Journal of Pharmaceutical and Applied Chemistry
An International Journal

10.18576//JPAC.2023.305116

Spectrophotometric Assay of Trifluoperazine-HCl Via Oxidation and Bleaching the Color of Bougainville

Ali M. Hussein[1,] and Nebbel S. Othman[1].*

[1] Department of Chemistry / College of Science University of Mosul, Mosul, Iraq.
[1] Department of Chemistry / College of Science University of Mosul, Mosul, Iraq.

Received: 15 May. 2023, Revised: 10 June. 2023, Accepted: 15 June. 2023.
Published online: 1 September 2023.

Abstract: A simple, sensitive, and easy spectrophotometric method has been suggested for the determination of trifluoperazine-HCl. The developed method is based on the oxidation of trifluoperazine-HCl (TFPH) with an excess of N-bromosuccinimide [NBS] and then the unreacted NBS used in bleaching the colour of Bougainville [BgVa], which is extracted from Bougainville flowers collected from Mosul city. All factors that affected the two main reactions have been studied, including the type and amount of acid used in the first reaction (oxidation of trifluoperazine-HCl), the amount of Bougainville, the medium of reactions, and the times required for completing both oxidation and bleaching the colour of BgVa. The optimum conditions have been recommended. The present assay obeyed Beer's law (R2 = 0.9991) over the range of trifluoperazine-HCl concentrations from 5 to 75 g/ ml. The value of molar absorptivity is found to be 4.22x104 L/mol.cm, and Sandell's index value is 0.0113 g/cm2. The values of molar absorptivity and Sandell's index indicated that the suggested method has good sensitivity towards the compound under investigation, Trifluoperazine Hcl, with no interference from additives. The present mothed was applied successfully to the assay of Trifluoperazine HCl in (Tablet).

Keywords: Trifluoperazine- HCl, oxidation , N-bromosuccinimide , spectrophotometry, Bougainville.

Introduction

Trifluoperazine hydrochloride is a white-coloured powder that is odourless, highly dissolved in water and alcohol, partially dissolved in diethyl ether, and kept isolated from light in dark containers [1]. The scientific name of trifluoperazine hydrochloride is 10-[3-(4-methyl-1-piperazinyl) propyl] trifluoperazine hydrochloride (2-trifluoro-methyl phenothiazine di-hydrochloride), and it has the following chemical structure as shown in Figure 1.

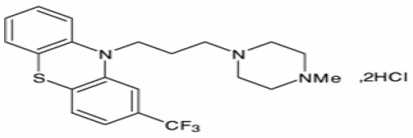


Fig. 1: Chemical structure of Trifluoperazine- HCl.

It has been known to induce QT prolongation and ventricular tachycardia, which can lead to sudden death [2], and is therefore used in the treatment of various mental diseases like schizophrenia. And depressive [3]. It was estimated via various methods, including electrochemistry using electrodes made of carbon. [4]. Various spectrophotometric methods were used, including oxidative coupling and other types of reactions [5–9]. Ultraviolet Spectrophotometric [10]. Also, other types of techniques have been used: the indirect atomic absorption method [11], the voltammetric method [12], potentiometric sensors [13], electrochemical sensing [14], flow injection analysis [15–17], RP-HPLC [18, 19], HPLC [20], derivative spectrophotometric, HPLC, and thin layer chromatography [21].

The dye used in the present work was a natural pigment extracted from the flowers of Bougainvillaea. It is easily obtained and extracted, does not need further purification, is not a toxic compound, does not emit any harmful gases to our environment, and its cost is not expensive.

Bougainvillaea is a type of organic compound belonging to the phenolic and flavonoid classes. The colourful flowers of bougainvillaea contain betacyanin [22]. Bougainvillaea has many uses for medical treatments such as stomach acidity, any problem in blood vessels, hepatitis, and various types of pain [23, 24].

EXPERIMENTAL

Apparatus

All Spectral measurements and absorption readings were carried out using a JASCO-360 spectrophotometer. Cells of glass and quartz with a light path of 1 cm were used. The pH was measured using a TRANS BP3001 pH meter and a BEL-sensitive balance was used to carry out the required weighing operations.

