Simultaneous Estimation of Trifluoparazine by UV-VIS Spectroscopy using of the Oxidative Coupling Reaction with Reagent Naphthalene-1, 5-Diamine

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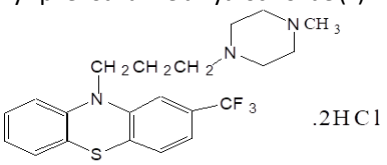
Abstract

A simple, rapid and sensitive spectrophotometric method was described for the determination of Trifluoparazine the method is based on the oxidative coupling reaction between Trifluoparazine and Naphthalene-1,5diamine in the presence of Potassium Iodate to form violet colored product with maximum absorptions at 535nm, which is soluble in water. Beer's law is obeyed in the concentration range of 10 to 50 µg.ml-1 with a molar absorptivity of 0.7975×104 L.mol-1.cm-1, and Sandell's index of 0. 0602 µg.cm 2, respectively. The correlation coefficient of 0.9994, with recovery average % of 99.6 Limit of detection (LOD), limit of quantification (LOQ) of 0.782 µg.ml- 1and 2. 609 µg.ml -1 with relative Error (RE) % of -0.2 to -0.5 and a relative standard deviation (RSD) % of 0.561 to 0.231. The proposed method has been used to successfully determine Trifluoparazine in pharmaceutical formulations (Tablet).

Keywords: Trifluoparazine, Spectrophotometric, Oxidative of Coupling, pharmaceutical.

1. Introduction

Trifluoparazine 10-[3-(4-methylepiprazin-1-yl) propyl]-2-trifluoromethyl- phenothiazine dihydrochloride (1)



Chemical structure of Trifluoparazine

Trifluoperazine hydrochloride is a white powder with a bitter taste, its melting point is 240 ° C, it is odorless, it has a pale white color that tends to yellow, it dissolves in water at a temperature of 20 ° C, it is photo sensitive, so it should be kept in a closed, opaque containers and away from light [1] Trifluoperazine hydrochloride is generally used as an antipsychotic and analgesic for treating psychiatric patients [2] and a narcotic, as well as for the treatment of anxiety and psychological states, i.e. schizophrenia, and used as a sedative for anxiety and aid in sleep, and used to treat vomiting and nausea [3], used to treat cases of hysteria, It is not recommended to take the drug for pregnant women [4] and lactating women without consulting a doctor because it has an unstable effect, and taking doses of it leads to an increase in weight and the mother may develop jaundice and has negative effects on the future newborn. It has been estimated by many different analytical methods such as high – performance liquid chromatography technology HPLC [5, 6] spectroscopic method [7-10], TLC technique [11],atomic absorption [12], and flow injection method [13]. The aim of the present work is to find out a simple, sensitive and specific spectrophotometric method to determine its validation for the estimation of Trifluoperazine hydrochloride from pharmaceutical preparations.

2. Experimental Part

Instrumentation Used

Spectrophotometric measurements were made using UV-visible double beam a type (T92+ Spectrophotometer, China), with using 1cm of matching quartz cells.

Materials and Solution of the Used

The substances employed in this study were all extremely pure equipped by my company (Fluka, bdh, SDI), and throughout the tests, methanol and distilled water were employed as solvents to preparing solutions.

Trifluoparazine standard solution (1000 µg.ml-1)

It was prepared by dissolving 0.1000 g of pure Trifluoparazine powder in an amount of a distilled water and then completing the volume to the mark in a 100 ml volumetric flask, A Concentration 250 µg .ml-1 was prepared by taking 25 ml of standard solution (1000 µg.ml-1) and dilute it in a 100 ml volumetric flask, then complete the flask to the mark with the same solvent.

Potassium Iodate of Solution (2x10 -2Molar)

It was prepared by dissolving 0.428g of the substance in a little distilled water and completed the volume to the mark with the same solvent in a volumetric flask of 100 ml.

Solution of sodium carbonate (2×10-2 Molar)

It was prepared by dissolving 0.212 g of sodium carbonate in an amount of distilled water (D.W) and filled the volume to the mark with the same solvent in a volumetric flask of 100 ml.

