

Spectrophotometric Determination of Trifluoperazine Hydrochloride Using Oxidative Coupling Reaction

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Abstract

A simple spectrophotometric technique has been developed for the determination of trifluoperazine hydrochloride (TFPH) pure and pharmaceutical formulations. The proposed method is based on the oxidative coupling reaction using ammonium ceric sulphate and sulphanilic acid producing a violet colored complex with maximum absorption at 545 nm. The Beer's law is obeyed over the concentration range of (0.5 – 20.0) $\mu\text{g ml}^{-1}$, while the detection limit and quantification limit are 0.1604 and 0.4860 $\mu\text{g ml}^{-1}$ respectively, with a correlation coefficient (R²) of 0.9980 and a molar absorptivity of $1.441 \times 10^4 \text{ L mol}^{-1}\text{cm}^{-1}$ with Sandell's sensitivity index of 0.3330 $\mu\text{g cm}^{-2}$. The precision and accuracy of the method are checked by calculating relative standard deviation (RSD) (<1.55%) and average recovery (99.509%). The value of the stability constant has been calculated and found to be $7.30 \times 10^5 \text{ L mol}^{-1}$. Different experimental parameters affecting the development and stability of the development and stability of the formed colored product are carefully studied and optimized. Possible interferences that related to the determination of (TFPH) in pharmaceutical tablets are studied and the results showed that the method is successfully applied for determination of TFPH in pharmaceutical formulation.

Keywords: Trifluoperazine hydrochloride, sulphanilic acid, ammonium ceric sulphate, spectrophotometric.

1. Introduction

Trifluoperazine hydrochloride (TFPH) is a typical antipsychotic drug of the phenothiazine group. It has a central antiadrenergic, antidopaminergic, minimal. Anticholinergic effects and commonly used antipsychotic drug (British Pharmacopoeia-(B.P)-(2001)). It has been known to induce QT prolongation and ventricular tachycardia, which can cause sudden death and hence is used in the treatment of various mental illnesses such as schizophrenia (Young et al. - 2005). TFPH is a white crystalline powder which dissolves easily in water and alcohol, while does not dissolve in the alkaline solution. It is sensitive to light so saves away from it (B.P. - 2005). The importance of TFPH has prompted many investigators to look for methods for its rapid determination. These methods include voltammetry (Huang et al. - 2006), capillary zone electrophoresis (Muijselaav et al. - 1996), fluorimetry (Kaul et al. -1978) turbidimetry (Amir et al. - 2003), titrimetric (potentiometric titrations)

(Krishnamurthy and Basavaiah - 1998 and Ahmed et al. - 2009), spectrophotometric (Jayarama et al. - 1986; El-Gundy et al.- 2001; Basavaiah -2004 and El-Saudagar et al. - 2007), extraction liquid chromatography (Shaghayegh et al. - 2011), high performance liquid chromatographic methods (Shettip and Venkatachalam - 2010).and liquid chromatographic methods(Shree - 2009; Temerdashev et al - 2006; Anna - 2007; Magdalena et al- 2006).

In this work, a spectrophotometric method is proposed for the determination of TFPH which based on its oxidation reaction by ammonium ceric sulphate then coupling the product with sulphanilic acid. This method is applied to determine TFPH in pharmaceutical formulations with obtaining is a satisfactory result in comparison with official method (B.P. - 2005).

2. Experimental

2.1. Apparatus

Spectral measurements were carried out on a (CECIL CE 3021-England) UV-Vis digital spectrophotometer, while other measurements were carried out with a (JENWAY 7305 -UK) UV-Vis spectrophotometer equipped with quartz cell of 1.0 cm path length. A digital analytical balance (METTLER TOLEDO AB204-S), pH meter (PHILIPS pw 9421), magnetic stirrer hotplate (Gallenkamp - 400), and water bath (LA bacon LWB-104) are used through this investigation.

2.2 Reagents and Solutions

All chemicals and reagents are used of analytical grade. TFPH is provided by Samara Drug Industry (SDI) - Iraq. Distilled water is used in all preparations.

2.3 TFPH Solution (1000 $\mu\text{g ml}^{-1}$)

A 0.1000 g of TFPH is dissolved in amount of distilled water and then made up to 100 ml in volumetric flask. The working solution of (250 $\mu\text{g ml}^{-1}$) is prepared by simple dilution of stock solution and stored in an amber glass bottle in a refrigerator.