Reagents

All chemicals used were of analytical reagent grade, the pure Trifluoperazine hydrochloride was provided by the State Company for Drug Industries and Medical Appliance-(Safa and Bioner) -Iraq.

Trifluoperazine hydrochloride (500 µg/ml) was prepared by dissolving 0.0500 g of pure drug compound in distilled water and then made up to 100 ml in a volumetric flask and kept

* Corresponding author E-mail: alialnimi542@gmail.com

protected from sunlight in a volumetric flask.

Solution N-bromosuccinimide ($1x10^{-3}$) M was prepared by the dissolving of 0.01779 g of pure NBS in distilled water and diluted to the mark in100 ml-volumetric flask and kept protected from sunlight in an ambient bottle.

Dilute hydrochloric acid solution (approximate 1M): It is prepared by withdrawing 8.4 ml of concentrated hydrochloric acid (11.8 M) and adding it to a volumetric flask of 100 ml containing a little water and completing the volume with distilled water to the mark.

Bougainville dye solution (0.1%) is prepared by dissolving 0.1 g of dry extracted Bougainville dye in 100 ml distilled water.

Preparation of pharmaceutical preparation:

5 Tablets (S.D.I) each tablet containing 5 mg trifluoperazine-HCl , were carefully weighed and after being crushed and mixed well, the amount of the powder equivalent to 0.0100 g of pure TFPH was weighed and dissolved in distilled water then filtered into a volumetric bottle of 20 ml and supplemented with distilled water up to the mark.

15 Tablets for (1 mg/tablet, S.D.I), were carefully weighed and after crushed and mixing well, an amount of the powder equivalent to 0.0100 g of pure TFPH was weighed and dissolved in distilled water then filtered into a volumetric bottle of 20 ml and supplemented with distilled water up to the mark.

Extraction of the dye from Bougainville flowers

Bougainville flowers were collected from the Al-Nour neighborhood / Mosul /Iraq in April 2022. It was washed well with distilled water, then left to dry. After drying, the leaves were crushed using a wooden mortar. Approximately 10 g of the powder was taken and placed in a 500 ml beaker. Using distilled water (95 ml) and 5 ml hydrochloric acid (0.1M) in dissolving. After it was left for a period of time estimated at 72 hours, the mixture was filtered using ordinary filter paper and the filtrate was taken and left at a temperature of approximately 40 degrees Celsius to volatilize the solvent and we obtained the solid that was used in the current work after purification for several times using pure ethanol.

Then FTIR spectra of the dye was recorded by SHIMADZU 8400_FTIR spectrometer using KBr pellets (400 - 4000 cm^{-1}) in the College of Pharmacy, University of Mosul (Figure 2).

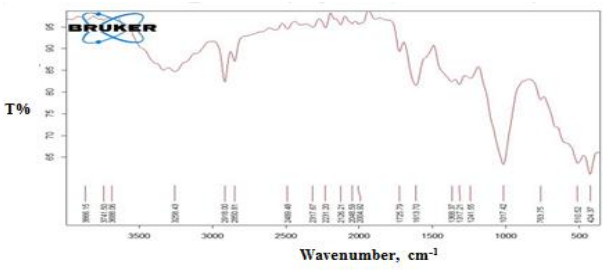
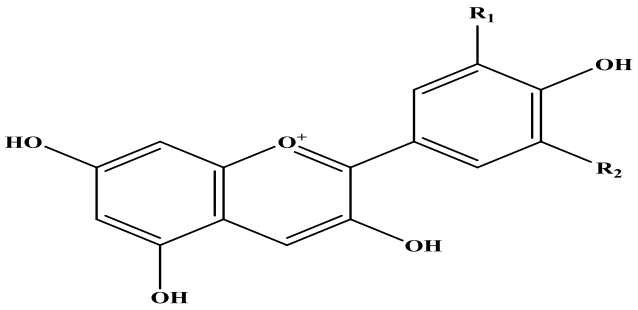


Fig. 2: The IR spectrum of extracted dye.

