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USE OF EXTRACTIVE SPECTROPHOTOMETRY AND ION-PAIR FORMATION WITH CONGO RED FOR THE DETERMINATION OF PROMETHAZINE HYDROCHLORIDE ANTIPSYCHOTIC DRUG IN PHARMACEUTICAL FORMULATION

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Abstract:
Promethazine hydrochloride is phenothiazine used as antipsychotic drug. A simple, rapid and sensitive extractive spectrophotometric method is described for the determination of promethazine hydrochloride in pure form and in its pharmaceutical formulation. The method is based on the ion-pair complex formation between the drug and the Congo red dye in acidic medium. The red coloured chromogen, being extractable with chloroform, could be measured quantitatively at 483 nm. All variables were studied to optimize the reaction conditions. The method obeys Beer's law and the precision and accuracy of the method were checked. The molar composition and stability constant of the ion –pair complex formed is determined at room temperature by Turner and Anderson method . The molar composition of complex Congo red : PromethazineHCl is 1:2. The stability constant is 1.2489×10^4. The detection limit is 19.4 to 83.5 µg $m1^{-1}$ and the molar absorptivity is 3.5298×10^3 L mol^{-1} cm^{-1} and Sandell's sensitivity is 0.1125 µg cm^{-2} per 0.001absorbance unit.

Key words: Extractive spectrophotometry, ion-pair complex, promethazine hydrochloride, congo red.

INTRODUCTION: Phenothiazines are widely used drugs in the treatment of mental disease. Promethazine hydrochloride is one of the phenothiazine which shows neuroleptic, antihistaminic and antibacterial activity. It ischemically2-RS-N,N-dimethyl-1-(10Hphenothiazine-10 yl)propan -2- amine hydrochloride. The structure of promethazine hydrochloride is as shown below.

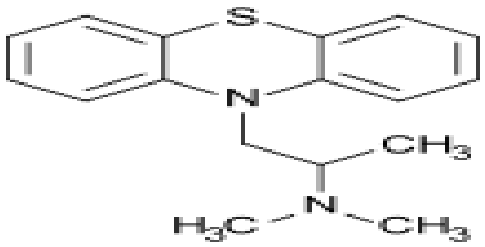

Figure 1: Structure of Promethazine

It is official in B.P. [1], USP [2] and I.P. [3]. Literature survey reveals that various methods for its determination are reported which include flow injection analysis [4, 5], chromatography [6, 7], spectroflorometry [8, 9], solid phase extraction [10]. The spectrophotometric method [11, 12] involved the chromogenic reaction with various reagents. Few extractive spectrophotometric methods [13-15] has been reported for the estimation of promethazine hydrochloride. The objective of the present study was to develop a simple economic extractive spectrophotometric method with easily available chromogenic reagent Congo red which can be used for routine quality control of drug in bulk and in its formation.

EXPERIMENTAL

Instrument : A Equiptronic model EQ282 visible spectrophotometer with a pair of 1 cm matched quartz cells was used for optical measurements.

Materials :

Standard stock solution : A 0.01M stock solution of pure promethazine hydrochloride (PMTH)(Sigma) was prepared in 0.1 N hydrochloric acid solution. From this stock solution working standard solution of 32 µg /ml was prepared by appropriate dilutions.

Congo red (CR) solution: A 0.01 M congo red solution was prepared in 0.1 N hydrochloric acid . The reagent solution of desired concentration was then obtained by further dilutions.

All chemicals used were of analytical grade. Chloroform and water used were double distilled.

METHOD:

Calibration curve: In a series of flasks an appropriate aliquots of standard PMTH solution were added and final volume was made to 15 ml. These aliquots were vigorously shaken for 15 minutes in two installments of 5 ml chloroform. The absorbance of one of the extracted layer was first scan in visible range for determination of maximum wavelength, λ_{max} (Figure 2). At this wavelength then absorbance for all other solutions of extracted chloroform were measured against reagent

blank and calibration curve was plotted for validation of Beer's Law (Figure 3).

Stability constant: 0.001M and 0.002M solutions of PMTH and CR were prepared by appropriate dilution. Different aliquots of drug and chromogenic reagent were mixed in varying proportion of mole fraction of drug. These aliquots were then similarly extracted with chloroform as discussed above. A Turner and Anderson [16] plot was plotted (Figure 4) to calculate stability constant of the complex formed.

Estimation of drug in tablet: Commercial tablet Phenargan were procured from local market. Twenty tablets were weighed and ground to fine powder in mortar. An amount of powder equivalent to 10 mg of drug was transferred to 100 ml volumetric flask. 0.1 N HCl was added and shaken thoroughly to dissolve the powder completely. The volume was made up to the mark and solution was filtered. Suitable aliquots were mixed with CR solution and extracted with 10 ml chloroform in two installments of 5 ml. Absorbance of extracted chloroform was obtain at $\lambda_{max.}$ the amount of drug in tablet was then calculated from calibration curve. The optical characteristic and results of error analysis is given in Table 1 and Table 2.

RESULT AND DISCUSSION

Congo red and promethazine hydrochloride forms ion pair complex in acidic medium. The drug and congo red individually are insoluble in water while the complex formed is insoluble in water and highly soluble in chloroform. This makes the basis of the proposed extractive spectrophotometric method.