Solution of Naphthalene-1,5diamine (3×10-2 Molar)

It was prepared by dissolving 0.474 g of the reagent in an amount of distilled water (D.W), and then filled the volume to the mark with the same solvent in a volumetric flask of 100 ml capacity.

Pharmaceutical preparation of Trifluoparazine (stelazine tablet)

Ten tablets are weighed (40 mg/ Tablet), and the grains are crushed well, then a certain weight of the powder is taken, which is equivalent to 0.1g of Trifluoparazine, depending on

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the type of tablets used, and it is dissolved in a little of distilled water and then filtered to separate the insoluble components, if any, then transferred to a volumetric flask of 100 ml capacity, and completed the volume to the mark with distilled water and then 25 ml is taken of this solution and transferred to a volumetric flask of capacity of 100 ml and filling the volume to the mark with distilled water to obtain a solution of 250 µg.ml-1.

The method's general principle

Principle is the coupling of the reagent Naphthalene-1, 5-diamine with the drug Trifluoparazine and in the presence of the oxidizing agent potassium iodate in an alkaline medium, a solution with a violet color is formed, which gave the highest wavelength at 535 nm versus the blank solution.

3. Results and Discussion

Preliminary study

Studying the absorption spectrum of the drug only

The absorption spectrum of the 250 µg.ml-1 of drug was recorded against the distilled water as a reference. This was done by transferring 2 ml of the 250 µg.ml-1 solution into a 25 ml volumetric flask and then filled the volume with distilled water to the mark. The absorption spectrum was taken as in Figure (1), which shows that the drug gives absorption at the wavelength of 305 nm.

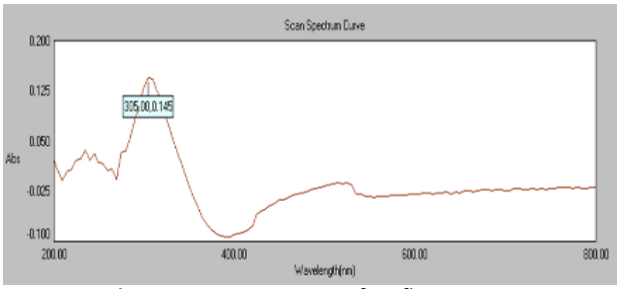

Fig. (1): Absorption spectrum of Trifluoparazine versus distilled water before coupling

Studying the absorption spectrum of the drug with the reagent Naphthalene-1,5diamine

In a volumetric flask with a capacity of 25 ml, 2 ml of drug solution with a concentration of 250 g.ml-1 was mixed with 1 ml of 3 x 10-2 M of a reagent solution Naphthalene-1,5diamine solution, and 1 ml of a solution of potassium iodate of 2×10-2 M, and 1 ml of sodium carbonate of 2×10-2 M, then filled the volume to the mark with D.W and shaking to homogenize the solutions. The absorption spectrum of the resulting violet color, was measured against the versus blank solution as a reference to obtain the wavelength and the highest value for the absorption was given at the wavelength of 535 nm, as in Figure (2).

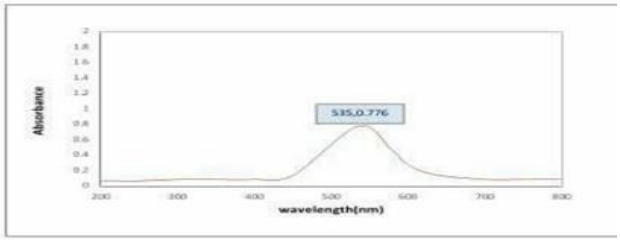

Fig. (2): Absorption spectrum between the drug and the Naphthalene-1, 5-diamine in the presence of potassium iodate

Examining the best conditions

After obtaining the absorption spectrum of the reaction solution, the reaction conditions were studied using 1 ml of the oxidizing agent solution potassium iodate, 1 ml of the used reagent solution Naphthalene-1,5diamine, 2ml of the standard Trifluoparazine solution with concentration of 250 µg.ml-1, and 1 ml of sodium carbonate solution in a final volume of 25 ml. The absorption of the solutions at the different wavelengths was measured against blank solution.

