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Research Article

Spectrophotometeric Determination of Trifluoperazine HCL in Pure Forms and Pharmaceutical Preperations

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ABSTRACT

A simple and accurate spectrophotometric method for the determination of Trifluoperazine HCl in pure and dosage forms was developed. The method is based on the reaction between Trifluoperazine HCl and p-chloroaniline in the presence of cerium ion as oxidizing agent which lead to the formation of violate color product that absorbed at a maximum wavelength 570nm while the blank solution was pink. Under the optimum conditions a linear relationship between the intensity and concentration of TRF in the range 4-50µg/ml was obtained . The molar absorptivity $3.74x10^3$ $L.mol^{-1}.cm^{-1}$, Limit of detection (2.21µg/ml), while limit of quantification was 7.39µg/ml. The proposed analytical method was compared with standard method using t-test and F-test , the obtained results shows there is no significant differences between proposed method and standard method. Based on that the proposed method can be used as an alternative method for the determination of TRF in pure and dosage forms.

Keywords: Spectrophotometric, Trifluoperazine HCl, p-chloroaniline reagent.

INTRODUCTION

Phenothiazine group has sixty four derivatives. They involved in being contain heterogeneous rings. These rings have a sulfur atom and a nitrogen atom. Among the most important of these derivatives was Trifluoperazine Hydrochloride (TRF)[1]. And which has the following structure and its structure formula was $C_{21}H_{24}F_3N_3S.2HCl$, and a molecular weight of 407.496g/mole shown in figure(1).

it commercially marketed in different pharmaceutical Preparations names like Iralzin , Terfluzine, Stellasil, Stellamide[2], It was a white crystalline powder has melting point 196 C° with high solubility in water and ethanol ,also disintegrate when exposed to light or air[3].

It mainly acts on dopamine receptor. The primary indication of trifluoperazine is schizophrenia. Trifluoperazine HCl is effective for the short-term treatment of generalized non-psychotic anxiety[4]. Literature survey reveals U.V. spectrophotometric[5-13], RP-HPLC methods[14-18], Potentiometric titration[19], Densitometry[20], Multi Walled Carbon Nanotubes[21], and Fluorescence Detection-FIA[22] for the estimation of Trifluoperazine hydrochloride alone and with other combination in Bulk, and Dosage forms.

The validity of spectrophotometric apparatus and the simplicity of analytical procedures make the technique very attractive for a wide range of applications. In this paper, a study of the determination of TRF in pure form and in different pharmaceutical preparations available in the Iraqi markets has been undertaken. The proposed method is based on the reaction of TRF with p - ChloroAniline as new chromogenic reagent in the presence of ceric ammonium sulphate as oxidizing agent. Different factors affecting this reaction are studied. The proposed method has the advantage of being rapid, simple, accurate, economic, sensitive and less-time consuming.

EXPERIMENTAL

Apparatus

A double beam UV-Vis (UV-1800) Shimadzu with 10mm glass cell spectrophotometric measurements. The pH meter/HM TDA electronic was used for pH measurements, and A four digit electronic balance – Sartorius Lab BP3015 was also used.

Reagents

All chemicals used were of analytical reagent grade, the pure trifluoperazine hydrochloride was provided from State Company for Drug Industries and Medical Appliance-(SDI) Sammara-Iraq.

Deionized water was used to prepare all solutions. Freshly prepared solutions were always employed.

A stock solution of 1000 µg/ml of trifluoperazine hydrochloride was prepared by dissolving of 0.1g in distilled water and then made up to 100ml in volumetric flask with the same solvent. The working solution of 100 µg/ml was prepared by simple dilution of stock solution and kept protected from sun light in ambient bottle.

A ceric ammonium sulphate (0.1M) was prepared by dissolving 6.5962gm in 100ml sulfuric acid (1%v/v), dilute concentration (0.005M) were also prepared from the stepwise dilutions of stock ceric ammonium sulfate with the same acidic solvent.