From the band presented in Figure 2, it can be concluded that the Bougainville flower extract contains anthocyanin pigments shown by their groups C=O, C–O, and C=C which is the structure of anthocyanin(Figure 3) [25].



R_1 and R_2= H,OH or OCH_3

Fig. 3: Basic structure of Anthocyanin [26].

RESULTS AND DISCUSSION

Color Spectrum

To determine the wavelength, the spectrum of the Bougainville dye that will be used in the subsequent measurements was taken by taking 1 ml of the dye and adding to it 1 ml of 1M HCl, completing the volume with distilled water to 10 ml, and taking the spectrum against the blank (Figure 4).

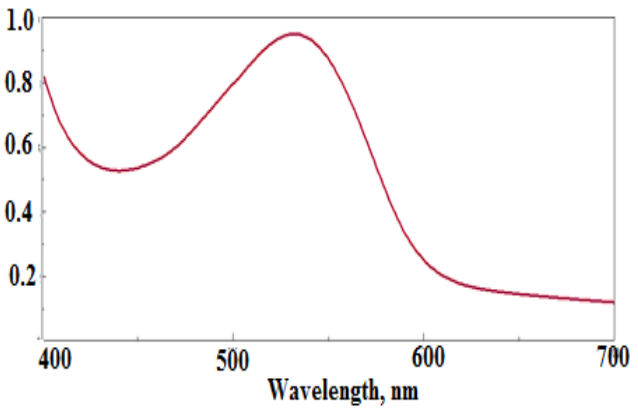


Fig. 4: Absorption spectra of Bougainville dye

Figure 3 shows the spectra of the Bougainville dye; the maximum absorption at 532 nm is used in all subsequent experiments.

Study of the Optimum Reaction Conditions

The effect of various parameters on the absorption intensity of the dye formed was studied and the reaction conditions are optimized.

Effect of Dye Volume

Different volumes of Bougainville dye were used, ranging between 0.1-1.5 ml of 0.1%, and the absorbance at the wavelength of 532 nm was measured against the blank solution and the results are shown in Figure 5.

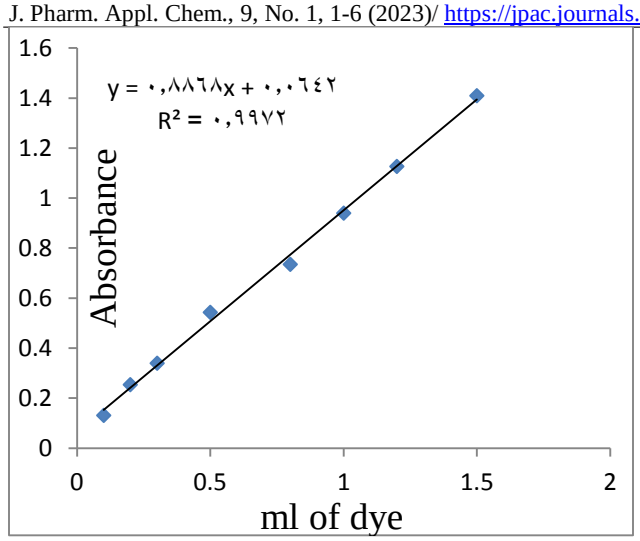


Fig. 5: Standard curve of Bgva dye.

The standard curve for different amounts of Bougainville. The results in Figure 4 show that the linearity continues to 1.5 ml with a determination factor of 0.9972.

1 ml of Bougainville was chosen to give it an acceptable absorbance so that it falls within the standard curve**.**

Selection of the optimal oxidizing agent

The oxidizing agents potassium periodate, N-bromosuccinimide and N-chlorosuccinimide were chosen to bleach the color of the dye by adding 1 ml to 10 ml volumetric containing 1 ml of dye and 1 ml of hydrochloric acid then the volume was supplemented with distilled water to the mark, and the solutions were left for 10 minutes, then absorbance was measured at the wavelength of 585 nm against the blank solution (Figure 6).