2.4 Sulphanilic Acid Solutions (1.0x10⁻² M)

A 0.1732 g of sulphanilic acid is dissolved in a small volume of distilled water, and then diluted to 100 ml in volumetric flask.

2.5 Ammonium Ceric Sulphate Solution (ACS) (5.0x10⁻³ M)

This solution is prepared by dissolving 0.3162 g of ammonium ceric sulphate in distilled water then completed to 100 ml with distilled water.

2.6 Sample Solution of Tablets Contain TFPH (250 µg ml⁻¹)

A 20.0 tablets (STELLASIL– Cairo– Egypt) (each contain 5.0 mg TFPH) are weighed (7.4160 g) and granulated to a fine particles, then weight 1.8540 g which dissolved in a small volume of distilled water, then the solution filtered by filter paper (589/4 S&S Round filter 150 mm) and the volume is completed to 100 ml.

3. Results and Discussion

3.1 Preliminary Investigations

To a 25 ml volumetric flask containing 1.0 ml standard TFPH (250 µg ml⁻¹) added 1.0 ml of (5.0x10⁻³ M) ammonium ceric sulphate (ACS) followed by adding 1.0 ml (1.0x10⁻² M) of sulphanilic acid, then diluted to the mark with distilled water. The blank solution is prepared in the same way except TFPH. The absorption spectrum of the colored complex (violet color) against blank solution shows maximum absorption at 545 nm.

The mechanism of the reaction is proposed, in which TFPH oxidizes by ACS, then the product coupled with sulphanilic acid producing violet complex, which completely soluble in water.

3.2 Selection of the Oxidizing Agent

Effects of different types of oxidizing agent (1.0ml of 5.0x10⁻³ M) (ammonium ceric sulphate, sodium per iodate, sodium hypochlorite, potassium bromate, ammonium persulphate and ferric chloride) are tested. Results indicate that ammonium ceric sulphate give that best absorption maxima, therefore it is used in subsequent experiments.

3.3 Effect of ACS Concentration

The effect of ACS in the range of (0.3 – 6.0 ml) of (5.0x10⁻³ M) on the sensitivity of the reaction has been studied. It is found that 4.0 ml of ACS (5.0x10⁻³ M) gives the optimum absorbance.

3.4 Selection of the Coupling Reagent

Different coupling reagent is tested depending on the highest value of $\Delta\lambda_{max}$ (λ_{max} of the complex - λ_{max} of the blank). It found that sulphanilic acid is the best coupling reagent due to gives the highest $\Delta\lambda_{max}$ = 299 nm (λ_{max} of sample against blank = 545 nm and λ_{max} of blank against water = 246 nm).

3.5 Effect of Sulphanilic Acid Concentration

The effect of sulphanilic acid is investigated in the range of (0.3 – 3.5 ml) of (1.0x10⁻² M) solution to a constant amount of TFPH (1.0 ml, 250 µg ml⁻¹). It is observed that the maximum color intensity is obtained with 1.0 ml, after which further increase in volume results nearly a constant absorbance.

3.6 Order of Addition

The effect of order of addition on the sensitivity of the method has been investigated. The results obtained that the order of addition (Drug sample (TFPH) + ACS sulphanilic acid) gave the best sensitivity and more intense color than probabilities and this order is selected in all subsequent experiments.

3.7 Effect of Oxidation Time and Temperature

The oxidation of the drug (TFPH) with ACS is tested during different periods (1:00 - 50:00 min) then adding the sulphanilic acid as coupling reagent. It has seen that the best complexation occurs between (2:00 - 15:00 min). Therefore, 5:00 min will select for the subsequent experiments because after this time there is a good stability in the absorbance up to 15:00 min. In contrast, the effect of temperature is also studied between (5 - 50 °C). It found that the highest absorbance can be recorded in the range of (15 - 30 °C), so it considered 25°C (room temperature) for the subsequent experiments.

3.8 Stability of the Colored Product

The stability of the formed product is tested during different time (0:00 – 60:00 min).

It is found that a high absorbance will be obtained after 5:00 min, which shows good stability up to 50:00 min.