The red coloured ion –pair complex formed shows broad absorption spectra with λ_{max} 483 nm (Figure 2). In Turner and Anderson plot (Figure 4) the maxima obtained at mole fraction = 0.666 of drug. Hence the molar composition of the complex formed is found to be PMTH : CR = 2:1. The stability constant was also calculated from same plot (Figure 4) by using equation

$$K = \frac{x}{(a_1 - x)(b_1 - x)} = \frac{x}{(a_2 - x)(b_2 - x)} \text{ and } x = \frac{a_1 b_1 - a_2 b_2}{(a_1 + b_1) - (a_2 + b_2)}$$

It is found to be 1.2489×10^4. The Beer's Law plot is found to be satisfactorily linear over the range of 19.4 µg ml^{-1} to 83.5 µg ml^{-1}. The ion-pair complex is intensely red coloured shows molar absorbtivity 3.5298×10^3 L mol^{-1} cm^{-1}. The recovery study of drug shows good percentage recovery of 99.794% with relative standard deviation of 0.1907 and standard deviation of ± 0.01903.

CONCLUSION:

The proposed method is simple, accurate and reproducible and can be used for routine quality control analysis of promethazine hydrochloride.

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Fig. 2: Maximum wavelength of absorption of complex (λ_{max})

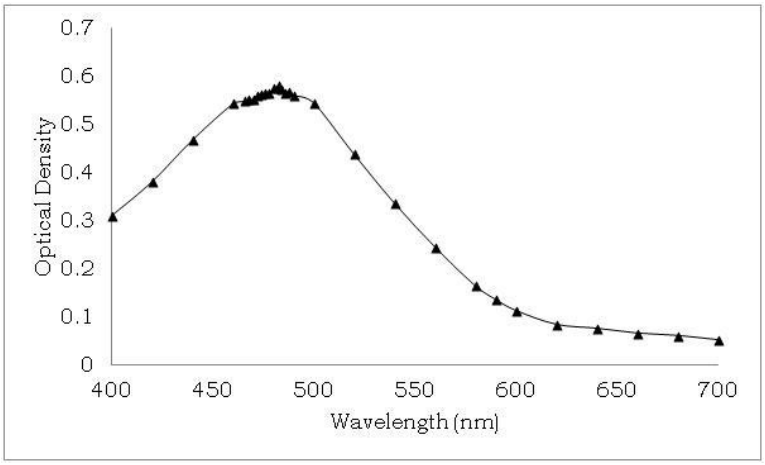

Fig. 3 : Beers law plot

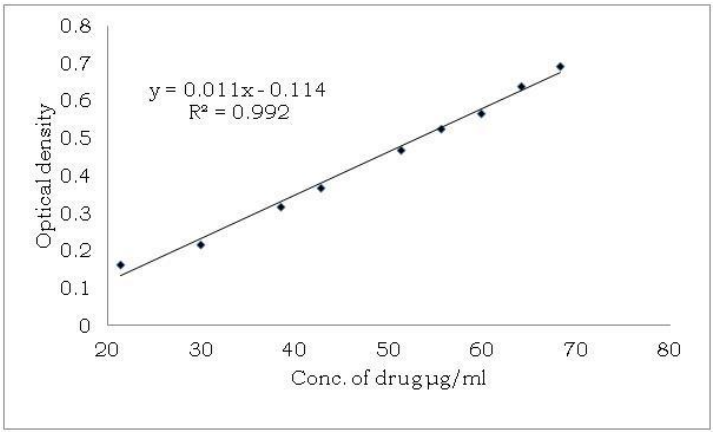

Fig. 4 : Turner Anderson plot

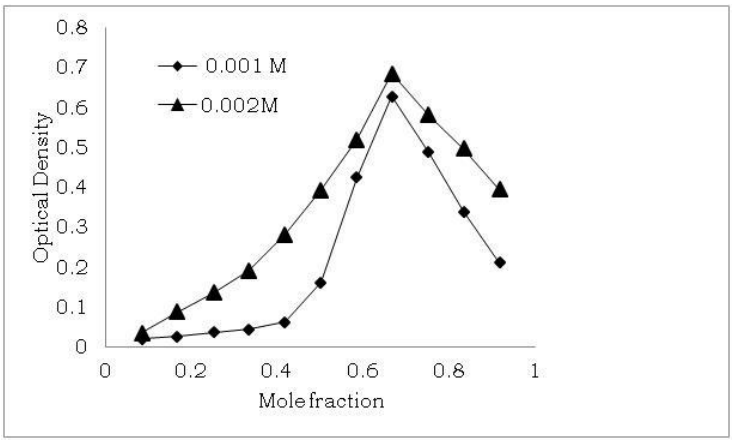

Table 1: Optical parameters of promethazine hydrochloride- Congo red complex

Parameters	
Colour of complex	Red
Maximum Wavelength of absorption (nm)	483
Molar composition of Complex (CR : PMTH)	1: 2
Beers law limit (µg ml^{-1})	19.4 – 83.5
Molar absorbtivity (l mol^{-1} cm^{-1}) x 10^3	3.5298
Sandell's sensitivity (µg cm^{-2} per 0.001 absorbance unit)	0.11256
Regression equation (y) slope (a) Intercept (b)	0.011 -0.114
Correlation coefficient (R^2)	0.992
Stability constant (x 10^4)	1.2489

y = ax + b , where x- concentration of PMTH , y – absorbance, b- Intercept.

Table 2: Statistical analysis of determination of promethazine hydrochloride

Tablet	Labeled amount mg/Tab	Amount found Mg/Tab	Recovery %	Error %	RSD	SD*
Phenargan-10	10	9.9794	99.794	0.2058	0.1907	±0.01903

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