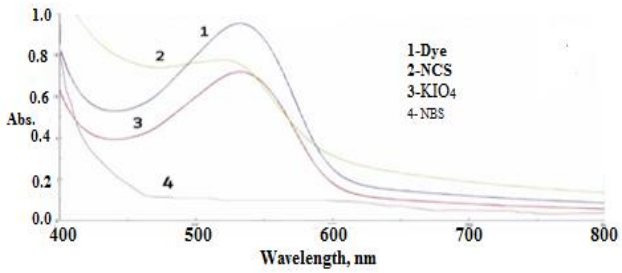


Fig. 6: Effect of different oxidizing agents on dye bleaching.

Figure 4 shows that the oxidizing agent N-bromosuccinimide gives the best results in the bleaching process, so it was chosen in subsequent experiments.

Effect of the amount of volume N-bromosuccinimied

The effect of the oxidizing agent NBS has been studied in different quantities (0.1 to 1.75 ml) in the oxidation of the drug compound under study in increasing quantities of it as was inferred from the results listed in Figure (7).

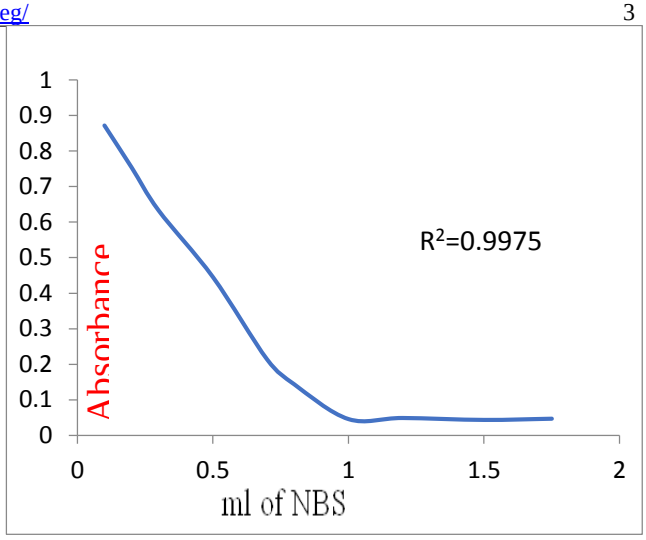


Figure 7: The effect of various volume of the oxidizing agent.

Results show that the optimal volumes of 1 ml of the oxidizing agent is the best in the oxidation process, it gave the excellent bleaching color of the dye, and therefore it was adopted in subsequent experiments.

Effect of the type of acid used in oxidation

Different types of acids were studied on the oxidation of 1 ml (100 µg) of Trifluoperazine hydrochloride, and 1 ml of different acids and 1 ml of NBSwas added. Absorbance of the remaining Bgva dye was measured after bleaching and at wavelength 585 nm and the results are shown in Table 1.

Table 1: Effect of the type of acid used in oxidation

)1M (Acid used	**Absorbance**
HCl	0.9402
H_2SO_4	0.6743
$HN0_3$	0.3215
CH_3COOH	0.4452

From the results in Table 1, it was noted that hydrochloric acid gave the highest intensity of absorbance of the remaining dye, which indicates that a larger amount of Trifluoperazine hydrochloride oxidized by NBS and less amount of NBS unreacted and used in bleaching color of the dye, therefore it was used in subsequent experiments.

Effect of the amount of hydrochloric acid

The effect of the amount of hydrochloric acid needed to complete the oxidation process of Trifluoperazine hydrochloride was studied, as shown in Table 2.

Table 2: Effect of hydrochloric acid amount.

MHCl١)ml(	0.25	0.5	0.7	1	1.5
Absorbance	٠,٣٢١ ٨	٠,٥١٧ ٦	٠,٧٦٨ ٣	٠,٩٣١ ١	٠,٦٤٣ ٢

Effect of oxidation time

The effect of the time required for the oxidation of Triflouperazine hydrochloride and bleaching the residual

dye was investigated by follow-up the absorbance of residual dye after various times from 2 - 25 minutes for oxidation of Triflouperazine hydrochloride by adding NBS and then after the addition of the dye left for various time from 2-25 minute before dilution a measuring the absorbance.

