ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 04, pp.49218-49222, April, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

FLOW INJECTION SPECTROPHOTOMETRIC DETERMINATION OF TRIFLUOPERAZINE HYDROCHLORIDE USING OXIDATIVE COUPLING REACTION

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ARTICLE INFO

Article History:
Received 17th January, 2017
Received in revised form
18th February, 2017
Accepted 06th March, 2017
Published online 30th April, 2017

Key words:
Trifluperazine hydrochloride, Ammonium ceric salphate, Sulphanilic acid, Flow injection.

ABSTRACT

A flow-injection (FI) spectrophotometric procedure is proposed for Trifluoperazine Hydrochloride (TFPH) determination in pharmaceuticals. The proposed method is based on the injection of 50 µL sample solution into an oxidizing agent stream of ammonium ceric salphate with the optimum flow rate of 2.0 ml min^{-1}. The violet [TFPH- sulphanilic acid (SA)] complex is monitored at 545 nm. The (FI) system and the experimental conditions were optimized. Under the optimum conditions, calibration graph was obtained for 0.5-120 µg $ml^{-1}$and the detection limit 0.0459 µg ml^{-1}. The correlation coefficient was 0.9990. The method was successfully applied to the determination of this drug in pharmaceutical formulations with a sample throughput of $120h^{-1}$. The results obtained by the proposed method were in good agreement with those obtained by the official method at 95% confidence level.

Citation: Kamal M. Mahmoud and Maadh T. Abdurhman, 2017. "Flow injection spectrophotometric determination of Trifluoperazine hydrochloride using oxidative coupling reaction", *International Journal of Current Research*, 9, (04), 49218-49222.

INTRODUCTION

Trifluoperazine HCl (TFPH), 10-[3-(4-methyl-1-piperazinyl) propyl]-2-(trifl uoromethyl)-10 Hphenothiazine hydrochloride, is a prominent compound in a large group of phenothiazine derivatives. TFPH has central antiadrenergic, antidopaminergic, and minimal anticholinergic effects (Prashanth, *et al*., 2014). is still widely used because it is an inexpensive and accessible drug, although administration of TFPH commonly causes side effects, including drowsiness, dizziness, rash, and anorexia, and occasionally more serious complications such as cardiac arrhythmias or sudden death (Kim *et al*., 2016). Several methods have been applied for the determination of trifluoperazine hydrochloride in dosage forms and in biological fluids. The different techniques used in this action include spectrophotometry (El – Gindy *et al*., 2001; Basavaiah 2004; El- Saudagar, *et al*., 2007; Hassouna, *et al*., 2012 and Maadh and Kamal, 2016), voltammetry (Huang *et al.,* 2006), capillary zone electrophoresis (Muijselaav *et al*., 1996), fluorimetry (Kaul *et al*., 1978) turbidimetry (Amir *et al*., 2003), Titrimetry (potentiometric titrations) (Krishnamurthy and Basavaial – 1998 and Ahmed *et al*., 2009), extraction liquid chromatography (Shaghayegh *et al.,* 2011), High performance liquid chromatographic methods (Shettip and Venkatachalama – 2010). And liquid chromatographic methods (Shree – 2009; Temerdashev *et al*., 2006; Anna, 2007; Magdalena *et al.,* 2006). In recent years, more strict regulation related to the quality control of pharmaceuticals has led to increasing demands on automation of the analytical assays carried out in appropriate control laboratories. The flow-injection analysis (FIA) procedure became a versatile instrumental tool that has contributed substantially to the development of automation in pharmaceutical analysis due to its simplicity, low cost and relatively short analysis time (Tzanavaras, Paraskevas *et al*., 2002; Rufino, *et al.,* 2008). The main purpose of this work was to develop a simple, fast and low-cost flow injection procedure for the quantification of Trifluoperazine HCl based on the spectrophotometric detection of the colored products formed by the oxidation of these drugs with sulphanilic acid. The resulting colored products of the above mentioned reaction measured at 545 nm.

