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Indirect Determination of Chlorpromazine Hydrochloride by Square Wave Voltammetry of Sodium Nitroprusside: Application to Pharmaceutical Formulations

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ABSTRACT

An indirect voltammetric method was developed for the determination of chlorpromazine hydrochloride (CPZ) via square wave voltammetric behavior of sodium nitroprusside (SNP) which gives a well-defined square wave voltammetric peak at (-0.589)V against the reference electrode (Ag/AgCl/Sat KCl). The addition of CPZ leads to the decrease of the reduction peak of SNP due to the interaction of SNP with CPZ. The decrease in the peak current (ΔI_p) was found to be linear and related to the concentration of CPZ within the range of concentration $[(0.490\times10^{-6})-(9.77\times10^{-6})]$ M with a correlation coefficient of (0.9948). The method had been successfully applied to determine the CPZ in a pure form and in pharmaceutical formulations.

Keywords: Chlorpromazine hydrochloride; Sodium nitroprusside; Square wave voltammetry.

التقدير غير المباشر للكلوربرومازين بواسطة فولتامتري الموجة المربعة لنيتروبروسيد الصوديوم: تطبيق الطريقة على المستحضرات الصيدلانية

الملخص

تم تطوير طريقة فولتامترية غير مباشرة لتقدير الكلوربرومازين عن طريق دراسة السلوك الفولتامتري لنيتروبروسيد الصوديوم (SNP). إذ لوحظ أن نيتروبروسيد الصوديوم أعطى موجة اختزال واضحة وجيدة عند الجهد (-0.589) فولت ضد قطب المرجع (Ag/AgCl/Sat KCl). ولوحظ عند إضافة الكلوربرومازين حدوث نقصان في تيار اختزال نيتروبروسيد الصوديوم نتيجة لحدوث تداخل بين نيتروبروسيد الصوديوم والكلوربرومازين. تمت دراسة العلاقة بين انخفاض التيار (ΔI_p) وتركيز الكلوربرومازين المضاف وتبين أنها خطية ضمن مدى التراكيز $[(0.490\times10^{-6})-(9.77\times10^{-6})]$ مولاري وكانت قيمة معامل الارتباط (0.9948). وقد طبقت هذه الطريقة بنجاح لتقدير الكلوربرومازين بشكله الحر وفي مستحضراته الصيدلانية.

الكلمات الدالة: الكلوربرومازين، نيتروبروسيد الصوديوم، فولتامتري الموجة المربعة.

INTRODUCTION

Sodium nitroprusside is an inorganic compound with the formula $Na_2[Fe(CN)_5NO]$. $2H_2O$. This red coloured salt, which is often abbreviated as SNP, is a potent vasodilator. This sodium salt is soluble in water and to a lesser extent in ethanol to give solutions containing the dianion $[Fe(CN)_5NO]^{2-}$ (Butler and Megson, 2002).

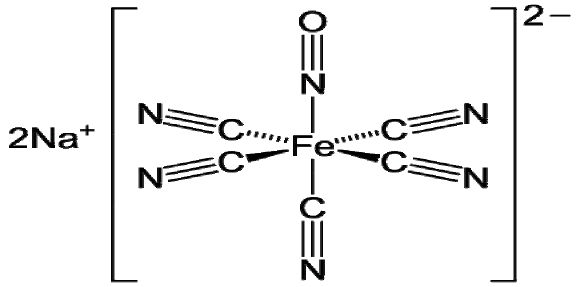

Fig. 1: The chemical structure of sodium nitroprusside, M.wt.=298 g/mole.

Chlorpromazine hydrochloride (CPZ), has the IUPAC name [3-(2-chloro-10H-phenothiazine-9-yl)-N,N-dimethyl-propan-1-amine] as shown in Fig. (2) (Healy, 2004).