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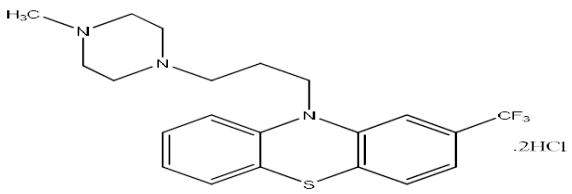


Figure 1: The Chemical structure of TRF.

A p-Chloroaniline (0.005M) was prepared through dissolving 0.0767gm in ethanol. Diluted sulfuric acid H_2SO_4 was prepared by dilution of concentrated sulfuric acid.

Recommended Procedure

Aliquots of standard solution of trifluoperazine hydrochloride covering the range (4 - 50µg) were transferred to a 25ml calibrated flasks. Then 2ml of $5x10^{-3}$M p-Chloroaniline solution and 1.5ml of $5x10^{-3}$M Cerric Ammonium sulfate were added to the flasks , the solutions were made up to the mark with distilled water and left for 20 min. The absorbance was measured at 570 nm against reagent blank.

Analysis of Tablets

Twenty tablets (each tablet containing 1mg or 5mg active ingredient TRF) were weighed and finely powdered. An amount of the powder equivalent to 100µg/ml of pure drug of trifluoperazine hydrochloride was weight, then dissolved in 25ml of distilled water, filtered and the filtrate was made up to 100ml in volumetric flask. The solution was further diluted as needed.

RESULTS AND DISSCUSION

The spectrophotometric method for the determination of TRF is based on the oxidative coupling reaction between TRF and p-chloroaniline in the presence of ceric ammonium sulfate as oxidant leading to form a violet colored product . The factors affecting the color development, sensitivity and linearity that obeyed Beer law were studied.

Spectral Characteristics

A violate color product is formed when TRF was allowed to react with p-chloroaniline in the presence ceric ammonium sulfate with a maximum absorption at 570nm as shown in figure(2). While figure(3) shows the colors of both the reaction product and blank solutions.

Study of the Optmium Reaction Conditions

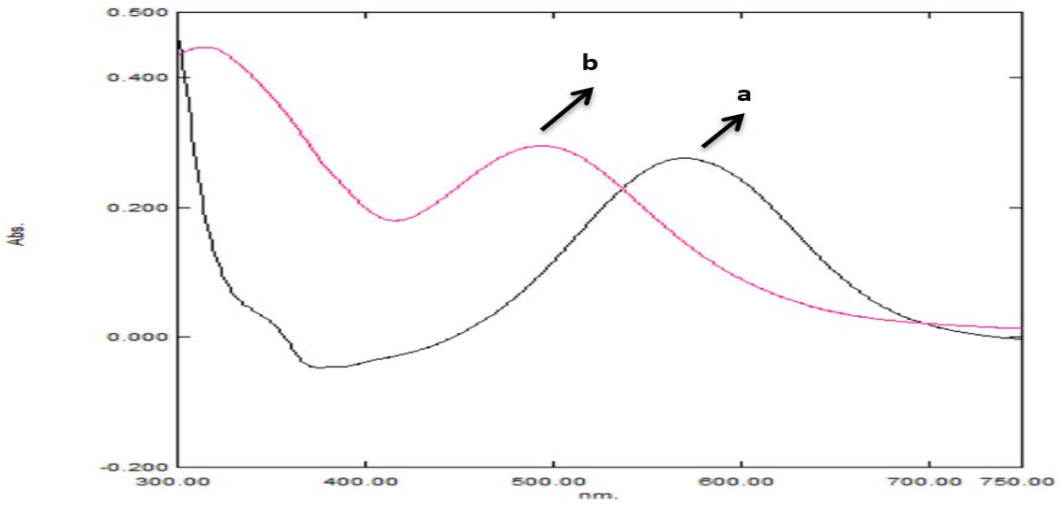


Figure 2: Absorption spectra of (a) Violate product(25µg/ml of trifluoperazine hydrochloride) against reagent blank, and (b) reagent blank versus distilled water.

