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RESEARCH ARTICLE……!!!

SIMULTANEOUS DETERMINATION AND VALIDATION OF CHLOROQUINE PHOSPHATE AND PARACETAMOL BY SIMULTANEOUS EQUATION AND FIRST ORDER DERIVATIVE METHODS IN BULK AND PHARMACEUTICAL FORMULATION

Manzoor Ahmed, Swarnalatha B M*, Sathish kumar Shetty

Department of Pharmaceutical Analysis, National College of Pharmacy, Shimoga - 577201, Karnataka, India.

KEYWORDS:

Chloroquine phosphate, Paracetamol, Simultaneous equation method, Derivative spectroscopic method.

FOR CORRESPONDENCE:

Swarnalatha B M*

ADDRESS:

Department of Pharmaceutical Analysis, National College of Pharmacy, Shimoga - 577201, Karnataka, India.

ABSTRACT

Two simple, accurate, rapid and precise UV Spectrophotometric methods have been developed for simultaneous estimation of Chloroquine phosphate and Paracetamol in bulk drug & tablet dosage form by Simultaneous equation method and Derivative spectrophotometric method using distilled water as solvent. The analytical wavelengths for Chloroquine phosphate and Paracetamol were 221nm and 243nm for simultaneous equation method and 213nm and 226nm for first order derivative method respectively. Beer's law obeyed in the concentration range of 2-10µg/ml for both the drugs with correlation coefficient of 0.999. LOD and LOQ was found to be 0.0537µg/ml and 0.1627µg/ml for Chloroquine phosphate and 0.0525µg/ml and 0.1591µg/ml for Paracetamol respectively in Simultaneous equation method and for first order derivative method LOD and LOQ was found to be 0.0577µg/ml and 0.1750µg/ml for Chloroquine phosphate and 0.0869µg/ml and 0.2633µg/ml for Paracetamol respectively. In both the methods the %RSD for intra-day and inter-day precision was within 2%. Both the methods were found to be rapid, specific, precise and accurate. Hence these methods can be applied for routine analysis of Chloroquine Phosphate and Paracetamol in combined dosage form. The above methods are validated according to ICH Guidelines.

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INTRODUCTION:

Paracetamol is used as an analgesic and antipyretic. It is official in the IP. Chloroquine phosphate is used mainly as antimalarial and anti-inflammatory. It is official in IP. Several methods are reported for individual estimation of PARACETAMOL and CHLOROQUINE. Combination of these two drugs used in the treatment of malaria.

Paracetamol (PARA), chemically know as N-(4-hydroxyphenyl)acetamide. It has weak activity on COX in the inflamed peripheral tissues which have high concentration of peroxides; however, it equals the blocking effect of asperin on this enzyme in the brain. Therefore, paracetamol is a potent antipyretic and is equi analgesic with asperin in therapeutic doses but devoid of significant anti-inflmmatory effect [1-2].

Chloroquine phosphate (CHQ), chemically known as 7-chloro-4[{4-(diethylamino)-1-methylbutyl} amino] quinoline, is a 4-aminoquinolein antimalarial drug. It is the prototype synthetic antimalarial drug most widely used to treat all types of malarial infections. The drug is also prescribed to decrease the symptoms of rheumatoid arthritis and to treat systemic and discod lupus erythematosus in adults [3].

The combination of Paracetamol and Chloroquine was significantly used in the treatment of malaria [4-5].

On literature survey, it was found that no method has been reported for simultaneous estimation of Paracetamol and Chloroquine in combined dosage form and no method is available in pharmacopeias. In the view of the need for a suitable methods for routine analysis in combined formulations, attempts are made to develop simple, precise and accurate analytical methods for simultaneous estimation of titled drugs and extend it for their determination in formulations [6-7].

MATRIALS AND METHODS:

Instrument

For UV-Visible Spectroscopy methods, Shimadzu model 1800 double beam UV-Visible Spectrophotometer with spectral band width of 1 ± 0.2nm, wavelength accuracy of ± 0.3nm and a pair of quartz cuvettes having 1cm path length was used. Distilled water was used throughout the experimental work.

Chemicals

Standard Paracetamol and Chloroquine Phosphate were procured from yarrow chem products, Mumbai.

METHODS [8-9]

Preparation of standard solutions

100 mg each of Paracetamol and Chloroquine phosphate were weighed separately and transferred into two different 100 mL volumetric flask. Both the drugs were dissolved in 50 mL of distilled water by ultrasonication and then volume was made up to the mark with distilled water to obtain a concentration of 1000µg/ml of each component (stock A).