4. Results

Choosing the best reagent

1 ml of each solution were taken from the used reagents, 2 ml of Trifluoparazine solution at a concentration of 250 µg.ml-1, 1 ml of potassium iodate solution as an oxidizing agent, and 1 ml of sodium carbonate solution of 2×10-2 M and the results shown in Table No. (1). we note that the Naphthalene-1,5-diamine reagent gave the highest absorption of the colored product formed at 535 nm versus the blank solution, the blank solution showed no absorption at this reagent, thus it was used in the following experiments.

Table (1): Choosing of the best reagent

(2× 10-2 M) of Reagent	Variable	Absorbance	?max
1_Naphthylamine_4_sulfanicacid	SB	0.529	447
	BW	0.087	412
Naphthalene_1,5_diamond	SB	0.776	535
	BW	0.098	516
4 –amin benzene sulfanicacid	SB	0.422	425
	BW	0.076	492

SB: It symbolizes the absorption spectrum of Trifluoparazine solution compared to a blank solution
BW: It represents of the blank solution absorptions spectrum in comparison to distilled water.

Volume impact of the coupling reagent

Impact of the volume of reagent Naphthalene-1,5diamine solution on the intensity of absorption was studied. Where a series of volumes were taken from the used (0.3-2) ml reagent with a concentration of 2×10-2 M, 2ml of the Trifluoparazine solution of 250 µg.ml-1,1ml of the oxidizing agent solution, and 1ml of sodium carbonate solution of 2×10-2 M. It was found that adding 1ml of the reagent was the best to give it the highest absorption. Results are in the Table (2).

Table (2): Volume impact of the coupling reagent

2×10-2 M of Reagent, ml	Absorbance	
	BW	SB
0.3	0.077	0.585
0.5	0.084	0.647
0.7	0.090	0.770
1	0.098	0.776
1.3	0.088	0.732
1.5	0.080	0.700
1.7	0.071	0.693
2	0.062	0.658

Choosing the best oxidizing agent

Several experiments were carried out to find the best oxidizing agent to form the colored product. Several Solutions of oxidizing agents were used of (2×10-2 M), each with a volume of 1 ml, and 1 ml of Naphthalene-1,5-diamine solution and added 1 ml of the sodium carbonate solution were has a concentration of(2×10-2 M) in a volumetric flask with a capacity of 25 ml. It was noted that the best oxidizing agent was potassium iodate, which gave a maximum absorption for the colored product formed at the wavelength of 535 nm. Results are in the Table (3).

Table (3): oxidizing agent choosing

λ max(nm)	Absorbance		(2×10-2 M) of Oxidizing agent
	Sample	Blank	
467	0.645	0.072	Potassium permanganate
506	0.704	0.080	Potassium persulfate
535	0.775	0.097	Potassium Iodate
425	0.589	0.060	Ammonium ferric sulfate

Volume effect of oxidizing agent

Effect of the volume of oxidizing agent solution with a concentration of 2×10-2 M on the intensity of absorption was studied, as different volumes (0.2-2) ml were used and it was found that 1 ml of potassium iodate solution is the best which gives highest sabsorption. Results are in the Table (4).

Table (4): Volume effect of oxidizing agent

Absorbance		2×10-2 M of KIO3 ,ml
SB	BW	
0.361	0.062	0.2
0.471	0.070	0.4
0.564	0.074	0.6
0.682	0.088	0.8
0.775	0.097	1
0.579	0.080	1.4
0.397	0.063	1.8
0.301	0.055	2

Choosing the best base

Overall, 1 ml of different types of bases with a concentration of approximately 2 x 10-2 M were used and their impact on the intensity of absorption was studied. Results are in the Table (5).

Table (5): Choosing of best base

NaOH	Ca(OH)2	Na2CO3	KOH	Base Solution 2×10-2 M
0.592	0.706	0.776	0.654	Absorbance

From the above table, we note that the sodium carbonate gave the highest absorption and therefore it was chosen in the subsequent experiments.

Effect of the amount of base used

Different quantities of the base used were added of sodium carbonate of (0.2-2) ml 2×10-2 M, to find out the optimum amount, it was found that 1 ml is the best which gives highest absorption therefore a volume 1 ml was used in subsequent experiment. Results are in the Table (6).

