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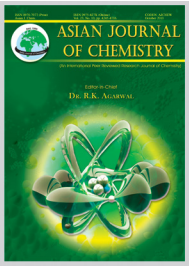

Spectrophotometric Determination of Centrophenoxine Hydrochloride with Colour Reaction of Rose Bengal

WEI-XING MA[1,2,3*], YAN ZHOU[1], QIAO LING WANG[1] and ZHENG ZHANG[1]

[1]School of Chemical Engineering, Huaihai Institute of Technology, Lianyungang 222005, Jiangsu Province, P.R. China
[2]Jiangsu-Marine Resources Development Research Institute, Lianyungang 222005, Jiangsu Province, P.R. China
[3]Key Lab of Applied Chemistry, Huaihai Institute of Technology, Lianyungang 222005, Jiangsu Province, P.R. China

*Corresponding author: Tel: +86 518 85895405, E-mail: weixingma650528@163.com; weixingma650528@126.com

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A new spectrophotometric method for determination of centrophenoxine hydrochloride was proposed based on the colour reaction of centrophenoxine hydrochloride with rose bengal to form ion association complex in the Clark-Lubs buffer media with pH 2.6, whose maximum wavelength was at 568 nm with the apparent molar absorptivity of complex was 5.589×10^3 L mol^{-1} cm^{-1}, Beer law was obeyed in the range of 2-21 mg L^{-1} for centrophenoxine hydrochloride. The proposed method was stable, accurate, sensitive and rapid and has been applied for the determination of centrophenoxine hydrochloride with satisfactory results.

Key Words: Centrophenoxine hydrochloride, Rose bengal, Spectrophotometry, Determination.

INTRODUCTION

Centrophenoxine hydrochloride or meclofenoxate hydrochloride is an ester of dimethyl aminoethanol and *p*-chlorophenoxy acetic acid. It is a known antiaging drug, which enables its passage through the blood brain barrier very easily and can stimulate brain metabolism, can increase lifespan and improve learning capacity. Therefore, it is used as a psychostimulant in the nootropic agent group available in capsule and tablet formulations approved for traumatic cataphora, alcoholic poisoning, anoxia neonatorum and children's enuresis in China.

Several procedures have been reported in the literature for the determination of centrophenoxine hydrochloride. These methods are spectrophotometry[1-5] and high performance liquid chromatography methods[6-9].

Visible spectrophotometric method has been widely applied to the determination of compounds of pharmaceutical preparations. In general, this method is faster and cheaper than the high performance liquid chromatography methods and more precise. In this work, a new spectrophometric method for the assay of centrophenoxine hydrochloride was developed,which was based on the colour reaction between centrophenoxine hydrochloride and rose bengal to form ion association complex in the Clark-Lubs buffer media with pH 2.6. In the proposed method, there are no complicated sample separation and extraction steps with satisfactory analytical results.

EXPERIMENTAL

All chemical reagents used were of analytical or pharmaceutical grade and distilled water was used throughout the experiments. Pharmaceutical grade centrophenoxine hydrochloride (99.95 % pure, CH) was obtained as gift sample from Nanjing Haichen Pharma Ltd., China. A standard solution of centrophenoxine hydrochloride containing 100 µg/mL was prepared in distilled water. 5×10^{-4} mol L^{-1} rose bengal solution was prepared by dissolving 0.5088 g of rose bengal and diluting the solution to 1000 mL with the distilled water. Clark-Lubs solutions were prepared at pH range from 2 to 4 based on the described procedure[10].

Different dosage forms of centrophenoxine hydrochloride such as Jiannaoling injection, Surueisu injection, Zhengsu injection and Teweizhi capsules were obtained commercially from different firms in China.

A Shimadzu UV-250PC model UV-Visible spectrophotometer (Tokyo, Japan) with 1 cm matched quartz cells was used for the absorbance measurements.

Assay procedure: An aliquot of the stock solution or sample solution containing 20-210 µg of centrophenoxine hydrochloride was transferred into a series of 10 mL volumetric flasks, 2 mL of 5×10^{-4} mol L^{-1} rose bengal solution and 2 mL of Clark-Lubs solution at pH 2.6 were added successively. Each flask was made up to volume with distilled water. The absorbance of the solution containing centrophenoxine

hydrochloride was measured at 568 nm against a reagent blank.

