

INDIRECT POLAROGRAPHIC DETERMINATION OF FLUPHENAZINE HYDROCHLORIDE USING PEROXOMONOSULPHATE

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Fluphenazine hydrochloride (FH), 2-[4-[3-(2-(trifluoromethyl)-phenothiazine-10-yl)propyl]piperazine-1-yl]ethanol dihydrochloride (Fig. 1), belongs to the piperazine class of phenothiazines [1]. It is a typical antipsychotic drug used for the treatment of psychoses, such as schizophrenia, dementia and others [2].

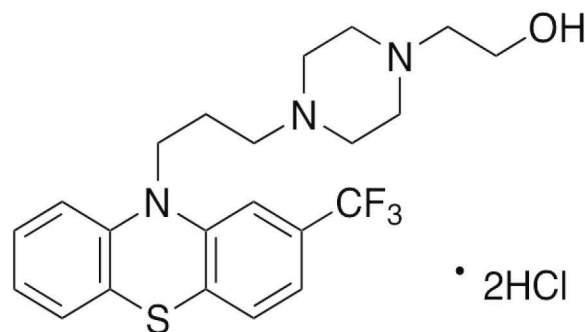


Fig. 1 The molecular structure of Fluphenazine hydrochloride

Numerous analytical methods are given in the literature for determining FH, either in pure form or in pharmaceutical preparations and biological fluids. The United States Pharmacopoeia (USP), on the other hand, describes the HPLC method for the determination of FH in its pure form, Fluphenazine Hydrochloride Injection and Fluphenazine Hydrochloride tablets, using UV detection at 254 nm where the limit of quantification (LOQ) is $2.4 \mu\text{g mL}^{-1}$. Although chromatographic methods offer a high degree of specificity, the sample purification and instrumental limitations preclude their use in routine studies. Therefore, there is a need for an alternative substitute to the HPLC methods, and voltammetry by virtue of its high sensitivity is a promising substitute.

The electrochemical behavior of FH can be successfully employed to elaborate simple, rapid and sensitive procedures for determining this API in pharmaceutical preparations [3]. Thus, after effectively accumulating at multi-walled carbon nanotubes/(3-mercaptopropyl)trimethoxysilane of the bilayer modified gold electrode Fluphenazine produces two anodic peaks at 0.78V and 0.93V (versus SCE). This method was successfully applied to the determination of FH in drugs, and the recovery was 96.4-104.4% [4]. A glassy carbon electrode with Methylene blue as a mediator was employed to sense the electrocatalytic determination of FH, using cyclic voltammetry. It was found that the peak current due to the oxidation of Methylene blue at the surface of the electrode (at a potential of about -180 mV) was proportional to the FH concentration. Linear analytical curves were obtained in the ranges of $1.0 \times 10^{-6} - 2.1 \times 10^{-4} \text{ mol L}^{-1}$ for FH. Though FH cannot be directly reduced on the mercury electrode, after nitrosation it can be determined by DPP on DME at the submicromolar level [5]. The HPLC and DPP methods are in good agreement; however, polarography enables a rapid analysis with a simple apparatus, does not require a tedious purification step, and it provides better reproducibility and accuracy.

The work of our laboratory showed a successful application of this approach in the assay of several phenothiazines.

The aim of this research was to develop a simple, accurate, precise and inexpensive method for the assay of FH in pharmaceutical formulations. In present paper, we report on the use of potassium peroxymonosulfuric acid (PMS) for the oxidation of FH to a polarography-active S-oxide Fluphenazine, and the development of a simple and sensitive method for its determination. The use of PMS has several advantages over other reagents applied in this field.

A potassium triple salt containing potassium peroxydisulfate (KHSO_5), potassium hydrogensulfate (KHSO_4), and potassium sulfate (K_2SO_4) in the molar ratio of 2:1:1 was used. This product is sold under the trade name Oxone®. Moreover, it is considered as “green” oxidizing agent since it has no toxic effects.

All the electrochemical experiments were conducted in a three electrode single compartment glass cell. An Ag/AgCl (3.0 mol/L KCl) electrode was used as reference electrode and auxiliary electrode was a Pt electrode. The working electrode was a hanging mercury drop. The polarographic measurements were carried out using Metrohm 797 VA Computrace system (Metrohm AG Ltd., Switzerland).

10 ml of 0.02 M HCl solution and 120 μl of the original Oxone solution were poured in an electrochemical cell. The solution was degassed with nitrogen for 120 s. after that aliquots of the FH solution (20-30 μl) were added to the cell. After each addition of the aliquot, the solution was stirred for 150 s, and then the voltammograms were recorded.

Differential pulse polarogram of FH after oxidation by hydrogenperoxomonosulfate is shown in Fig. 2.