Table (6): Effect of the amount of base used

Absorbance		2×10-2 M of Na2CO3, ml
SB	BW	
0.587	0.070	0.2
0.632	0.076	0.4
0.690	0.082	0.6
0.760	0.090	0.8
0.776	0.097	1
0.704	0.0087	1.4
0.654	0.0074	1.8
0.610	0.076	2

Sequence of additions Impact

It was found that the best addition sequence which gives the highest absorption in (D+R+O+B). Results are in the Table (7).

Table (7): sequence of additions Impact

Absorbance		Order of Addition	No.
SB	BW		
0.712	0.093	D+R+O+B	I
0.776	0.098	B+O+D+R	II
0.693	0.089	O+B+R+D	III
0.648	0.083	R+O+D+B	VI

Potassium iodate (O), reagent solution Naphthalene-1, 5-diamine (R), Trifluoparazine solution (D), and base solution Sodium carbonate (B).

Impact of temperature

The formed product was studied using different temperatures, and it was found from the results that the absorbance remains stable within the range (15-60) degrees Celsius, and the absorbance decreases at high temperatures, and it was found that the colored product was gives the highest absorption at room temperature (25 oC). Results are in the Table (8).

Table (8): Impact of Temperature

Temp. °C	15	20	25	30	35	40	45	50	55	60
Absorbance	0.635	0.695	0.775	0.664	0.641	0.523	0.520	0.485	0.442	0.396

The reaction Products Stability

The stability reaction was studied using different time periods at room temperature (25°C) to know the stability of the formed product, were taken 2 ml of the Trifluoparazine solution 250 µg.ml-1, and take equivalent 20 µg.ml-1 from the drug and added 2ml of the reagent solution of Naphthalene-1,5diamine (3×10-2 µg .ml-1) ,1ml of of potassium iodate 2×10-2 µg.ml-1, and 1 ml of the sodium carbonate solution in a 25 ml volumetric flask, the volume was subsequently filled to the mark with distilled water, the product formed was found to be stable for 60 minutes, as shown in Table (9).

Table (9): The reaction Products Stability

20 µg.ml-1 of Trifluoparazine	
Time (min)	Absorbance
5	0.552
10	0.572
15	0.629
20	0.645

30	0.776
40	0.774
50	0.774
60	0.772

Spectrum of ultimate absorption

The final absorption spectrum was measured after fixing the optimal conditions shown in table (10) using 2 ml of Trifluoparazine solution at a concentration of 250 µg.ml-1, 2ml of reagent solution of Naphthalene-1,5diamine at a concentration of (3×10-2 M), 1ml of potassium iodate at a concentration of (2×10-2 M), and 1ml of sodium carbonate at a concentration of (2×10-2 M), and complete the volume to the mark in a 25ml volumetric flask with distilled water, then final absorption spectrum of the violet product was measured against the blank solution, it was found that it gives the highest absorption at the wavelength 535 nm. As illustrated in Figure (3).

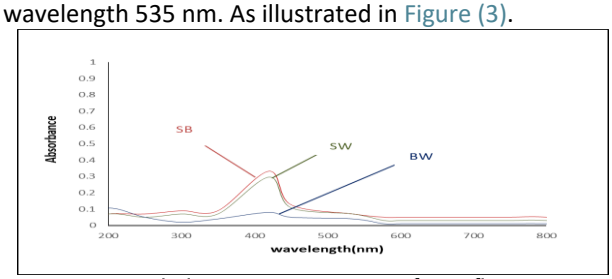

Fig. (3): Final absorption spectrum for trifluoparazine determination

SB: It symbolizes the absorption spectrum of Trifluoparazine solution compared to a blank solution.
SW: It symbolizes the absorption spectrum of Trifluoparazine solution versus the distilled water
BW: It symbolizes the absorption spectrum of the blank solution versus distilled water.
The optimal conditions for the determination of Trifluoparazine are summarized in the Table (10).