From the above stock A solution, 10 ml of aliquot was pipetted out in a 100 mL volumetric flask and the volume was made up to the mark with distilled water to obtain a concentration of 100µg/mL of each component (stock B).

From the above stock B solution further dilutions were made to get the concentration range of 2-10µg/mL for both the drugs.

Preparation of sample solution:

20 tablets of Paracetamol and Chloroquine phosphate in combination were weighed and powdered. Tablet powder equivalent to 100 mg of Paracetamol was weighed accurately and dissolved in 70 mL of distilled water and sonicated for 15 min then filtered and the filtrate was diluted upto 100 mL with distilled water (stock A).

From the above stock A solution, 10 ml of aliquot was pipetted out in a 100 mL volumetric flask and the volume was made up to the mark with distilled water to obtain a concentration of 100µg/mL of each component (stock B).

From the stock B further dilutions were made to get the concentration of the drugs within the range.

Method A (Simultaneous equation method)

The standard solutions of PARA and CHQ were scanned seperately in the range of 200 to 400 nm against distilled water as blank and wavelengths of maximum absorbance were determined. The absorbances of all dilutions were recorded at selected wavelengths λ1 (243 for PARA) and λ2 (221 for CHQ) and calibration curves were plotted[10]. The overlay spectrum of these drugs is shown in Fig 3.

The concentration of both drugs in mixture can be calculated by using following equations

$Cx = A_1ay_2 – A_2ay_1 / ax_1ay_2 – ax_2ay_1$

$Cy = A_1ax_2 - A_2ax_1 / ay_1ax_2 - ay_2ax_1$

Where,

C_x = absorbance of Sample at 243 nm

C_y = absorbance of Sample at 221nm

ax_1 = absorptivity of Paracetamol at 243nm

ax_2 = absorptivity of Paracetamol at 221nm

ay_1 = absorptivity of Chloroquine Phosphate at 243nm

ay_2 = absorptivity of Chloroquine Phosphate at 221nm

Method B (First order derivative)

For the estimation of Paracetamol and Chloroquine Phosphate by first order derivative spectroscopy, zero crossing point for both drugs were obtained and the wavelengths were selected in manner such that at the zero crossing of one drug, the other drug should show substantial absorbance. From the first order derivative spectra of standard Paracetamol and Chloroquine Phosphate, zero crossing point of Paracetamol was found at 243nm and zero crossing point of Chloroquine Phosphate was found at 221nm and wavelength selected for their estimation was 226nm for PARA and 213nm for CHQ.

VALIDATION OF THE METHOD:

All the methods were validated according to ICH guidelines by carrying out analysis of six replicate samples of tablet. Recovery studies were carried out at three different levels i.e., 80%, 100%, 120% by adding the pure drug to previously analyzed tablet power sample. From the amount of the drug found, percentage recovery was calculated[11-12**]**

RESULTS AND DISSCUSION

The linearity range in both the methods for PARA and CHQ was 2-10µg/ml. The % R.S.D. was found to be less than 2, which indicates the validity of method. Linearity was observed by linear regression equation method for PARA and CHQ in different concentration range. The Correlation coefficient of these drugs was found to be close to 1.00, indicating good linearity. The assay results obtained by proposed methods are in fair agreement, hence it can be used for routine analysis of both the drugs in combined dosage forms. There was no interference from tablet excipients was observed in these methods. It can be easily and conveniently adopted for routine quality control analysis. Both the methods are accurate, simple, rapid, precise, reliable, sensitive, reproducible and economic and are validated as per ICH guidelines.