Experimental

Apparatus

The schematic design of FI-system used in this modified method was a multichannel peristaltic pump (Manostat-Barnant Company) provided with silicon pump tubes (0.8 mm i.d.) used to deliver the flow streams, a six-way injection valve (Rheodyne-USA, with variable homemade loop volumes) and PTFE tubes with homemade Y-pieces and mixing coils (0.8

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mm i.d., different length) used to connect and mixing of different flow streams. The colored product formed was monitered spectrophotometrically using JENWAY 6300 spectrophotometer that's connected to a recorder (type PM 8251A PHILIPS-one line recorder), through a flow cell (Sterna-micro flow cell, 100 µL and 1.0 cm path length).

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.

TFPH solution (1000 µg 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 (100 µg ml^{-1}) is prepared by simple dilution of stock solution and stored in an amber glass bottle in a refrigerator.

Sulphanilic acid solutions (SA) (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 vol-umetric flask.

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.

Sample solution of tablets contain TFPH (250 µg ml^{-1})

From three deferent companies 20 tablets are weighed (each tablet contain 20.0 mg TFPH) and granulated to a fine particles, then apportion equivalent to 250 µg ml^{-1} of TFPH is weighed into 100 ml volumetric flask, then the solution filtered by filter paper (589/ 4 S&S Rundfilter 150 mm) and the volume is completed to the mark.

General procedure

The FIA manifold shown in Fig.(1-I) was used for determination of TFPH. 5.0 × 10^{-3} M (ACS), and 1.0 × 10^{-2} M (SA) solutions were propelled at flow rates of 2.0 ml min^{-1}. A 60 µL of 100 µg mL^{-1} TFPH was injected into oxidizing agent stream in a reaction coil-1of 30-cm then react with reagent (ACS) in a reaction coil-2 of 20-cm, while the colored product was formed, the peak heights were recorded at 545 nm.

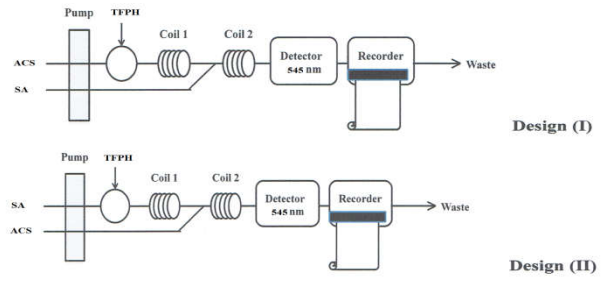

Fig. 1. Schematic diagram of FIA-Spectrophotometric designs (I and II)

For determination of TFPH

Optimization of manifold designs

Two manifolds designs shown in Fig. (1- I and II) had been tested for the determination of TFPH. Among these two manifolds it was found that the manifold (I) was the best in the stability and peak height (mm) obtained, compared with the manifold (II), which gives lower measuring. Therefore, design (I) had been selected in further studies.

Optimization of experimental parameters

Optimization of chemical parameters

The effect of different concentrations range (1.0×10^{-4} - 5.0× 10^{-3}M) of ACS was investigated, while keeping other conditions constant, it was found that a 1.0×10^{-3} M of ACS was found to be the most suitable concentration for obtaining maximum absorbance Fig. (2), and was chose for further use, SA was found necessary for developing the colored product and increase its stability the effect of SA was studied in the concentration range (1.0 ×10^{-1}- 1.0 ×10^{-3}M) and a greatest absorbance intensity with lower baseline intensity was obtained with 1.0 ×10^{-2} M of SA for determination of TFPH Fig. (3).