RESULTS AND DISCUSSION

Absorption spectra: Centrophenoxine hydrochloride is designated chemically as 4-chlorophenoxy-acetic acid 2-(dimethylamino)ethyl ester hydrochloride, or (*p*-chlorophenoxy)acetic acid 2-(dimethylamino)ethylester hydrochloride. It react with rose bengal in Clark-Lubs solution at pH 2.8 to form the colouring complex. The absorption spectra of reagent rose bengal and the complex was shown in Fig. 1. From Fig. 1, it was found that the maximum absorption wavelength of the reagent obviously at 520 nm and the maximum absorption wavelength of the complex at 568 nm, Δλ is 48 nm. Hence, 568 nm was selected for further studies.

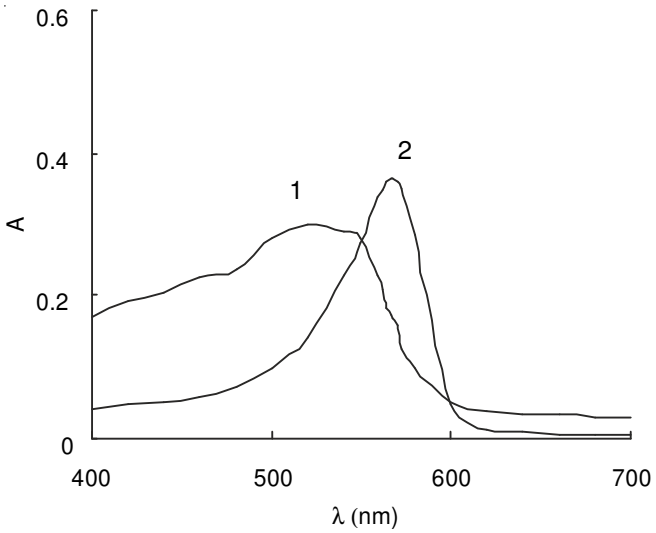
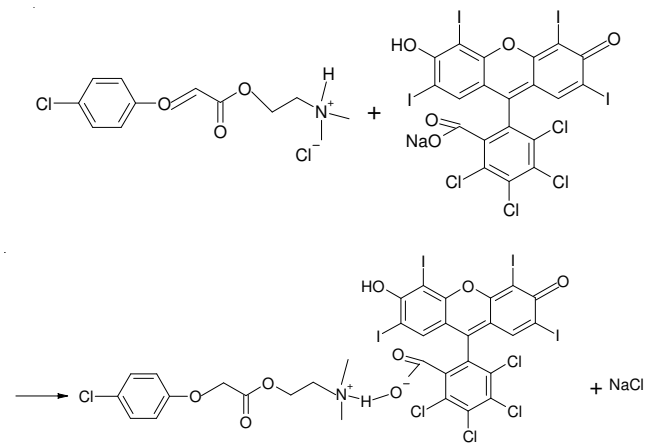


Fig. 1. Absorption spectra: (1) rose bengal (against water), (2) rose bengal + centrophenoxine hydrochloride (against rose bengal), [centrophenoxine hydrochloride] = 10 μg mL^{-1}; [rose bengal] = 1.0 × 10^{-4} mol L^{-1}

The composition ratio of the complex was measured with the molar ratio method. The result indicated that the ratio of centrophenoxine hydrochloride and rose bengal in the ion association complex was 1:1. According to the above, the suggested colour reaction was shown in **Scheme-I**.



Scheme-I: Reaction equation of rose bengal with centrophenoxine hydrochloride

Effect of temperature: The effect of temperature on the absorbance in the range of 15-50 ºC was investigated and the results were shown in Table-1. It was seen that the absorbance was almost constant at 20-30 ºC. For the reason of simple operation, room temperature range from 20 to 30 ºC was chosen as optimum temperature for further study.

TABLE-1
EFFECT OF TEMPERATURE

Temperature (ºC)	15	20	25	30	40	50
Absorbance*	0.187	0.209	0.208	0.209	0.178	0.135

*10 μg mL^{-1} centrophenoxine hydrochloride; 1.0 × 10^{-4} mol L^{-1} rose bengal; pH 2.6

Effect of reaction time: The effect of reaction time was studied. As shown in Fig. 2, centrophenoxine hydrochloride reacted with rose bengal within at most 8 min at room temperature. The formed colour complex remained steady at least 112 min.