Table (10): Summary of optimum condition	
Experimental Condition	
Λmax	535 nm
Amount ml of (2×10-2 M) potassium iodate	1ml
Amount ml of (2×10-2 M) Naphthalene-1,5diamine	1ml
Sodium carbonate	1ml
Temperature	25 Co
Solvent	Distilled water
Oxidative time	5 min

Calibration curve

The calibration curve was created as follows after determining the optimum conditions of the method. Increasing volumes (1 - 5 ml) of Trifluoparazine solution at a concentration of 250 µg.ml-1 were added to volumetric flask 25 ml capacity containing 1ml Naphthalene-1,5diamine of (3×10-2M), 1 ml of potassium iodate solution of (2 × 10-2M), and 1 ml of sodium carbonate with a concentration of 2×10-2 M. Then the absorbance of all solutions was measured against the blank solution at a wavelength of 535 nm. Results indicated in Figure (4) that follows law Beer's within the limits of concentration from (10 – 50 µg.ml-1) of Trifluoparazine solution, and the molar absorption coefficient was calculated its value was 0.7975×104 L.mol-1.cm-1, and Sandell's sensitivity was calculated and found to be equal to 0.0602 µg.cm-2, and the correlation coefficient is 0.9992.

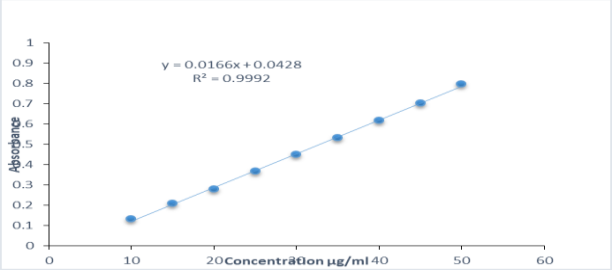

Fig. (4): Calibration curve for the determination of Trifluoparazine when reacted with Naphthalene-1,5diamine in the presence of oxidizing agent potassium iodate

Method validation

Three different concentrations of Trifluoparazine with a concentration of 250 µg.ml-1 were used to verify the accuracy and precision of the method represented by Relative Error RE%, Recovery percentage (R %), and Relative standard Deviation RSD%. By taking an average of six readings for each of them, the recovery rate was 99.24% and the relative standard deviation (0.792-0.892%), and results in the Table (11) are shown, meaning that the method is of high accuracy and has good agreement.

Table (11): The accuracy and compatibility					
RSD %	**Average of Recovery %**	**Recovery %**	**RE%**	**Conc. Of Measured µg.ml-1**	**Conc. OfMP. µg.ml-1**
0.792	99.24	99.8	-0.2	9.98	10
0.895		99.1	-0.9	19.8	20
0.892		98.83	-1.16	29.65	30

Detection limit

The limit of detection was determined by measuring the absorption of the lowest concentration (10 µg.ml-1) at 535 nm from the calibration curve, as shownin the Table (12).

Table (12): Detection Limit			
LOQ µg .ml-1	**LOD µg .ml-1**	**∂**	**Concentration of µg.ml-1**
2.609	0.782	0.0043307	10

The nature of colored product

Two continuous change approaches (Job's method) and (molar ratio method) were used to determine the nature of the colored product formed and the source of the drug's connection with the reagent.In both methods, the concentration of the trifluoperazine solution and the reagent solution1-naphthalene-1, 5-diamine is the same concentration 3x10-2 M. In the Job method, a series of volumetric bottles with a capacity of 25 ml was taken. Different volumes of the drug solution were placed, ranging from (1-9) ml to bottles containing decreasing volumes of the reagent (9-1 ml) and and diluted with distilled water to the limit of the mark, and measurement of the absorption of these solutions at 535 nm in

comparison to their blank solutions. Figure (5) shows that the correlation ratio between the drug and the reagent is 1:1,

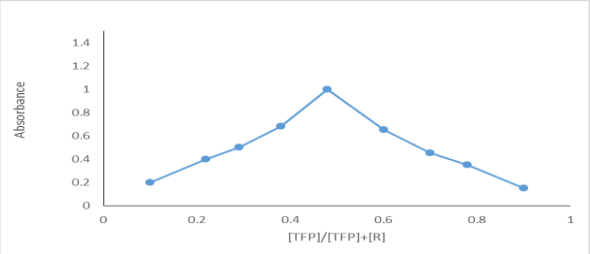

Figure (5): Shows method of continuous changes (Job method)

To ensure that the reaction ratio between the trifluoperazine and the reagent is 1:1, the molar ratio method was used where 2 ml of the drug solution was placed in a series of 25 ml volumetric bottles, different volumes of the reagent (0.3-3 ml) were added to it, and the rest was supplemented with the addition of solutions in the optimal volumes, then completed with distilled water, diluted to the mark. The absorption of these solutions was measured at wavelength 535 nanometers against the blank solution for each of them. With the method of continual changes, it was discovered that the molar ratio agrees with the blank solution.