3.9 Recommended Procedure

To a 25.0 ml calibrated flask which contain 1.0 ml of 250 µg ml⁻¹ of the working standard solution of TFPH (equivalent to 10 µg ml⁻¹) added 4.0 ml of ACS (5.0x10⁻³ M), then after 5:00 min added 1.0 ml of sulphanilic acid (1.0x10⁻² M) and complete with distilled water. The blank solution is prepared in the same manner in the absence of TFPH. The absorbance is measured against a reagent blank after 5:00 min, at 545 nm. The unknown concentration derived from the calibration graph or computed from the regression equation derived using Beer's law.

3.10 Calibration Graph & Statistical Data

Under the optimum experimental conditions and applying the recommended procedure, a calibration graph is obtained by taking different volume of TFPH (0.05 - 4.0 ml, 250 µg ml⁻¹). Fig (1) shows a straight line of the calibration graph which obeyed the Beer's law in the concentration range of (0.5 - 20.0 µg ml⁻¹) of TFPH with a correlation coefficient of (0.9980) and detection limit of 0.1604 µg ml⁻¹. The mo-

lar absorptivity and Sandell's index are found to be $1.441 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$ and $0.333 \mu\text{g cm}^{-2}$ respectively.

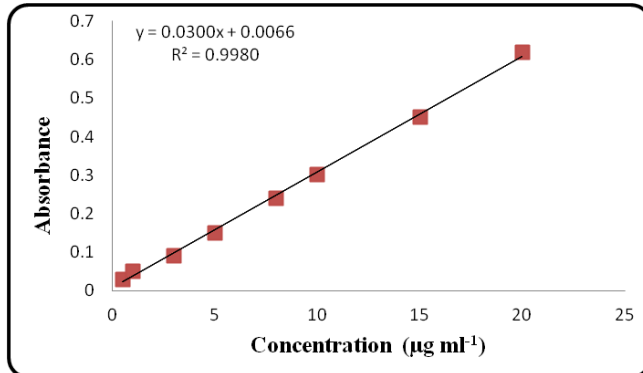


Fig. (1): Calibration Curve for Determination of TFPH By Oxidative Coupling with Sulphanilic Acid Reagent.

3.11 Accuracy and Precision

In this study the absorbance for three different concentrations (2.0, 10.0 and 16.0 $\mu\text{g ml}^{-1}$) of TFPH are measured for five replicated times ($n=5$). The results are shown in Table (1), which indicates a good accuracy and precision, because the average recovery approaches 99.509% and $\text{RSD} \leq 1.55\%$.

Table (1): Results of Accuracy and Precision

Conc. of TFPH ($\mu\text{g ml}^{-1}$)	Recovery (%) *	Average Recovery (%)	RSD (%)
2.0	98.960	99.509	1.550
10.0	99.400		0.434
16.0	100.167		0.344

* Average of five determination.

3.12 The Nature of the Colored Product and Its Mechanism

The stoichiometric relation between oxidized TFPH and sulphanilic acid has been studied employing the Molar ratio method (Nabil - 1994). The results which are shown in Fig. (2) indicate that the reaction between the oxidized drug and the reagent (1:1)

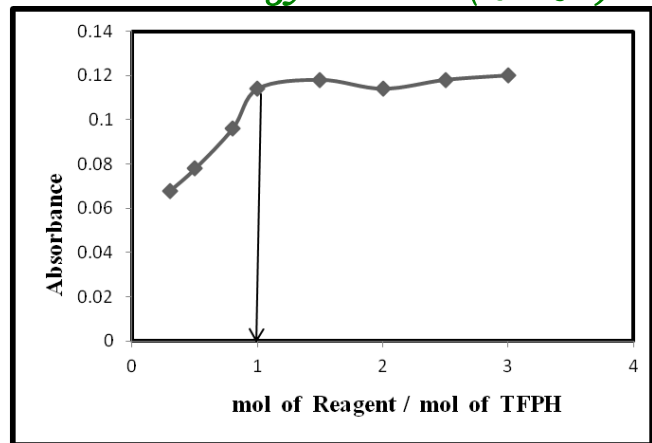


Fig. (2): Molar ratio Method of the Formed Product by Oxidative Coupling of TFPH with Sulphanilic Acid Reagent.

The proposed mechanism for the reaction can be written as shown in Fig. (3).