The oxidizing agent N-brormosuccinimide in the acidic medium and then left for different periods of time - and then adding the known amount of dye Bougainville and then diluting it to the mark limit and measuring the absorption at the maximum wavelength 532 nm and the results are shown in Table 3.

Table 3: Effect of oxidation time on the drug compound and short pigmentation.

Standing time of oxidation (minute)	Standing time minute before dilution					
	2	5	10	15	20	25
2	٠,٢٢٨	٠,٥٨٣	٠,٧٩٦	٠,٨٦٣	٠,٨١١	٠,٨٠٦
5	٠,٥٨١	٠,٧٨١	٠,٨١٠	٠,٨٩١	٠,٨٧٦	٠,٨٦٦
10	٠,٨٦٣	٠,٨٨٠	٠,٩٠٠	٠,٩٢١	٠,٩١٨	٠,٩٠٨
15	٠,٩٣٨	٠,٩٣٩	٠,٩٤٠	٠,٩٤٤	٠,٩٣٦	٠,٩٣١
20	٠,٨٧٦	٠,٩١٦	٠,٩١٠	٠,٨٨٦	٠,٨٦٥	٠,٨٥١
25	٠,٨٤٤	٠,٨٥٦	٠,٨٧٤	٠,٨٧١	٠,٨٥٢	٠,٨٤١

The results showed that the best time for oxidation of Trifluoperazine hydrochloride is 15 minutes, and the best time for shortening the color of Bougainville is 15 minutes, so it was adopted in subsequent experiments.

The effect of temperature and time on the stability of the color of the remaining Bougainville dye

The effect of temperature on the intensity of the remaining Bougainville color was studied. It was noted that changing the room temperature gave the best results. Therefore, the room temperature was adopted to give it the highest absorption. The results are shown in Table 4.

Table 4: The effect of temperature on the intensity of the remaining BgVa color.

Tem .^{0}C	Absorbance / minute standing							
	5	10	15	20	30	40	50	60
10	٠,٨١٣	٠,٨١٢	0.811	0.810	0.810	0.809	0.806	0.805
RT	٠,٩٤٣	٠,٩٤٢	٠,٩٤٤	٠,٩٤٣	٠,٩٤٢	٠,٩٤٤	0.943	0.941
40	٠,٦٦٢	٠,٥٧٥	٠,٤٤٤	٠,٤٢١	٠,٤٠٣	٠,٣٩٦	٠,٣٦٦	٠,٣٤٤

The sequence of adding reaction components

Several experiments were carried out with different sequences to add the oxidizing agent in order to obtain the best absorption of the remaining dye. Results Table 5.

Table 5: Finding the best sequence for adding components.

Reaction component	Order number	Absorbance
S+H^++OX+BgVa	I	٠,٩٤٣٢
S+ BgVa +OX+H^+	II	٠,٦٣٥٨
BgVa+OX+H^++S	III	٠,٨٧٦١

S (Trifluoperazine-HCl) + H (Hydrochloric acid) + OX (NBS) +BgVa (Bougainville)

From the results in the table, the sequence I followed in the previous and subsequent experiments was adopted. In order to give it the highest absorption intensity of the remaining dye, which indicates the largest amount of the drug compound oxidized.

Optimum conditions

After creating the optimal conditions via various experiments, these conditions are listed in Table 6,

Table 6: The optimal conditions.

Variable	Optimality
Dye ,concenteration,V	Bougainville ,0.01M,1ml
Oxidant,M,ml	NBS,1x10^{-3}M,1
Volume of HCl,M,ml	1,1

Working method and standard curve.

Adding an increasing volume of trifluoperazine hydrochloride solution (500µg/ ml) to a set of 10 ml volumetric flasks, and 1 ml of hydrochloric acid and 1 ml of an NBS solution (1x10^{-3} M) were added, then the solutions are left for 15 minutes at room temperature, then 1 ml of the dye is added and left for 15 minutes. The volumes are supplemented with distilled water to the mark, then the absorbance is measured against the blank solution at a wavelength of 532 nm. Figure (8) represents the standard curve for the determination of trifluoperazine hydrochloric, which follows Beer's law in the concentration range (5-75) µg / ml, the molar absorption value is 4.22 x 10^4 l/.mol.cm, and the Sandell,s significance is 0.0113 µg/cm^2 which indicates the high sensitivity of the method.