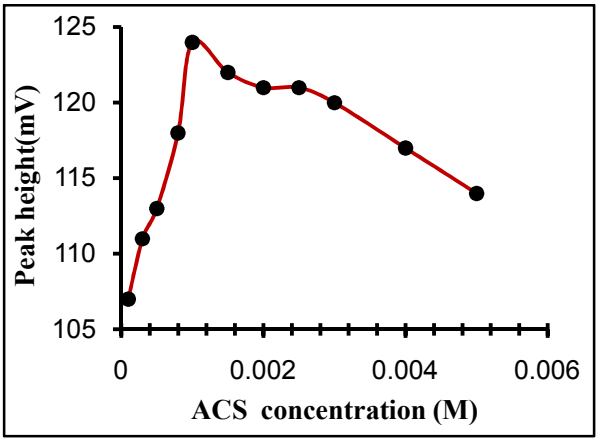

Fig.2. Effect the concentration of ACS

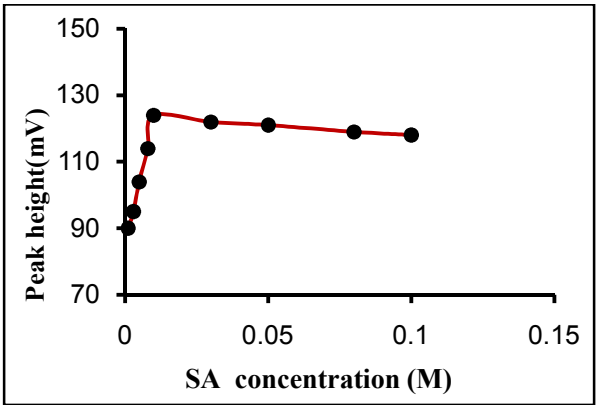

Fig.3. Effect the concentration of SA

Optimization of physical parameters

The variables studied under the optimized reagent concentrations were the flow rate, the injected sample volume and the reaction coil length. The effect of flow rate on the

sensitivity of the colored reaction product was investigated in the range (0.5-5.0 ml min^{-1}) the result obtained showed that a flow rate of 2.5 ml min^{-1} gave the highest absorbance as shown in Fig.(4) and was used in all subsequent experiments. The volume of the injected sample was varied between 50 – 150 µL using different length of sample loop, the result obtained showed that injected sample of 75 µL gave the best absorbance and good reproducibility Fig. (5). Effect of mixing coil length on the peak height was examined in the range of (0.0 - 120 cm). Two optimum values shown in Fig. (6). The results show that the optimum conditions was observed for the two reaction coil (a and b) used in the system were (80 and 30 cm) respectively.

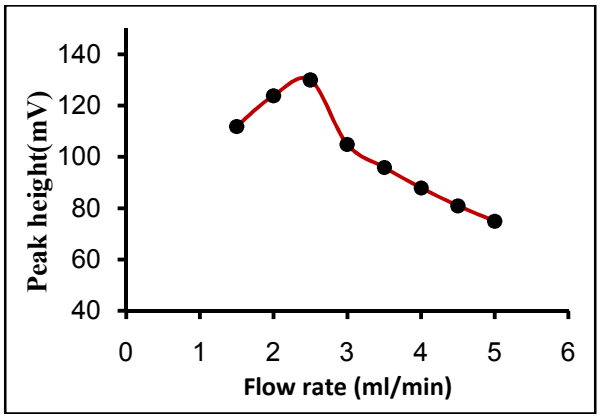

Fig.4. Effect of flow rate on the peak height

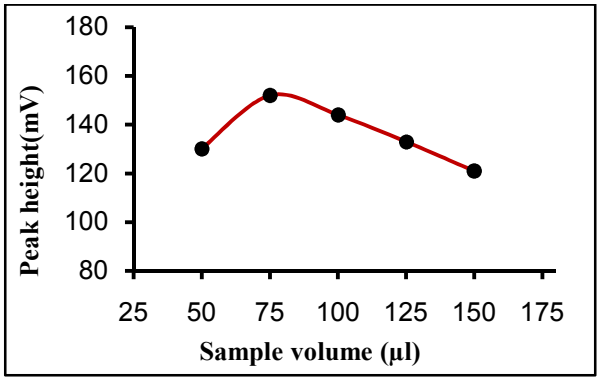

Fig.5. Effect of sample volume on the peak height

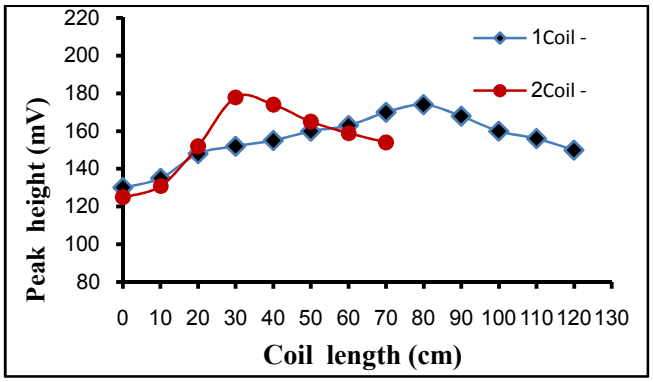

Fig.6. Effect of coil length on the peak height

Calibration graph

Under the recommended conditions, the calibration curve was produced by plotting the peak height (mm) against the concentration of TFPH (µg ml^{-1}). Beer′s law was obeyed over the concentration range of 0.5-120 µg $ml^{-1}$of TFPH, with a correlation coefficient of 0.9990 as in Fig. (7) and detection limit of 0.0459 µg ml^{-1}.