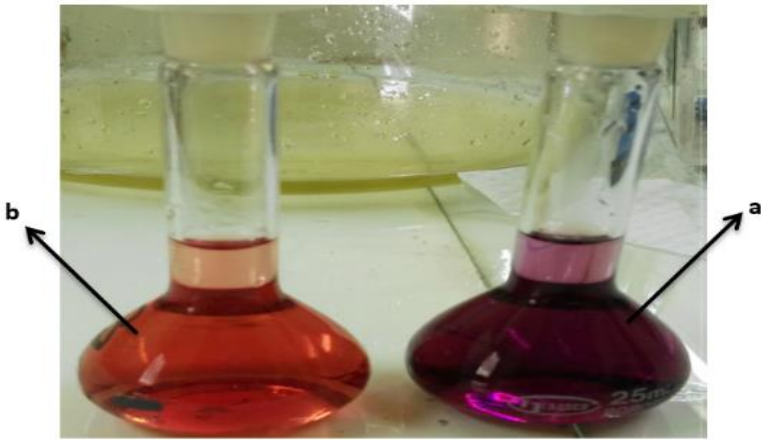


Figure 3: The colors of (a) violate product solution, (b) blank solution.

Table 1: Analytical data of the proposed method.

Parameters	Value
λ_{max}	570nm
Color	Violet
Regression equation Y = a + b [C]	A = 0.0161 + 0.0092 [C]
Correlation coefficient (r^2)	0.9975
Linearity percentage (%r^2)	99.75%
Linear dynamic range(µg/ml)	4-50
Molar absorptivity, ξ (L/mol. cm)	$3.74x10^3$
Slope , b (ml/µg)	0.0092
Intercept, a (a=y-bx)	0.0161
Standard deviation of slope, (Sb)	0.0002
Standard deviation of intercept, (Sa)	0.0059
Sandell sensitivity , S(µg/cm^{-2})	$0.108x10^{-3}$
Standard deviation of the residual, (Sy/x)	0.0093
Calculation T-test, (T_{cal})	53.79
Limit od detection, LOD (µg/ml)	2.21
Limit of quantification, LOQ (µg/ml)	7.39

The effect of various parameters on the absorption intensity of the dye formed was studied and the reaction conditions are optimized. It was found that a 0.005M solution of p-chloroaniline in the range 0.1-4ml and a 0.005M solution of ceric ammonium sulfate in the range 0.1-3ml were necessary to achieve the maximum absorption of the product. The color intensity decreased below the lower limit and above the upper limit. Therefore, 2ml of p-chloroanline and 1.5ml of ceric ammonium sulfate were recommended for all subsequent measurements.

To obtain optimum results the order of addition of reagents was also studied and should be followed as given under the general procedure (TRF + p-chloroaniline + ceric ammonium sulfate), otherwise a loss in color intensity was observed.

The effect of temperature and stability time were also studied by following the color development at room temperature and at different temperatures in thermostatically controlled water-bath. The absorbance was measured at 5min intervals against reagent blank treated similarly. It was observed that formation of color product for trifluoperazine Hydrochloride was achieved its maximum absorbance after 5minute at room temperature and remain stable for at least 45minute.

Analytical Data

A linear relationship was obtained for the absorbance of the color product when the concentration of the drugs was in the range 4-50 µg ml^{-1} in the final measured solutions as