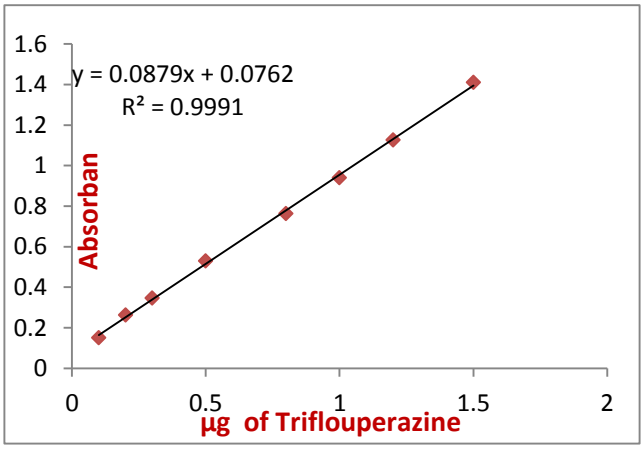


Fig. 8: Standard curve of determination Trifluoperazine Hydrochloride.

Analysis of Trifluoperazine hydrochloride

The method was applied by taking different volumes of a standard solution of 500 µg / ml to obtain concentrations of 10-50 µg / ml for tablet content (1 mg/tablete) and 15-35 µg / ml for tablet contenet (1 mg/tablet), and it was treated according to the working method described for standard solutions. The results obtained are shown in Table (7).

Table 7: The results of application of method.

Pharmaceutical preparation	µg TFPH /ml present	µg TFPH /ml measured	Recovery*%	Drug content found mg)(	t exp**
Trifluoperazine HCl 1mg/ tablet	10	9.92	99.20	0.9920	2.4641
	50	49.98	99.96	0.9996	0.7641
Trifluoperazine HCl 5mg/ tablet	15	14.96	99.73	4.9865	0.2037
	35	34.97	99.91	4.9955	2.2044

*Average for four determinations. ** $t = (\bar{X} - \mu) \times \frac{\sqrt{N}}{s}$

Estimation by the standard addition method

The calculated t-value for concentrations 10 and 50 µg/ml of Triflouperazine-HCl 1mg is 3.4641 and the calculated t-value for concentrations 15 and 35 of Triflouperazine HCl 5mg is 2.2044 is less than the tabular value with 3 degrees of freedom and at a confidence level of 95%, which indicates the success of the method.

In order to prove that the proposed method is free of interferences of additives used in manufacturing drugs, the standard addition method was applied to the medicinal product drops, as the obtained results are shown in Figure 9 and 10 and Table 8 that the standard addition method agrees well within the acceptable range of error, which indicates that the results of the method are satisfactory and free from interference.

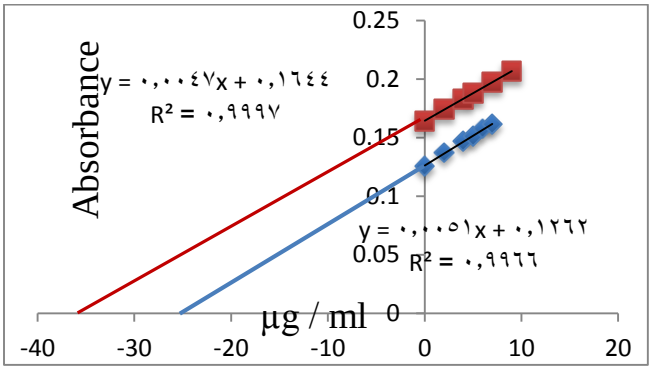


Fig. 9: Standard addition method of Trifluoperazine-HCl (1mg/ tablet, S.D.I. Iraq).