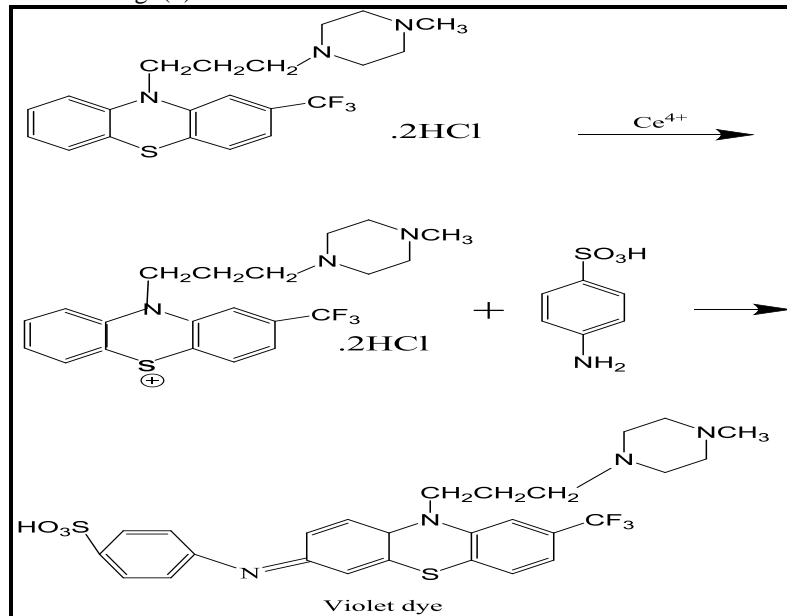


Fig. (3): The Proposed Mechanism for the Reaction of TFPH & Sulphanilic Acid.

3.13 Calculation of the Stability Constant

The analysis of the results that have been obtained from the molar ratio method to calculate the stability constant for the product of the TFPH drug reaction with sulphanilic acid reagent can be fixed by calculation using the following equation:

$$K = \frac{[C(1-\alpha)]}{\alpha^2 C^2} \rightarrow \frac{1-\alpha}{C \alpha^2}$$

$$\alpha = \frac{A_m - A_s}{A_m}$$

Am: is the greatest value of the absorption.

As: at the equivalence point absorption value (when the ratio of product 1:1).

The value of the stability constant has been calculated and found to be $7.30 \times 10^5 \text{ L mol}^{-1}$. Where Am value was (0.120) then As value was (0.114), under optimal experimental conditions this reveals that the product is of high stability.

3.14 Effect of Interferences

To improve the efficiency and selectivity of the proposed method for determination of TFPH, the effect of some foreign substances (glucose, fructose, maltose and starch) have been studied, which normally are present in the dosage forms, of pharmaceutical preparation. This study is performed by comparing the absorbance obtained when TFPH present alone and in the presence of different concentration of interferences (80 - 320 $\mu\text{g ml}^{-1}$) reach to (8 -32) times of the amount of TFPH (10.0 $\mu\text{g ml}^{-1}$). The results found that a substance is considered not to interfere if the variation in the absorbance of pure TFPH & TFPH with interferences equal or less than $\pm 5.0\%$ of the recovers. Table (2) illustrated the recovers after addition of additives by (8 - 32) fold excess the amount of TFPH.

3.15 Applications

The proposed method was successfully applied for the determination of TFPH in pharmaceutical preparation, while the same formulations are also analyzed by the British Pharmacopeia (B.P. – 2013) as standard method. The results are compared by using t –test & F – test at 95% level of confidence.

4. Conclusions

This method is considered to be simple, rapid, sensitive, inexpensive and accurate for the determination of TFPH in pure form and pharmaceutical formulations. The method dose not require the removal of excipients, any chemical sample pretreatment, solvent extraction step, and expensive reagents and solvents.

Table (2): Effect of Interferences

Foreign Compound	Recovery (%) of 10.0 $\mu\text{g ml}^{-1}$ of TFPH per ($\mu\text{g ml}^{-1}$) Foreign compound added		
	80	160	320
Glucose	99.93	100.06	99.93
Fructose	99.53	100.33	99.79
Maltose	99.39	99.83	100.06
Starch	100.20	100.06	99.25

Table (3): Comparison with Standard Method

	B.P. meth od	STELLA SIL (Egypt)	Triflida rou (Iran)	Iralzi n (SDI)
\bar{x}	0.303 7	0.2999	0.3016	0.304 7
Recov-ery%	99.77	100.01	100.13 2	100.0 98
SD	0.000 68	0.00088	0.0010 8	0.001 25
RSD%	0.22	0.29	0.356	0.409
T - exp	*2.26 2	2.174	0.847	0.503
F - exp	*3.18	1.682	2.536	2.46

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