinical cure and suppressive prophylaxis of all types of malaria, except that caused by resistant p. falciparum. It completely cures sensitive falciparum disease, but relapses in vivax and ovale malaria are not prevented, though interval between relapses may be increased. 2. Extraintestinal amoebiasis. 3. Rheumatoid arthritis. 4. Dicoid lupus erythematosus-very effective; less valuable in systemic LE. 5. Lepra reactions. 6. Photogenic reactions. 7. Infectious mononucleosis; affords symptomatic relief.

Doses

In the suppression of malaria, 500 mg once weekly; in the treatment of malaria, 0.5 to 1.5 g daily. In the treatment of malaria, by intravenous or intramuscular injection; for an adult, the equivalent of 200 to 300 mg of chloroquine base. In the treatment of hypatic amoebiasis, 0.5 to 1.0 g daily in divided doses. Chloroquine phosphate tablet should not be chewed.

Chloroquine base 150 mg 2 tablets BD. RESOCHIN, CLOQUIN, LARIAGO, NIVAQUINP 150 mg and 300 mg, 100 mg per 10 ml in oral susp., 40 mg/ml injections are available in pharmaceutical formulations.

Side effects

Toxicity of chloroquine is low, but side effects are frequent and unpleasant: nausea, vomiting, anorexia, uncontrollable itching, epigastria pain, uneasiness difficulty in accommodation and headache. Suppressive doses have been safely given for 3 years. Parenteral administration can cause hypotension, cardiac depression, arrhythmias and CNS toxicity including convulsions (more likely in children). Prolonged use of high doses may cause loss of vision due to retinal damage. Corneal deposits may also occur and graying of hair cans reversible on discontinuation.

Only a few methods viz, HPLC, Spectrofluorimetry, electrophoresis, UV-visible spectrophotometry appeared in the literature for the determination of CQ in bulk and pharmaceutical formulations. There is a need for simple spectrophotometric method for the analysis of Chloroquine in pharmaceutical formulations. No spectrophotometric methods in UV region are reported in the literature for Chloroquine analysis. In this paper, simple and sensitive Ultra violet spectrophotometric method for the analysis of chloroquine was described. The method is based on difference absorbance of Chloroquine in acid and base medium.

No interference was observed in the analysis of Chloroquine from common excipients found in pharmaceutical formulation. The proposed method is economic when compared with HPLC methods.

MATERIALS AND METHODS

Instrumentation

After due calibration of the instrument, spectral and absorbance measurements are made using ELICO UV-160 A double beam Spectrophotometer manufactured by M/S ELICO private Limited, Hyderabad, India. Pure Chloroquine sample was kindly gifted by BAL Pharma, Bangalore. All the chemicals used were of analytical grade. All the solutions were freshly prepared with double distilled water. Reagents were prepared a fresh for every method.

Since the drug was stable in 0.1 M Sodium hydroxide and 0.1 M Hydrochloric acid ,Freshly prepared 0.1 M Sodium hydroxide and 0.1 M Hydrochloric acid were selected as the solvents for the developed method.

Preparation of Reagents

Hydrochloric acid (0.1 N)

Hydrochloric acid solution (0.1N) is prepared by diluting the requisite volume of concentrated AR hydrochloric acid (Ranbaxy make) with distilled water and standardized by usual procedure.

NaOH solution (0.1N)

It is prepared by dissolving 4 gms of sodium hydroxide (Merck) to 1000 ml with distilled water.

Preparation of Standard solution of drug

Chloroquine solution

50 mg of Chloroquine was weighed separately and dissolved in 0.1 M Hydrochloric acid and 0.1 M Sodium hydroxide separately. The solutions were made up the volume to 50 mL in volumetric flasks with 0.1 M Hydrochloric acid and 0.1 M Sodium hydroxide separately. One ml of this solution contains 1mg/ml. The stock solution is further diluted to get desired concentration.

METHOD

In to a series of 25 ml standard flaks containing Chloroquine drug solution ranging from 0.5-2.5 ml are taken. To each flask 1ml of 0. 1N hydrochloric acid is added. These flasks are scanned over the wave length range of 280-365 nm against reagent blank prepared by taking various drug solutions (0.5-2.5 ml) in volumetric flasks containing 1 ml of 0.1 M sodium hydroxide solution .From the absorbance values two wavelengths at 285 and 345 nm are selected one at positive peak and another at negative peak, the amplitude is calculated from these values. The results are presented in figure.II.