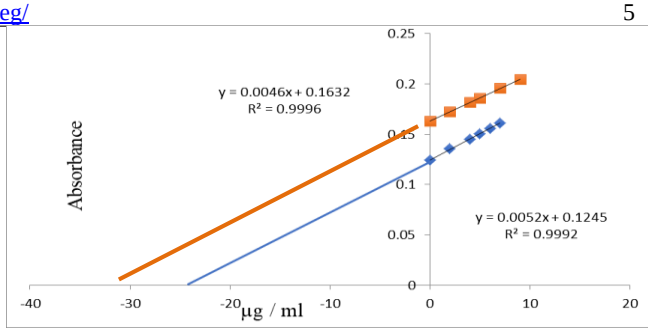


Fig. 10: Standard addition method of Trifluoperazine-HCl (5mg/ tablet, S.D.I. Iraq).

Table 8: The results of standard addition method

Pharmaceutical preparation	µg TFPH present	µg TFPH measured	Recovery* (%)	Drug contain mg
Trifluoperazine-HCl/tablet (1mg, S.D.I. Iraq)	25	24.74	98.96	0.9896
	35	34.97	99.91	0.9991
Trifluoperazine-HCl/tablet (5mg, S.D.I. Iraq)	25	23.94	95.76	4.788
	35	35.47	101.34	5.067

*Avreage for four determinations.

Conclusion

Suggested a sensitive spectrophotometric method for the determination of Triflouperazine hydrochloric in pharmaceutical preparations by oxidizing Triflouperazine hydrochloric with the oxidizing agent N-bromosuccinimide and then estimating the unreacted oxidizing agent by shortening the color of Bougainville and the measurement is done at the wavelength of 532 nm. The method was successfully applied for the determination of Trifluoperazine hydrochloride in its Tablet pharmaceutical preparation.

References

[1] British Pharmacopoeia Incorporating the 3th Ed.of the European pharmacopeia,2001,CD-Rom.

[2] Se-Young C., Young-Sang K., Su-Hyun J., Inhibition of human ether-a-go-go-related gene K+ channel and IKr of guinea pig cardiomyocytes by antipsychotic drug trifluoperazine, J. Pharmacol. Exp. Ther. 313 (2005):888-95.

[3] Walash ,M.I.,Rizk,M.,Abou-Ouf, Titrimetric determination of some N-substituted phenothiazine derivatives. Analyst, 108;(1983):626-32.

[4] Aveen K.Mohammed, Ali I.Khaleel. Determination of triflouperazine hydrochloride by new constructed

coated carbon selective electrodes. J. University of Garmian., (2019):398-410.

[5] Mohammad J. Hamzah, Rawa M. Taqi, Muna M. Hasan, Raid J. Al-Timimi, Spectrophotometeric determination of triflуoperazine-HCl in pure forms and pharmaceutical preperations. IJPCR,9(5); (2017): 337-342.

[6] Hussein A. Mohammad Othman N. Sabeeh. Development spectrophotometric determination of trifluoperazine hydrochloride in dosage forms by used oxidative coupling reaction. In: AIP Conference Proceedings. AIP Publishing LLC, (2023): 030004.

[7] MarwanT.J. Spectrophtomertic determination of triflouperazine hydrochloride in pharmaceutical preparations by oxidative coupling reaction, Sys Rev Pharm. 11 (6); (2020): 58-68.

[8] Hussein A. Mohammad, Othman N. Sabeeh. Development of a new indirect method for the determination of Trifluuperazine HCl in pharmaceutical formulations. Journal of Pharmaceutical and Applied Chemistry, (2023), 9(2): 1-16.

[9] AI-Rashidy A., AI –DOURY M. F., AI-Taiee A. K. Spectrophotomertic determination of triflouperazine hydrochloride using oxidative coupling reaction, Tikret J.Pharma. Sci.,13(1); (2018):1-10.

[10] Jalal MT. Spectrophotometric determination of trifluoperazine HCl in pharmaceutical preparations by oxidative coupling reaction. Sys Rev Pharm. 2020;11(6):58-68.

[11] Nief R. A. Ultraviolet spectrophotometric determination of trifluoperazine. HCl in pharmaceutical preparations and environmental wastewater samples: Application to content uniformity testing, Res.& Rev. J. Pharma. Analysis. (2014): 2347-2340.