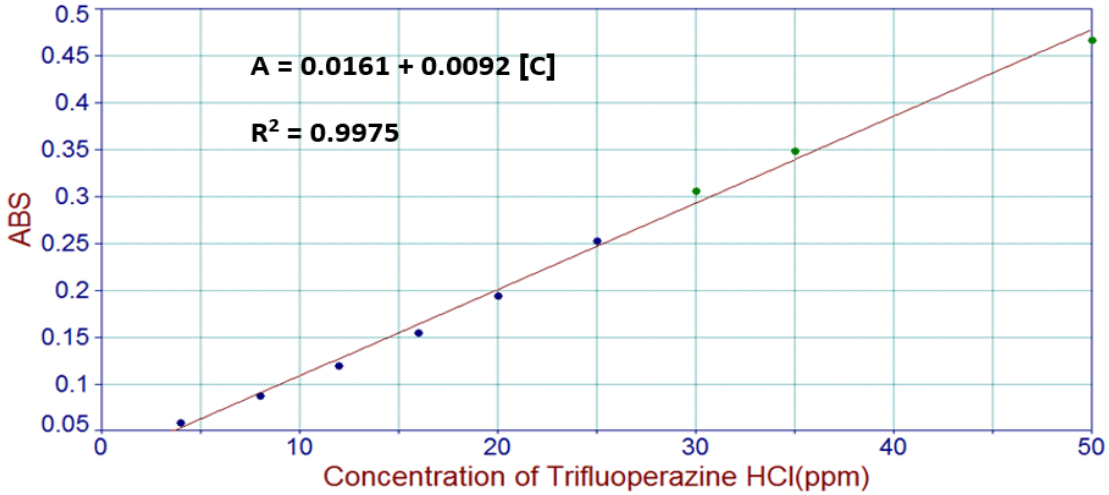


Figure 4: The calibration graph for determination of TRF.

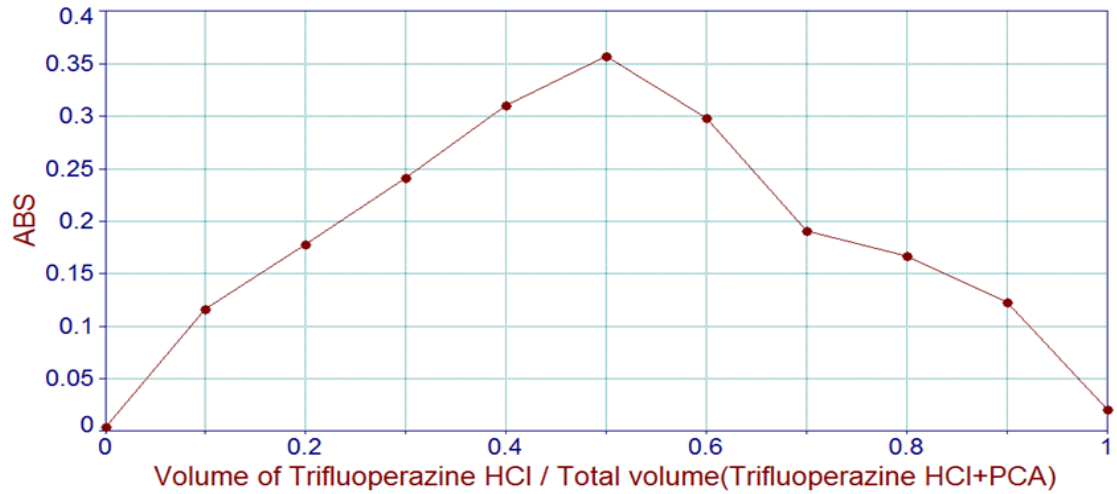


Figure 5: Job's method of formed product by reaction of TRF with p-chloroaniline reagent.

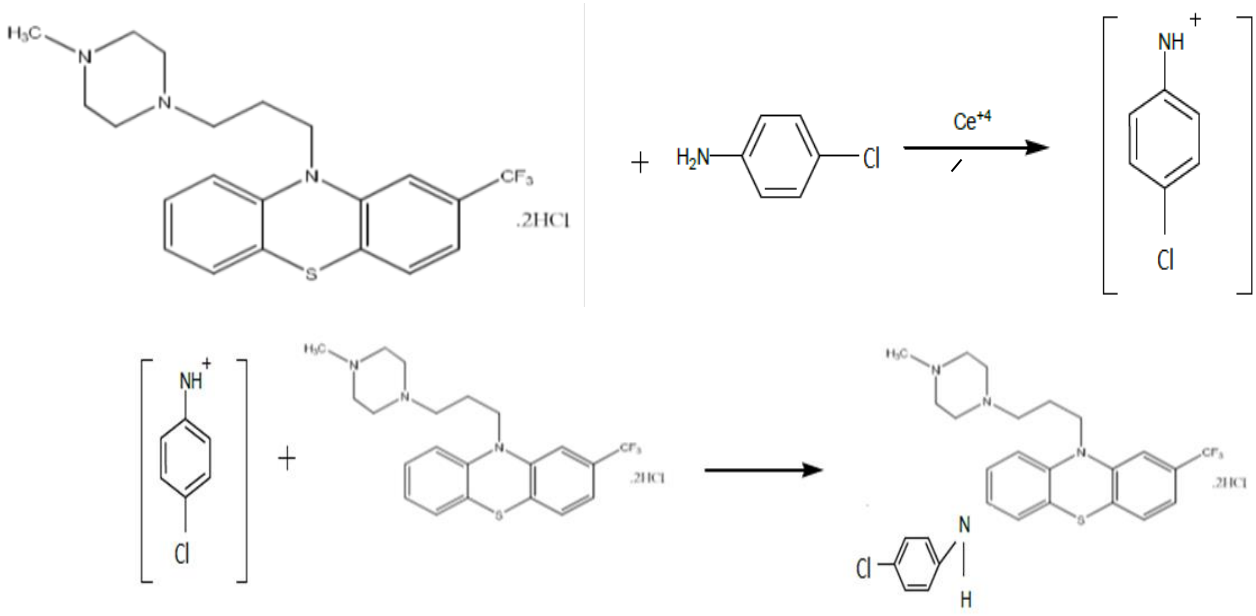
Table 2: Accuracy and Precision of the proposed analytical method.