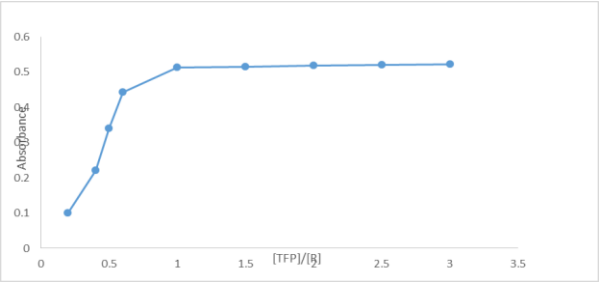

Figure (6): show the molar ratio method between the drug and reagent

Applications

The method can be used to test the following pharmaceutical formulations (Tablets), each of which contains 1mg of trifluoperazine.

The Direct method

Three different concentrations (10, 15, 20 µg/ml) of the preparations solution (Tablets) were taken, and then the absorptions was measured at a wavelength of 535 nm versus the blank solution by the same steps followed in the calibration curve, and the average of six was calculated Measurements for each concentration, and results in the Table (13) was indicated.

Table (13): The direct method

RSD %	Average of Recovery %	Recovery %	RE%	Conc. Of Measured µg .ml 1	Conc. Of T F P (Tablet) µg.ml-1
0.561	99.6	99.8	-0.2	9.98	10
0.477		99.4	-0.5	14.92	15
0.231		99.8	-0.2	19.96	20

Table (13): shows that the proposed method was successful in recognizing the trifluoperazine -containing medicinal product. The average recovery value was 99.6% percent in this case.

Method of Standard Additions

The standard additions method was used to show its accuracy in estimating trifluoperazine in pharmaceutical preparations and to show the efficiency of the proposed method. The method included adding fixed quantities of the preparation solution (1.5-1 ml) blocked at a concentration of 250 µg/ml in two volumetric vials of 25 ml capacity, then Add increasing volumes (0.2,0.4,0.6,1) ml of the standard drug solution with a concentration of 250 µg / ml. The above solutions are used in the same way as preparation for its user when preparing the calibration curve, then we measure the absorption of all solutions against the blank solution at a wavelength of 535 nm and the results are shown in Table (14) and Figure (7).

Table (14): Determination of T F P in tablets by the standard addition method

Amount taken µg /ml	Amount Measured	Recovery %
10	9.96	99.6
15	14.98	99.92

From the table, it turns out that the method of standard addition agrees well with the direct method within the acceptable range of error, which is what is shown the method is satisfactory.

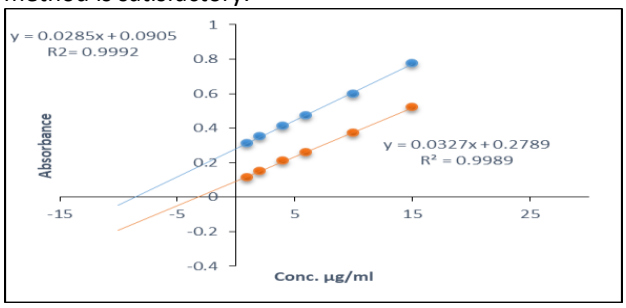

Fig. (7): Standard addition curve of trifluoperazine in tablets

5. Conclusions

Many reagents were used as oxidative coupling for trifluoperazine, as well as many methods were used to determine this drug in its free form and in its pharmaceutical preparation But in this proposed method was used a suitable coupling reagent (1-naphthalene-1, 5-diamine) in the presence of an oxidizing agent and in an alkaline medium for the purpose of using this method as a routine method for the determination of this drug. Where this method gave a linear relationship, accuracy and high harmonic with a relative standard deviation ranging between (0.792-0.892%) and a recovery rate of 99.24%, so it turns out that this method is a simple, fast and highly sensitive.

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