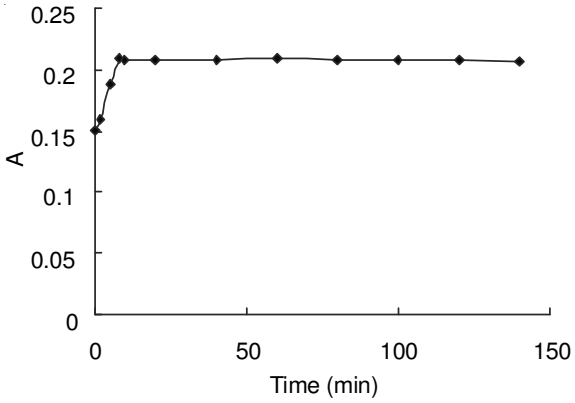


Fig. 2. Effect of reaction time: [centrophenoxine hydrochloride] = 10 μg mL^{-1}; [rose bengal] = 1.0 × 10^{-4} mol L^{-1}; pH 2.6

Effect of pH: The pH effect of the Clark-Lubs buffer solution on the absorbance were studied and the result shown in Fig. 3, When its pH was in the range of 2.2-3.4, the system had maximal and steady absorbance. The best scope of buffer solution dose was in the range of 1.5-2.5 mL. Therefore, 2 mL of Clark-Lubs buffer solution at pH 2.6 was used in this study.

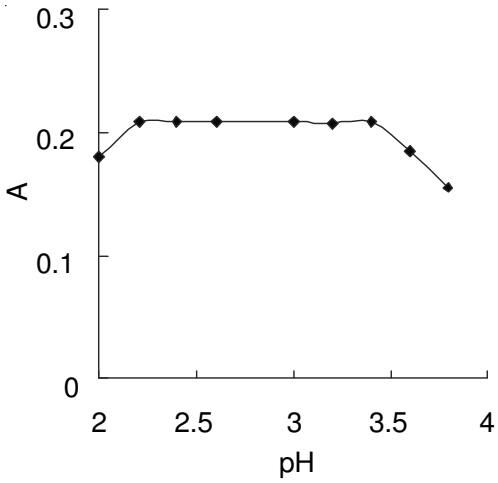


Fig. 3. Effect of pH: [centrophenoxine hydrochloride] = 10 μg mL^{-1}; [rose bengal] = 1.0 × 10^{-4} mol L^{-1}

Effect of rose bengal solution: The volume of rose bengal solution was studied as the colour reagent for centrophenoxine hydrochloride, the results shown as Fig. 4 suggested that the system has maximal and steady absorbance when the dose of colour reagent rose bengal solution was in the range of 1.5-3 mL. Therefore, 2 mL of 5×10^{-4} mol L^{-1} rose bengal solution was chosen in present study.

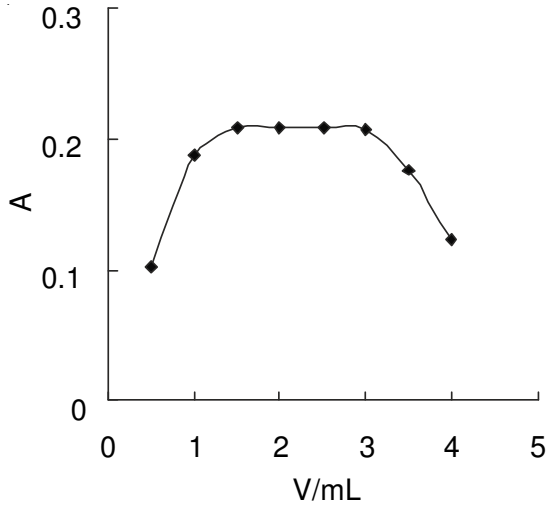


Fig. 4. Effect of rose bengal solution: [centrophenoxine hydrochloride] = 10 μg mL^{-1}; pH 2.6

Working curve and detection limit: A series of standard centrophenoxine hydrochloride solutions with different concentration were prepared. Under the chosen experimental conditions, the absorbance of these solutions were measured. The working curve was drawn and shown in Fig. 5. The results showed that Beer's law was obeyed in the concentration range of 2-21 μg mL^{-1} for centrophenoxine hydrochloride. The linear regression equation was A = 0.019C + 0.0186 with the regression coefficient γ = 0.9994. The reagent blank was determined 11 times and the detection limit of assay was 0.24 μg mL^{-1} by 3S/K method (S is the standard deviation of the reagent blank for 11 times determination, K is the slope of the working curve).