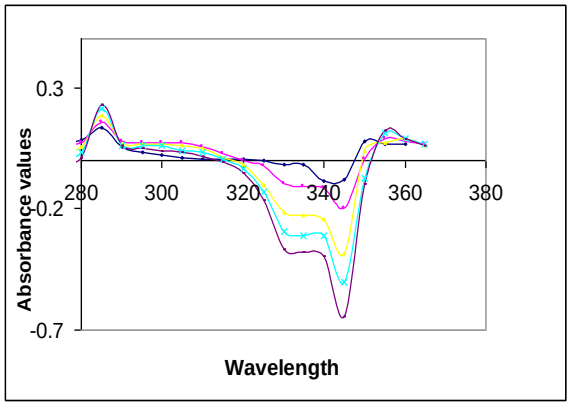

Figure II. Spectrum of Chlroquine

Calibration and amount of drug

The calibration curve is plotted between amplitude values and amount of drug (concentration of drug). The calibration curve is found to be linear over a concentration range of 50 to 250ug/ml of chloroquine.The amount of chloroquine present in the sample is estimated from the calibration graph.The data and results are presented in table I and figure III.

Table I

Amount of drug drug(µG/ML)	Absorbance(+ve) at 285nm	Absorbance(-ve) at 345nm	Amplitude
50	0.039	-0.250	0.373
100	0.064	-0.338	0.714
150	0.079	-0.535	1.025
200	0.087	-0.711	1.339
250	0.093	-0.879	1.678

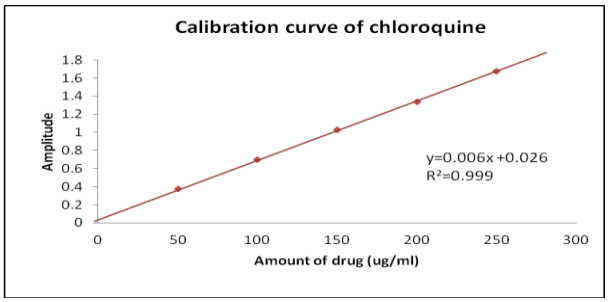

Figure III: Calibration curve of Chlroquine

Pharmaceutical analysis

Tablets powdered equivalent to 50 mg of the drug is weighed accurately and transferred into 50 ml standard flask and shaken well with 30 ml of methanol for five minutes. The solution is filtered into 50 ml standard flask and the volume is adjusted to 50 ml with methanol. One of the drug solutions is further diluted to five ml with distilled water to obtain the working concentration. The procedure described above of the proposed assay method is followed and the drug content of the sample is then estimated from the calibration curve. The results are present in table. II.

Table II:Assay of Chloroquine by Difference absorbance method in pharmaceutical formulations

Sample	Labelled Amount (mg)	*amount Found by Reference Method± s.d*	*amount Found by Proposed Method± s.d*	% of label Claim	Rsd%*	T^*_{cal}	F*
Tablet1	250	249.526 ±0.074	249.522 ±0.084	99.81	0.033	0.079	0.778
Tablet2	500	499.525 ±0.073	499.522 ±0.087	99.90	0.017	0.057	0.710
Tablet3	500	500.017 ±0.004	500.018 ±0.005	100.01	0.001	0.542	0.721

Average ± Standard deviation of six determinations, the t & F-values refer to comparison of the proposed method with reference method.

RESULTS AND DISCUSSION

The method is applied for the estimation of chloroquine in pharmaceutical formulation. The drug solution in acidic medium is scanned over the UV region by taking the basic drug solution as blank. From the absorbance values, spectrum is constructed. Two wave lengths are selected one at 285nm and another at 345nm. The sum of the absolute values at these wavelengths is called amplitude. The amplitude is proportional to the amount of drug. The calibration curve was plotted with the amplitude values verses amount of drug. The Standard deviation, Coefficient of variation and t_{cal} of the chloroquine is calculated from five measurements of replicate samples. The values of Standard deviation and Coefficient of variation and t_{cal} were shown in Table.II. The values of standard deviation and Coefficient of variation are low, indicates high accuracy and reproducibility of the method. The data of assay values of commercial formulations is subjected to statistical evaluation for student 't' test to study the proposed method. The calculated 't' values are less than 't' theoretical values with 4 (n-1= 5-1) degrees of freedom at 5% level of significance indicate that there is no significant difference between proposed method and standard method.

The proposed method is simple, less time consuming and it can be successfully adopted for the estimation of chloroquine in tablets. Please refer table.III.

Table III: Optical characteristics

Parameters	Method-value
λmax (nm)	285 and 345
Beer's law limit (µg/ml)	50-250
Correlation coefficient (r2)	0.999
Regression Equation (y=mx+c)	y=0.006x +0.026
Intercept (c)	0.026
Slope (m)	0.006

CONCLUSION

The Standard Deviation, % R.S.D. and Standard Error calculated for the method are low, it indicates high degree of precision of the method. The % R.S.D. is also less than 2 % as required by ICH

guidelines. The results of the recovery studies shows the high degree of accuracy of the proposed method. Hence the developed method is simple, rapid, precise, accurate, cost effective and can be employed for the routine analysis of Chloroquine in both bulk and tablet dosage form.

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