Using The Interaction of Sodium Nitroprusside With Modecate And Tegretol, As an Indirect Method For Their Determination Using S.W.V. Technique

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الملخص

تم ت دراسة الخواص الفولتامترية لنيتروبروسيد الصوديوم (Sodium Nitroprusside) النقي بطريقة مباشرة في محلول الفوسفات المائي المنظم (pH=7.0)(10ml) باستخدام تقنية فولتامتري الموجة المربعة (S.W.V) إذ أظهر موجة اختزال واضحة عند الجهد (-0.592) فولت ضد قطب ا لمرجع (Ag/AgCl/SatKCl)، وتم ايجاد المنحنى القياسي لنيترو بروسيد الصوديوم اذ كانت العلاقة خطية ضمن مدى التركيز [(0.99×10^{-7})-(14.77×10^{-7})] مولاري وكانت قيمة معامل الارتباط (0.9985). كذلك تم ايجاد المنحنى القياسي لمحاليل كل من الموديكيت والتكريتول ضمن مدى الت ركيز [(9.84×10^{-11})-(1.360×10^{-9})] مولاري للموديكيت بوجود (14.77×10^{-6}) مولاري من نيتروبروسيد الصوديوم و[(9.89×10^{-11}) -(9.8×10^{-10})] مولاري من التكريتول في وجود (9.9×10^{-6}) مولاري من نيتروبروسيد الصوديوم على التوالي.

تم تطبيق الطريقة للتقدير غير المباشر لكل من الموديكيت والتكريتول كل على انفراد من خلال الترابط بين نيتروبروسيد الصوديوم مع هذه الأدوية.

Abstract

A square wave voltammetric (S.W.V.) method has been developed for the quantitative analysis of sodium nitroprusside (SNP), sodium nitroprusside gives a peak at (-0.592) volt against the reference electrode (Ag/AgCl/sat KCl) in phosphate buffer (pH= 7.0). A calibration curve was constructed for the range [(0.99×10^{-7}-(14.77×10^{-7})]M the method was applied for indirect determination of medicate and tegretol individually via the interaction of SNP with these drugs. So, a calibration curve was constructed by adding appropriate amounts of modecate of the

range [(9.84 x 10^{-11} – 1.360 x 10^{-9})] M in the presence of (14.77 x 10^{-6})M SNP. An other calibration curve was constructed by adding appropriate amounts of tegretol of the range [(9.89 x 10^{-11} – 9.8 x 10^{-10})] M in the presence of (9.9 x 10^{-6})M of SNP.

Key words : S.W.V. Technique, Modecate, Tegretol.

Introduction

Sodium nitroprusside (SNP): Is the chemical compound with the formula [$Na_2(Fe(CN)_5NO).2H_2O$] with achemical structure as shown in Fig. 1.

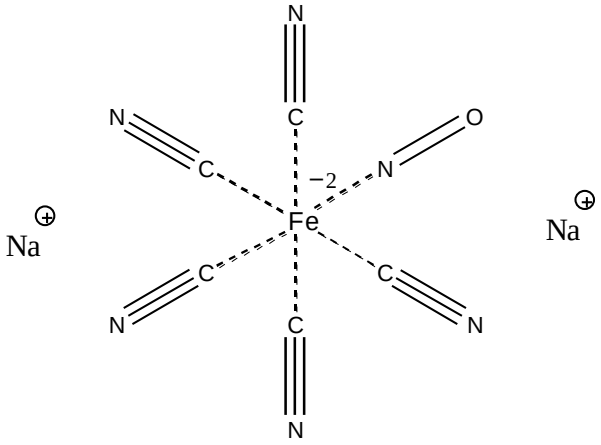

Fig 1: Chemical structure of sodium nitroprusside M. wt = 298 gm/mole

This salt serves as a source of nitric oxide, a potent peripheral vasodilator that affects both arterioles and venules (venules more than arterioles)[(1)]. SNP is often administered intravenously to patient who are experiencing a hypertensive emergency. The principal pharmacological action of SNP is to relax a smooth muscle and consequent dilatation of peripheral arteries. Dilatation of the coronary arteries also occurs[(2)]. This drug can cause very large decreases in blood pressure, serious injury or death could result. Sodium nitroprusside, with larger than the recommended doses, might cause cyanide poisoning[(3,4)]. Several methods are available for measuring SNP. The spectrophotometric method of analysis for SNP developed utilizing the molar absorptivity values at the maxima absorbency appearing in the electronic spectrum at 394 and 498 nm[(5,6)].