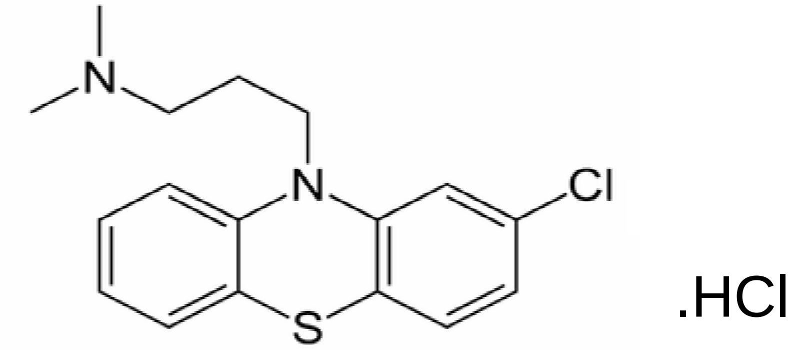

Fig. 2: The structural formula of Chlorpromazine hydrochloride, M.wt.= 355.33 g/mole.

CPZ is a typical antipsychotic and it was synthesized in 1950. CPZ was the first drug developed with specific antipsychotic action, and would serve as the prototype for the phenothiazine class of drugs, which later grow to comprise several other agents.

CPZ works on a variety of receptors in the central nervous system, producing anticholinergic, antidopaminergic, antihistaminic, and weak antiadrenergic effects. (Diaz, 1997).

Several methods have been described for the determination of CPZ including high-performance liquid chromatography procedures coupled with different types of detectors [fluorescence (Butterfield *et al.*, 1980), ultraviolet (Stevenson and Reid, 1981), (Rukadze *et al.*, 1999) and electrochemical detection (Murakami *et al.*,1982)].

A novel spectrophotometric method has been established to determine CPZ using potassium ferricyanide. The method has been successfully applied to determine CPZ in pharmaceutical and serum samples (Li-tao *et al.*, 2011).

CPZ was also determined by a spectrophotometric method which is based on the oxidative coupling ability of 3-methylbenzothiazolinone-2-hydrazone [MBTH] with the drug in presence of $FeCl_3$ under acidic condition. The proposed method has been successfully applied to routine pharmaceutical analysis of the sited drug (Vijay Raju *et al*., 2011).

An original, simple and sensitive flow-injection spectroelectoranalytical method has been described for the determination of CPZ in a pure form or in pharmaceutical formulations (Daniel and Gutz, 2005).

The electrochemical behaviour of CPZ in sulphuric acid was investigated voltammetrically using rethenium electrodes and it was subsequently determined by the same method. The proposed voltammetric method was applied to the determination of CPZ in tablets (Dermis and Biryol, 1989).

CPZ and promethazine were also determined by differential pulse stripping voltammetry using glassy carbon electrode in Britton-Robinson buffer of pH=9. The proposed method was applied to determine these two drugs in a set of synthetic mixtures and blood samples (Ni *et al*., 2001).

Carbon paste electrode has been developed for the potentiometric determination of CPZ Drug focused on the fabrication of carbon paste ion selective electrode for determination of the drug under investigation using potentiometric titration with sodium tetra phenyl borate (Frag *et al*., 2012).

The present work involves an indirect method for determination of CPZ through the square wave voltammetric behavior of SNP.

EXPERIMENTAL

Apparatus

Voltammetric measurements were carried out using a metrohm instrument, model 797 VA, computerized with stand three – electrodes containing an HMDE as a working electrode, an (Ag/AgCl-Sat KCl) as reference electrode and a platinum wire as an auxiliary electrode. The pH of the solutions was controlled with a (HANA) pH meter.

Reagents

All of the chemicals used were of analytical-reagent grade. The supporting electrolyte used for all experiments was phosphate buffer which was prepared by mixing certain volumes of (0.2) M of each of K_2HPO_4 and KH_2PO_4.

A Sodium nitroprusside solution (1.0×10^{-3} M) was freshly prepared by dissolving (0.00298) g SNP (Fluka) and the volume was completed to 10 ml in a volummetric flask.

A Chlorpromazine hydrochloride solution (1.0×10^{-3} M) was freshly prepared by dissolving (0.00355) g CPZ (NDI-Iraq) in distilled water and the volume was completed to 10 ml in a volummetric flask.