Fig 1: Chemical Structure of PARA

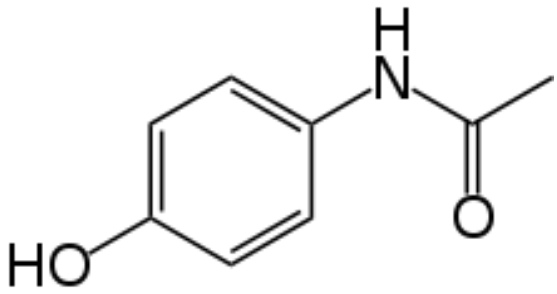


Fig 2 : Chemical Structure of CHQ

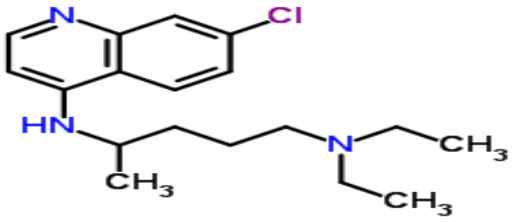


Fig 3: Overlay Spectrum of Standard Mixture

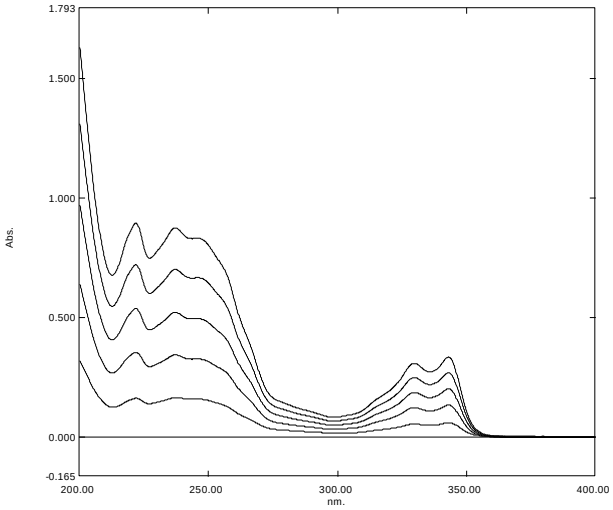


Fig 4 : Calibration Curve of PARA at 243nm

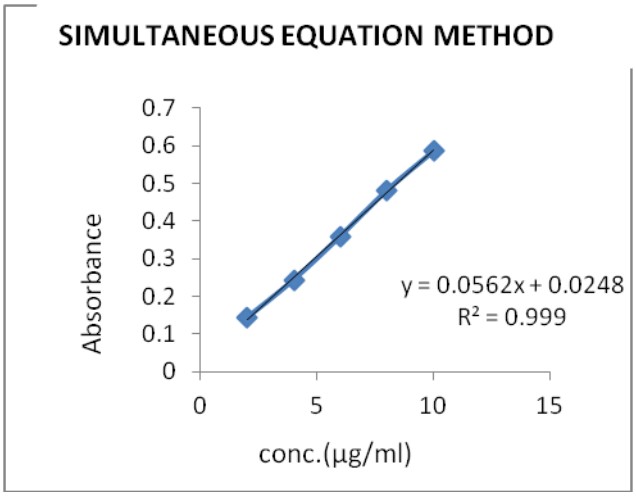


Fig 5 : Calibration Curve of CHQ at 221nm

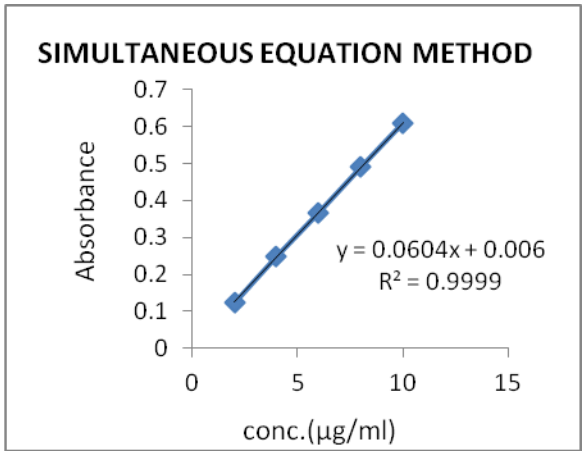


Fig 6 : overlay Spectrum of Standard Mixture

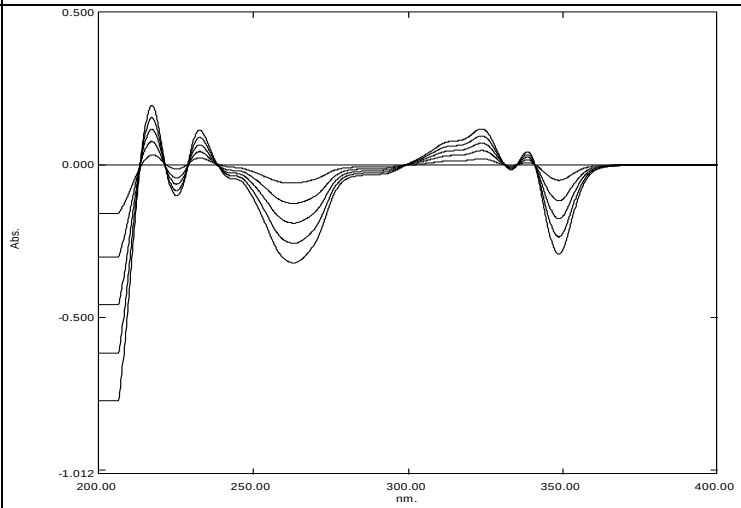


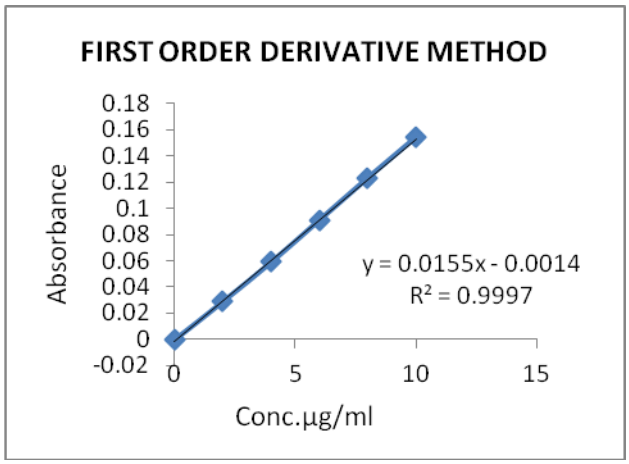
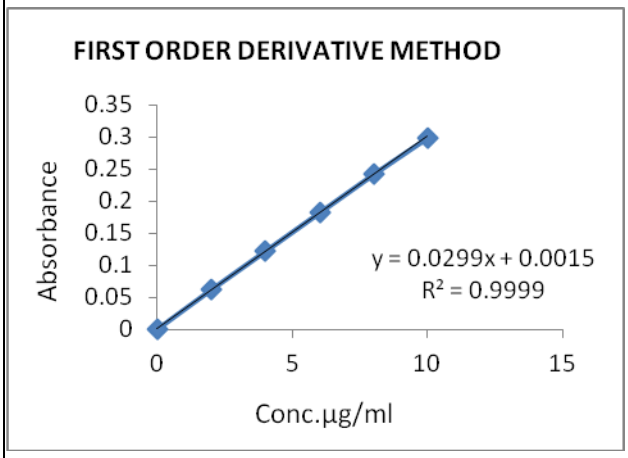
Fig 7 : Calibration Curve of PARA at 226nm	Fig 8 : Calibration Curve of CHQ at 213nm
	

Table 1: Summary of validation Parameters by Developed Methods

Parameter	Method A		Method B	
	PARA	CHQ	PARA	CHQ
Wavelength	243	221	226	213
Linearity Range (µg/ml)	2.0-10.0	2.0-10.0	2.0-10.0	2.0-10.0
Regression equation (y = a + bc)	y = 0.0562x + 0.0248	y = 0.0604x + 0.006	y = 0.0155x +0.0014	y = 0.0299x + 0.0015
Slope (b)	0.0562x	0.0604x	0.0155x	0.0299x
Intercept (a)	0.0248	0.006	0.0014	0.0015
Correlation Coefficient (r^2)	0.9999	0.9999	0.9999	0.9999
LOD (µg/ml)	0.0525	0.0597	0.0869	0.0577
LOQ (µg/ml)	0.1591	0.1627	0.2633	0.175

Table 2 : Statistical Validation Data For Accuracy Determination

Level of % Recovery	Components	Amount present (µg/ml)	Amount of Standard drug added (µg)	Method A			Method B		