Concentration of TRF ($\mu g.ml^{-1}$)		% Recovery*	% R.S.D*	% Error*
Taken	Found			
12	11.93	99.41	0.480	-0.583
16	15.58	97.41	0.662	-2.580
20	20.40	102.05	3.065	2.051

Table 5: The application of proposed method for determination of TRF in pharmaceutical tablets.

Pharmaceutical Formulation	Concentration Taken(µg/ml)	Concentration* Found(µg/ml)	%Recovery*	%Error*	%RSD*
SALABID(1mg)	10	9.73	97.33	-2.66	0.593
IRALZIN(5mg)	10	10.14	100.14	1.46	0.542
STELLASIL(1mg)	10	9.66	96.66	-3.33	1.194

*Average of three determinations.



shown in figure(4) . A =a + bC, where A is the absorbance of a 1-cm layer; b, slope; a, intercept and C, concentration of the measured solution in µg ml^{-1}, obtained by the method of least squares. The apparent molar absorptivity was found to be in the order of $3.74x10^3$ l. mol^{-1}. cm^{-1} with the Sandell sensitivity of $0.108x10^{-3}$µg.cm^{-2}. These values together with the limits of detection and quantification compiled in Table 1 indicate the reasonably high sensitivity of the method. Table 1 also shows the linear equation for absorbance versus concentration, together with the correlation coefficients, indicating excellent linearity.

Accuracy and Precision

The accuracy and precision of the method, were investigated by determining the Trifluoperazine. HCL at three different concentrations. The results tabulated in Table (2) indicated that the method is satisfactory. and have high accuracy and precision.

Stoichiometric Relationship

Job's method of continuous variation was employed, using 1mM of both standard solution of TRF and p-chloroaniline solutions. Into a 25ml volumetric flasks a series of solutions were prepared in which the total volume of drug and reagent was kept constant at 10 ml. To these solutions 1.5ml of ceric ammonium sulfate was added. The flaks were left for 20minute at room temperature, then the color intensity of each flask was measured against reagent blank at 570nm. The obtained results are shown in figure(5), indicated that a 1:1 TRF to p-chloroaniline is formed. Therefore, the reaction probably occur as in the reaction scheme showing below.

Analytical Applications

The developed method was successfully applied to determination of TRF in different pharmaceutical formulations available in Iraqi markets using standard addition method and the recommended analytical procedure. The obtained results were tabulated in table (5). The results shows the high recoveries and low percentage errors. The proposed method was also compared with the standard method adopted by BP using t-test and F-test respectively. The calculated t (0.558) and F (5.661) values were less than tabulated t (2.443) and F (9.277) at 95% confidence interval. Based on that the new proposed

method can be used as an alternative analytical method for the determination of TRF dosage forms.

CONCLUSIONS

Although TRF have been determined by a variety of techniques, the method described here was simple, highly sensitive (spectrophotometry), convenient and don't require special working conditions, unlike many other reagents. The produced assay results that are not significantly
different from those of the official monographs assay methods. It can easily be used in the quality control of TRF dosage forms.

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