Chlorpromazine hydrochloride tablet solution

The tablet was obtained from (SDI). Ten tablets of CPZ labelled with amount of (50) mg per tablet were completely grounded and homogenized. (0.02414) g of the powder was accurately weighed and dissolved in 10 ml of distilled water. After the mixing was completed, the mixture was filtered with an ordinary filter paper and the clear filtrate was used for the determination.

Procedure

The square wave voltamogram was recorded for the sample using a cell containing (10)ml of phosphate buffer at pH=7.0 at optimum conditions [Table 1] to obtain the blank current. Then 150 ml of (14.77×10^{-6})M of SNP was added and the voltamogram was then recorded to give the Ip of SNP, then an appropriate amount of (10^{-4})M of CPZ was added to the cell and the voltamogram was recorded to determine the CPZ in pure and in tablets.

RESULTS AND DISCUSSION

Typical square wave voltamogram of (9.9×10^{-6}) M SNP in phosphate buffer at pH=7.0 is shown in Fig. 3.

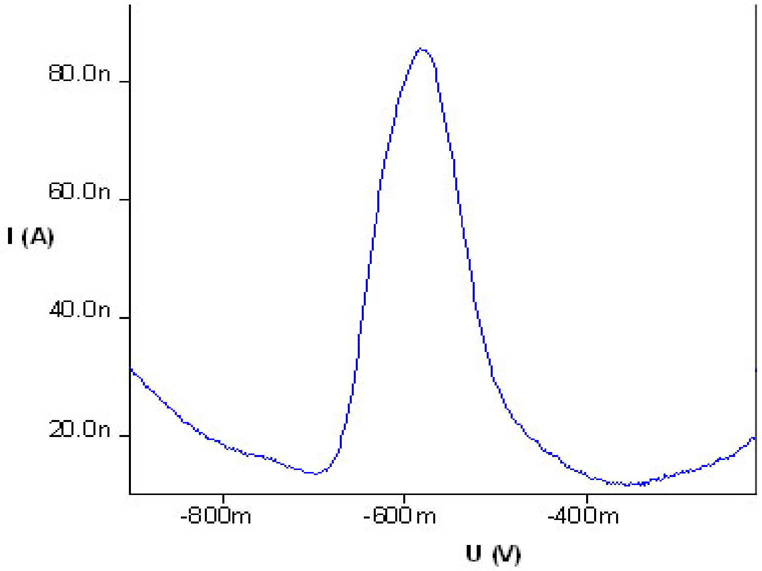

Fig. 3: Square wave voltamogram of (9.9×10^{-6})M SNP at (pH=7.0)

It can be seen from Fig. 3, that SNP showed a well-defined peak which is appeared at (-0.589)V versus (Ag/AgCl, Sat KCl) electrode.

Optimum Conditions

The square wave voltamogram of (9.9×10^{-6})M of SNP was investigated in phosphate buffer (pH=7.0) by variation of all the parameters of the measurements, the optimum values obtained are tabulated in Table (1).

Table 1: The optimum values obtained which give either the highest peak current or the best resolution of the peak

Condition	Value	Condition	value
Initial pot.	-0.1 V	Frequency	50 Hz
Final pot.	-0.9 V	Equilibration time	50 s
Voltage step	0.002 V	Deposition time	60 s
Amplitude	0.04 V	Deposition potential	-0.9 V

Effects of pH

The square wave voltamogram of (14.77×10^{-6}) M of SNP was investigated at different pH values (3 – 9) using the optimum conditions (Table 1) in phosphate buffer. The peak current (Ip) and the peak potential (Ep) obtained are shown in (Table 2).

Table 2: Effect of pH on SWV peak potential and peak current of (14.77×10^{-6}) M of SNP

pH	Ep (V)	Ip(nA)
3	-0.370	53.9
5	-0.470	128.5
7	-0.591	140.5
9	-0.701	110.44

The peak current (Ip) is clearly dependent on pH. A maximum current response was found at (pH=7.0). On the other hand, the peak potential (Ep) is found to be greatly dependent on pH and moves to more negative values with increasing the pH values. Linear plot of Ep versus pH was obtained in (Fig. 4) with a slope (-0.0560)V/pH and (R=0.9988) which is very near to the theoretical value obtained by Hammett (0.059) V/pH (Hammett, 1940).