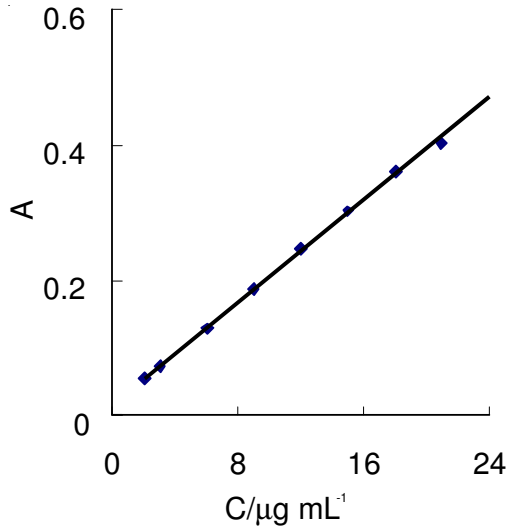


Fig. 5. Working curve

Recovery study: In order to study accuracy of the proposed method, recovery studies were carried out by the standard addition method. Known quantities of pure centrophenoxine hydrochloride were mixed with definite amounts of pre-analyzed formulations such that final concentration of centrophenoxine hydrochloride was within Beer's law limits and the mixtures were analyzed as before. The total amount of the drug was then determined and the amount of the added drug was calculated by difference. The results of recovery are given in Table-2. The average recoveries obtained were quantitative, its recoveries were at range of 98.28-99.80 % for determined wavelength at 568 nm. These results indicated good accuracy of the proposed method for determination of centrophenoxine hydrochloride.

TABLE- 2
RECOVERY STUDY FOR THE SPIKED CONCENTRATION OF CENTROPHENOXINE HYDROCHLORIDE TO THE PRE-ANALYZED DOSAGE FORMS

Formulation	Label claim (mg)	Amount added (mg)	Amount found[a]	Recovery (%)	RSD (%)
Jiannaoling injection	100	25	124.62	98.28	0.29
Jiannaoling injection	200	50	249.60	99.80	0.35
Surueisu injection	100	20	119.87	99.03	0.43
Zhengsu injection	100	30	129.88	99.60	0.38
Teweizhi capsules	100	20	119.79	98.95	0.45

[a]Each value is the mean of five measurements

Analytical application: The proposed method was applied for the determination of centrophenoxine hydrochloride in commercial injections and capsule. The results obtained were statistically compared to those of official method by students *t*-test for accuracy and the variance ratio *F*-test for precision as recorded in Table-3. The experimental values of t at 95 % confidence level did not exceed the theoretical value of 2.31, the experimental value of F for p = 0.05 also did not exceed the theoretical value of 6.39, indicating lack of significant difference between the proposed method and the official method. The results are shown in Table-3.

TABLE- 3
DETERMINATION OF CENTROPHENOXINE HYDROCHLORIDE IN PHARMACEUTICAL PREPARATIONS USING THE PROPOSED METHOD

Preparation	Labeled amount (mg)	This method recovery% ± SD[a]	Official method recovery% ± SD[a]
Jiannaoling injection	100	99.47 ± 0.42 F = 1.35; t = 1.47	99.38 ± 0.78 F = 1.25; t = 1.57
Jiannaoling injection	200	100.2 ± 0.57 F = 1.18; t = 1.76	99.98 ± 0.54 F = 1.90; t = 1.89
Surueisu injection	100	100.5 ± 0.62 F = 1.23; t = 1.79	99.95 ± 0.59 F = 1.53; t = 1.73
Zhengsu injection	100	99.24 ± 0.81 F = 1.33; t = 1.75	99.32 ± 0.87 F = 1.31; t = 1.76
Teweizhi Capsules	100	99.35 ± 0.29 F = 1.26; t = 1.53	99.30 ± 0.45 F = 1.56; t = 1.67

[a]Each value is the mean of five measurements

Conclusion

This paper demonstrated that the ion association complex reaction between centrophenoxine hydrochloride and rose bengal can be utilized as an useful method for the spectrophotometric determination of centrophenoxine hydrochloride. The proposed method has the advantages of being simple, cheap, accurate, rapid and requires minimum equipments and chemicals. These advantages encourage the application of the proposed method in routine quality control of the investigated centrophenoxine hydrochloride in industrial laboratories.

ACKNOWLEDGEMENTS

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