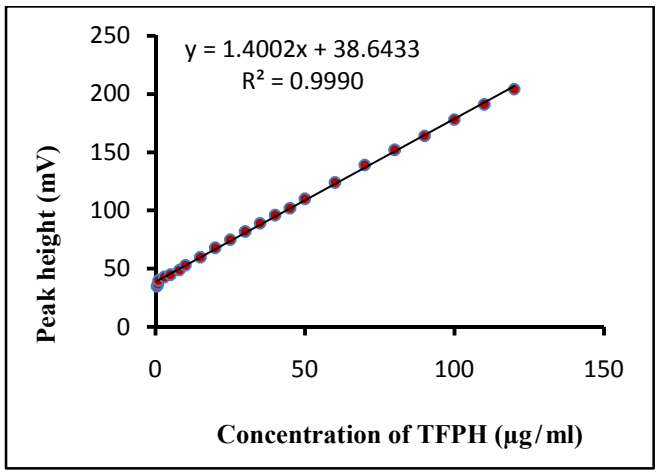

Fig.7. Calibration graph for FIA spectrophotometric determination of TFPH

Accuracy and precision

Accuracy and precision of the current system were measured through application of three different concentration of TFPH in the linear range with five replication for each concentration, the result shown in Table (1).

Table 1. Accuracy and precision of the FIA- spectrophotometric determination of TFPH

Analyte	Analyte concentration (µg ml^{-1})		Recovery %	RSD %
	TFPH taken (µg ml^{-1})	TFPH found (µg ml^{-1})		
TFPH	6	5.6825	101.28	1.17
	54	53.9613	99.82	0.39
	105	105.0968	100.11	0.24

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 signal obtained when TFPH present alone and in the presence of different concentration of interferences (100 - 400 µg ml^{-1}) reach to (5 -20) times of the amount of TFPH (20 µg ml^{-1}). The results found that a substance is considered not to interfere if the variation in the peak height of pure TFPH & TFPH with interferences less than ± 5.0% of the recovers. Table (2) illustrated the recovers after addition of additives by (5 - 20) fold excess the amount of TFPH.

Table 2. Effect of interferences

Foreign compound	Recovery (%) of 20.0 µg ml^{-1} of TFPH per (µg ml^{-1}) foreign compound added		
	100	200	400
Glucose	99.25	100.54	99.09
Fructose	100.06	100.67	100.17
Maltose	99.79	101.28	99.12
Starch	99.93	100.09	99.58

Table 3. Comparison of the present method with standard method for determination of TFPH (B.P.- 2013)

Product manufacture and country (tablets)	TFPH content (mg)	Proposed method			Standard method			t	F
		TFPH found (mg)	Rec. %	RSD %	TFPH found (mg)	Rec. %	RSD %		
STELLASIL (Egypt)	5.0	5.123	101.543	1.652	4.982	99.91	0.980	1.028	1.865
Trifldaron (Iran)	5.0	4.698	98.879	1.823	4.789	98.23	0.568	0.980	3.209
Iralzin (SDI)	5.0	4.928	99.915	0.231	4.916	99.87	0.199	0.687	1.060

Tabulated value of t = 2.776 , F = 6.39

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 result shown in Table (3).

Conclusion

FI-Spectrophotometric method utilizes for determination of TFPH in injection samples and the proposed method was also simple, rapid, and precise. As comparison in sensitivity between batch (Maadh and Kamal, - 2016) and FIA techniques observed that batch techniques more sensitivity than FIA technique in which linear ranges for both techniques (0.5 – 20.0 μg ml^{-1}) and (0.5 –120 μg ml^{-1}) respectively and detection limit for batch method 0.1604 μg ml^{-1} while for FI method gave 0.0459 μg ml^{-1}. However, FIA had some advantages over the batch method due to simplicity and rapidity.

Acknowledgements

The authors would like to thanks the presidency of Salahaddin University-Hawler, College of Science, and Department of Chemistry (Iraqi Kurdistan Region – Erbil) to their help and taking permission for working in the post graduate laboratories.

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