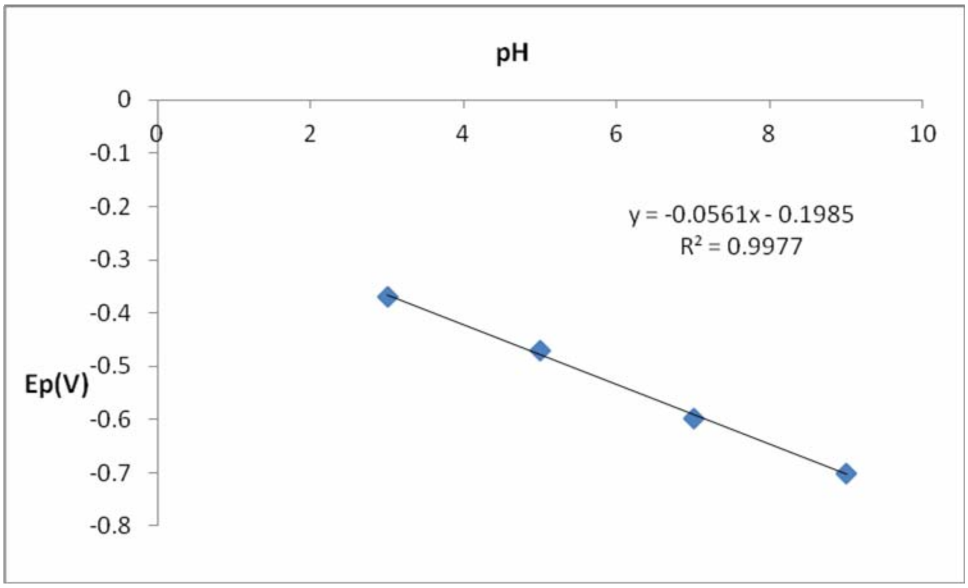

Fig. 4: The relation between Ep and pH of (14.77×10^{-6})M of SNP

Stability of SNP in aqueous phosphate buffer at (pH 7.0)

The square wave voltamogram of (14.77×10^{-6})M of SNP was recorded at different times in phosphate buffer at (pH=7). The results obtained are tabulated in (Table 3).

Table 3: Effect of time on SWV peak of (14.77×10^{-6}) of SNP at pH=7.0 in aqueous solution

Time (min)	Ip (nA)
5	163
10	159
15	134
20	157
25	142
30	144
35	143
40	157
45	150
50	150
55	151
60	157

It can be seen from (Table 3) that SNP is stable for 60 minutes.

Analytical considerations

Using the optimum conditions shown in (Table 1), the calibration curve was constructed using a serial dilution of the standard SNP (10^{-3})M in aqueous – phosphate buffer (pH=7.0)(10 ml).The results are listed in (Table 4).

Table 4:The effect of concentration on the peak current of (0.99×10^{-6}) – (38.46×10^{-6}) M of SNP at (pH=7.0) in aqueous solution at Ep=-0.591 V

Conc. (M),$\times10^{-6}$	Ip (nA)
0.999	14
1.990	28
2.991	41
3.980	55.8
4.975	70.5
5.964	86.2
6.951	103
7.936	115
8.919	130
9.900	144
14.778	183
19.608	199
24.390	221
29.126	240
33.816	268
38.462	288