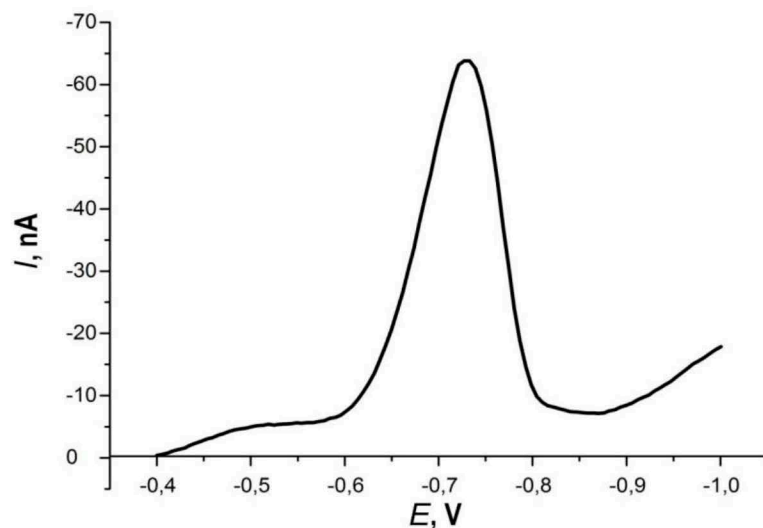


Fig. 2. Differential pulse polarogram of FH after oxidation by hydrogenperoxomonosulfate. 10 ml of 0.02 M hydrochloric acid solution; $C(\text{KHSO}_5) \approx 0.02 \text{ mg / ml}$, $C(\text{Fluphenazine}) = 2.3 \mu\text{g / ml}$, scan speed: 0.1 V / s, pulse amplitude: 0.06 V, pulse time: 0.007 s, $E_p = -0.73 \text{ V}$

The resulting calibration graph looked like:
 $I = (2.57 \pm 0.02) \cdot 10^4 c + (1.38 \pm 0.27)$ (Fig. 3).

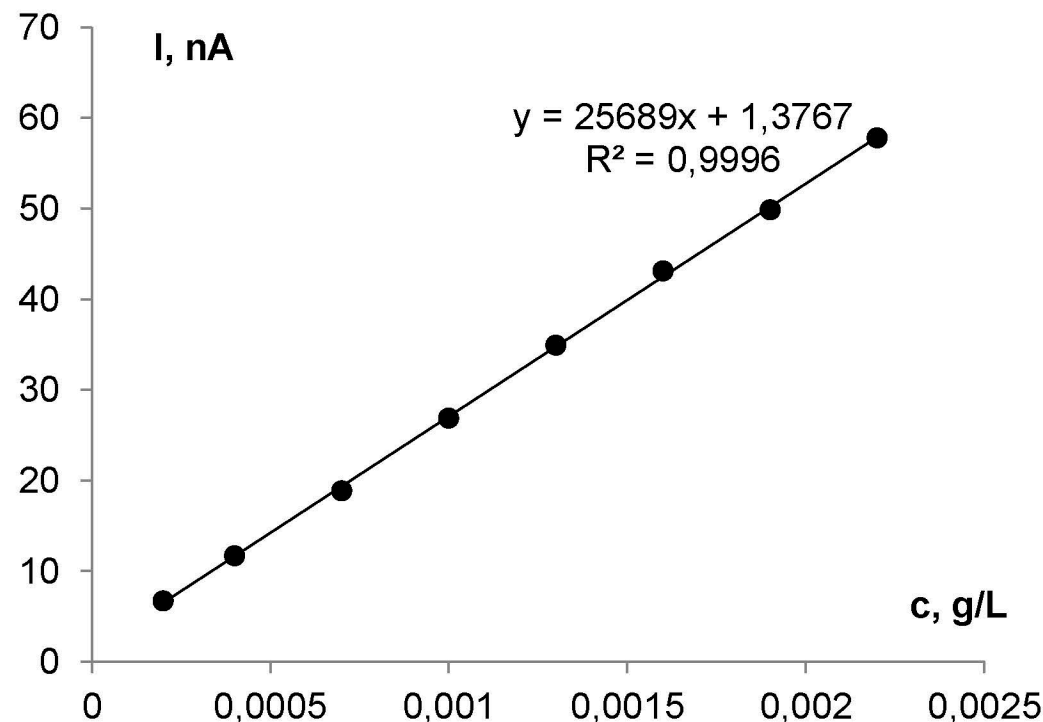


Fig. 3. Dependence of current electrochemical reduction of the oxidation product of Flufenazine on the concentration of Flufenazine

According to the calibration graph, the limit of detection (LOD) and LOQ were calculated; they were 0.03 $\mu\text{g/ml}$ and 0.1 $\mu\text{g/ml}$, respectively. The method was applied to the determination of FH in tablet, 5 mg, manufactured by Mediphar Laboratories (Dbayeh - Lebanon); RSD was 1.7-1.8 % ($\delta^* = -1.2 \dots - 0.2\%$) (Tabl. 1). (μ - Certificate data).

Tabl. 1 The results of quantitative determination of fluphenazine in tablets

Taken for analysis	Content found Fluphenazine hydrochloride,%	Metrological characteristics, P = 0.95
0.6455 g of powder tablets Fluphenazine HCl, Mediphar Laboratories (Dbayeh - Lebanon) (dilution 200)	4,80 4,94 5,00 4,95 5,02	$\bar{X} = 4.94$ $S_{\bar{x}} = 0.0385$ $\Delta\bar{x} = 0.107$ RSD = 1.74% $(\bar{X} - \mu)100\%/\mu = -1.2\%$
0.6455 g of powder tablets Fluphenazine HCl, Mediphar Laboratories (Dbayeh - Lebanon) (dilution 100)	5,02 4,94 5,02 4,87 5,10	$\bar{X} = 4.99$ $S_{\bar{x}} = 0.039$ $\Delta\bar{x} = 0.109$ RSD = 1.76% $(\bar{X} - \mu)100\%/\mu = -0.2\%$

The calculation was performed according to the average content found by the method of USP 39 (4.93 mg / tablet).

References

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