[12] Ameen W. Qassim,Zuhair A. K., Ashraf S.R. An indirect atomic absorption spectrophotometric determination of triflouperazine hydrochloride in pharmaceuticals, Arabian J. Sci. and Eng. 36; (2011): 553–563.

[13] Stankovi´c D., T. Dimitrijevi´c D., Kuzmanovi´c M. P., Krsti´c B. B. Voltammetric determination of an antipsychotic agent trifluoperazine at a borondoped diamond electrode in human urine, RSC Adv., 5;(2015): 107058-107063.

[14] Ahmed K. H., Suhaam T. Ameen., Bahruddin Saad., Suad M AI-Aragi.. Potentiometric Sensors for the Determination of Trifluoperazine Hydrochloride in Pharmaceutical Preparations Analytical Sciences 25(11):1295-9 DOI:10.2116/analsci.25.1295, November 2009.

[15] Sura M., Eman A.Electrochemical sensing for trifluoperazine determination at a pth/mwnts film-modified graphite electrode, Egyptian Journal of Chemistry 65 (4), 13-17, 2022.

[16] Moath .T.A. Flow injection spectrophotomertic determination of Triflouperazine Hydrochloride Using Oxidative Coupling Reaction, International J. Current Research.9(4); (2017): 49218-49222.

[17] Kamal M. and Maadh T.A. Flow injection spectrophotometric determination of triflouperazine hydrochloride using oxidative coupling reaction, Inter. J. Current Res.9(4); (2017): 49218-49222.

[18] Bhadani S., Ekta P. R. Development and validation of RP-HPLC method for simultaneous estimation of chlordiazepoxide, trifluoperazine hydrochloride and trihexyphenidyl hydrochloride in tablet dosage from, Inter. J. Current Res. in Pharma.1(1); (2015): 50-59.

[19] Suman P. A Novel RP-HPLC method development and validation for simultaneous estimation of trifluoperazine and isopropamide in tablet dosage form. Inter. J. Pharma. Sci. and Drug Res., 7(1); (2015): 105-109.

[20] Jameel M .Dhabab…Assaf H.Taufeeq Separation and determination of trifluoperazine and prochlorperazine in pharmaceutical preparations by HPLC, J. Assoc. of Arab Univ. for Basic and Appl. Sci., 13(1); (2013): 14-18.

[21] El-Gindy, A., El-Zeany, B., Awad, T., & Shabana, M. M. Derivative spectrophotometric, thin layer chromatographic densitometric and high performance liquid chromatographic determination of trifluoperazine hydrochloride in presence of its hydrogen peroxide induced-degradation product. Journal of pharmaceutical and biomedical analysis, (2002); 27(1-2): 9-18.

[22] Saleem H., Usman A., Mahomoodally M. F., and Ahemad N., Bougainvillea glabra (choisy): A comprehensive review on botany, traditional uses, phytochemistry, pharmacology and toxicity, J. Ethnopharmacol., 266: 113356.

[23] Ogunwande I. A., Avoseh O. N., Olasunkanmi K. N., Lawal O. A., R. Ascrizzi, and Flamini G. Chemical composition, anti-nociceptive and anti-inflammatory activities of essential oil of Bougainvillea glabra, J. Ethnopharmacol.,(2019); 232: 188–192.

[24] Markandan S., Abdullah A., K. H., Subramaniam V., and Stockham K., Determination of antioxidant activities, total phenolic and flavanoid contents in Bougainvillea glabra bracts at various methanol concentrations, in AIP Conference Proceedings, (2016); 1784(1): 30038.

[25] Pratima S. and Mahak S., Comparative study of proximal analysis of fresh pomegranate flower powder and dry pomegranate flower powder -a waste

management study, Plant Arch., (2020); 20: 88-90.

[26] Eker, M. E., Aaby, K., Budic-Leto, I., Rimac Brnčić, S., El, S. N., Karakaya, S., ... & de Pascual-Teresa, S. A review of factors affecting anthocyanin bioavailability: Possible implications for the inter-individual variability, Foods, (2019); 9(1): 1-18.