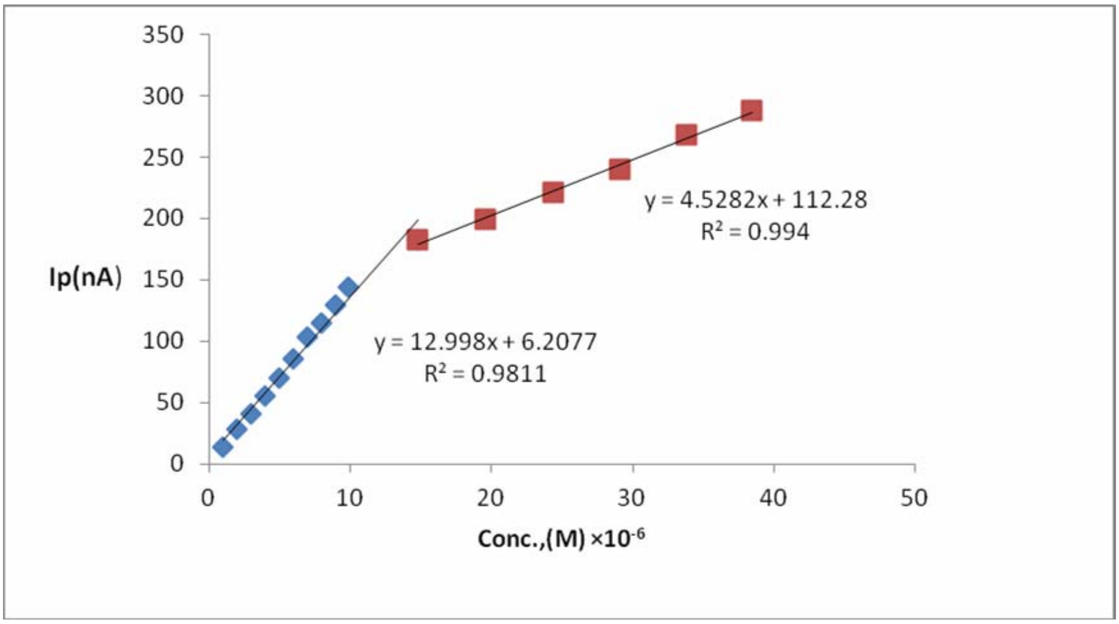

Fig. 5: The relation between peak current (Ip) and concentration of SNP at (pH=7.0) in phosphate buffer

The plot of peak current Ip versus molar concentration of SNP is shown in Fig.(5). Regression analysis on standard SNP indicated two straight lines, the first one with a concentration range of [(0.99×10^{-6})–(14.77×10^{-6})] M, with a correlation coefficient of (R=0.9905). The second with the concentration range [(14.77×10^{-6})-(38.462×10^{-6})] M with correlation coefficient of (R=0.9970). This behavior may be due to the change of the rate of diffusion with concentration and increased gradually by increasing concentration. It is well-known that the rate of reduction depends mainly on the rate of diffusion (Willard *et al*., 1974). The lowest experimental determination limit was (0.99×10^{-6}) M.

The calibration curve of CPZ in the presence of SNP

The square wave voltamogram of (14.77×10^{-6}) M of SNP in phosphate buffer at (pH=7.0) was recorded, successive amounts of CPZ were then added and the SW voltamogram was recorded after each addition. The results are shown in (Table 5). The peak current Ip of SNP was found to be decreased gradually with the addition of CPZ. This behavior is due to the interaction of SNP with CPZ. The plot of ($\Delta I_{pcorr.}$) versus concentration of the CPZ added is shown in (Fig. 6), where the Ip_o=156 nA represents the peak current of SNP only.

Table 5: The peak current of CPZ (0.490×10^{-6}) – (9.777×10^{-6}) in the presence of (14.77×10^{-6}) M of SNP in phosphate buffer (pH=7.0)

Conc. (M),$\times10^{-6}$	I_p (nA)	$\Delta I_{pcorr.}$ (nA)
0.490	154	15.38
0.975	153	16.38
1.456	147	22.38
1.932	141	28.38
2.403	138	31.38
2.870	133	36.38
3.791	121	48.38
4.694	103.6	65.78
5.581	84.4	84.98
6.451	69.3	100.08
7.305	55.1	114.28
8.144	46.8	122.88
8.968	35.5	133.88
9.777	28.6	140.78