				Total amount recovered (µg)	% Recovery	RSD	Total amount recovered (µg)	% Recovery	RSD
80%	PARA	4	3.2	7.15	99.31	0.16	7.21	101.14	0.16
	CHQ	4	3.2	7.15	99.31	0.14	7.18	99.72	0.21
100%	PARA	4	4	7.99	99.88	0.43	7.95	99.38	0.26
	CHQ	4	4	8.1	101.25	1.23	7.98	99.75	0.19
120%	PARA	4	4.8	8.72	99.09	0.31	8.79	99.89	0.41
	CHQ	4	4.8	8.77	99.21	1.08	8.84	100.46	0.57

Table 3 : Statistical Validation Data for Intra-day Precision

Parameter	Method A		Method B	
	PARA	CHQ	PARA	CHQ
Mean	99.806	99.833	99.694	99.666
Standard Deviation	0.5101	0.3496	0.28707	0.2981
Relative Standard Deviation	0.5111	0.3502	0.2879	0.2991
Standard Error	0.2082	0.1427	0.1172	0.1217

Table 4 : Statistical Validation Data for Inter-day Precision

Parameter	Method A		Method B	
	PARA	CHQ	PARA	CHQ
Mean	99.667	99.7	99.888	99.861
Standard Deviation	0.7454	0.8283	0.5443	0.6617
Relative Standard Deviation	0.7478	0.8308	0.5449	0.6627
Standard Error	0.3043	0.3382	0.2222	0.2702

CONCLUSION:

The developed simultaneous equation method and first order derivative method was found to be simple, rapid, accurate, sensitive and specific. Hence the above methods for the simultaneous estimation of PARA and CHQ in combined dosage form can be used for routine analysis in bulk and its formulation.

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