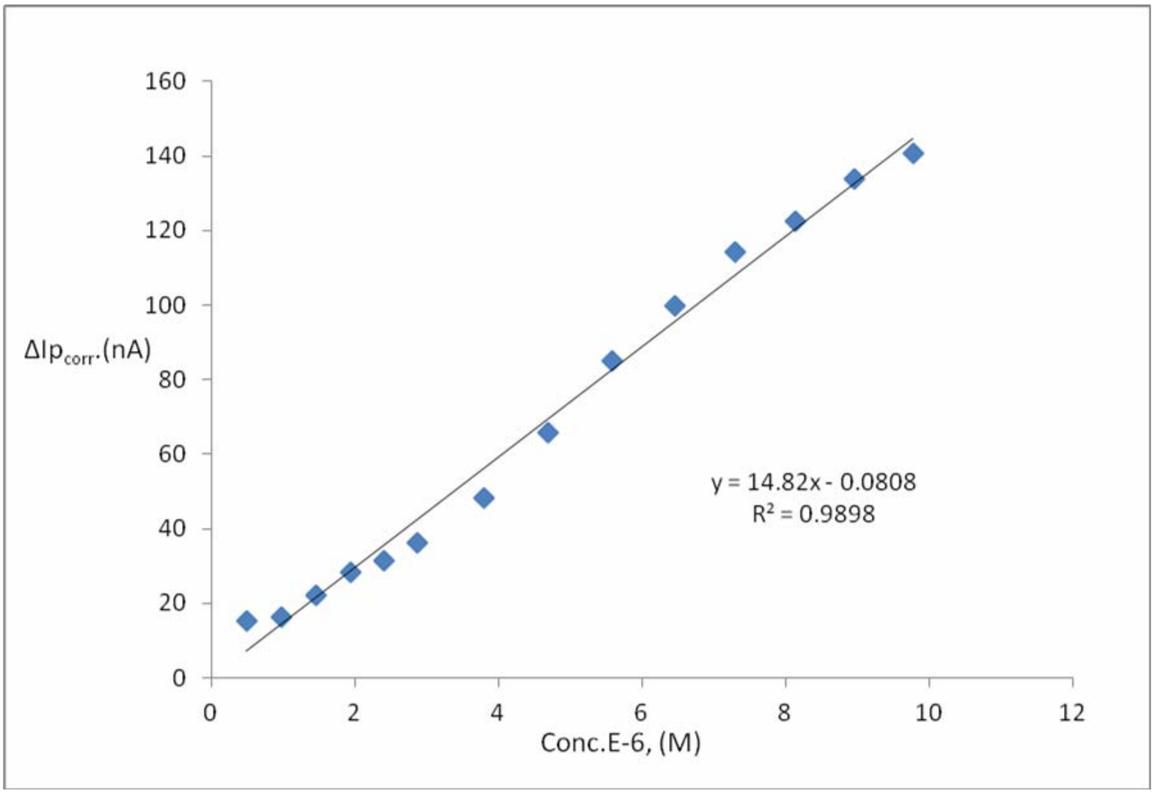

Fig. 6: The plot of $\Delta I_{Pcorr.}$ versus the concentration of CPZ at (pH=7.0) phosphate buffer

Application of SWV of SNP to determine the concentration CPZ in tablet:

Using the optimum conditions in (Table 1), this method was successfully applied to determine the concentration of CPZ in tablets and to calculate the recovery of the drug. The results are tabulated in (Table 6).

Table 6 : The results of the CPZ in tablet

Taken Conc. (M) $\times10^{-6}$	Found Conc. (M) $\times10^{-6}$	Recovery %	Error	ΔI_p (nA)
1.932	1.917	99.212	0.787	12.60
2.870	2.847	99.183	0.816	34.02
5.140	5.105	99.330	0.669	72.66
6.018	5.969	99.193	0.807	84.81
8.144	8.264	101.466	-1.466	104.51
8.968	9.184	102.410	-2.410	112.60

Comparison between the methods:

A comparison between the present method and the British pharmacopoeia standard method (British Pharmacopoeia, 2007) for the determination of CPZ in tablets showed that there is an ability to use the present method to determine the concentration of CPZ in pharmaceutical preparation. The results are shown in (Table 7).

Table 7: Comparison between the present method and the British pharmacopoeia standard method

Drug	Recovery %	
Largactil (50mg) (NDI)	Present method	British pharmacopoeia method
	102.410	106.00

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