Modecate[(7)] (fluophenazine decanoate): it is chemical compound with formula $C_{32}H_{44}F_3N_3O_2S$.

Modecate is a long acting piperazine phenothiazine antipsychotic drug which exhibits a more propensity for procuding extrapyramidal reactions than the group of phenothiazine antipsychotic drugs, and used via injection some times. It may occur less hypertension but less potentiating effect on central nervous system (CNS) depressants, anesthetics sedating than the group of phenothiazien antipsychotic drugs.

Several methods have been reported for the determination of fluphenazine hydrochloride in raw material, phamrmaceutical preparations and biological fluids, such as spectrophotometry[8], spectrofluorometry[8], HPLC and cyclic voltammetry.

These methods were either not sufficiently sensitive, tedious, or required highly sophisticated instrumentation that precluded their use. Therefore, there is still a need for a much more sensitive and simple method for the determination of the studied drugs, especially in biological fluids[8].

Tegretol (carbamazepine): It is anticonvulsant[9] it is used as a treatment of epilepsy and its scientific name is carbamazepine, its formula is $C_{15}H_2N_2O$ = 236.3 gm/ mol .A standard method of the determination of tegretol is GLC (Gas Liquid Chromatography)[10].

The present work involves the use off square wave voltammetric method for trace determination of SNP, and the application of the method for indirect determination of modicate and tegretol individually.

Experimental :

Apparatus:

All experiments were performed using the (797 VA computrace) from metrohm company. A three electrode systems were used. The working electrode was Hanging mercury drop electrode (HMDE); the reference electrode was (Ag/AgCl, Sat KCl electrode) and the counter electrode was a Pt-wire electrode. pH-measurement were made using PW 9421-Philips pH-meter.

Reagents: The chemicals used were obtained from Merck, Roth and Ninavah industry of drugs.

Preparation of 1 x 10^{-3}M of sodium nitroprusside solution was prepared by dissolving a 0.00298 gm of sodium nitroprusside in D.W. then the volume was completed to 10 ml with distilled water using (10 ml) volumetric flask, from this solution other dilutions were made.

Modecate (fluphenazine decanoate)

Modecate solutions (1× 10^{-3}) M: was prepared by dissolving 236 microlitter of the original solution from the ampoul in benzyl alcohol in 10 ml volumetric flask to the mark. other dilutions were made using benzyl alcohol.

Tegretol (carbamazepine) (1× 10^{-3}) M solution was prepared by dissolving 0.0023 gm of the drug in 10 ml volumetric flask then the volume completed to 10 ml with distilled water and from this solution other dilutions were prepared.

Phosphate buffer pH = 7.0 [11]

A weight of 8.7091g of the K_2HPO_4 was dissolved in 250 ml in a volumetric flask to give 0.2M of K_2HPO_4 .

Also a eight of 6.8044096 was dissolved in 250 ml volumetric flask to give 0.2M of of KH_2PO_4 . Then 30.5 ml of 0.2M K2HPO4 + 19.5 ml of 0.2M of KH_2PO_4 and the volume was completed with D.W. to 100ml using a 100ml volumetric flask. This gives phosphate buffer pH= 7.0, and its pH was checked using a pH – meter.

Procedure :

A- The square wave voltammetry mode was used following the optimum conditions: voltage step (0.001) V; Amplitude (0.03); deposition time (10) sec; frequency (20) HZ; equilibrium time (5) Sec. the solution was de-oxygenated by passing through it a slow stream of purified nitrogen gas for 300 seconds to remove the dissolved oxygen. The square wave voltammogram was recorded on a deoxygenated (10 ml) phosphate buffer solution at (pH = 7.0) the blank current was recorded, appropriate amounts of sodium nitroprusside stock solution were add (and altering the time of N_2 gas to 30 second) to yield the desired concentration and the voltage-current was recorded again. The calibration curve was then constructed.

B- For indirect determination of modecate and tegretol the above procedure was followed in phosphate buffer (pH=7.0)(10ml) with presence of ($14.77x10^{-6}$)M. of SNP for modecate experiment and a ($9.9x10^{-6}$)M. of SNP for tegretol experiment then successive amounts of modecate or tegretol were then added and S.W. Voltammogram were recorded again, the decrease in peak current was then plotted versus the concentrations of modecate or tegretol added (calibration curves).

Result and Discussion

Typical square wave voltammogram of ($2.99x10^{-6}$) M SNP in (10ml) phosphate buffer at (pH=7.0) is shown in fig 2.

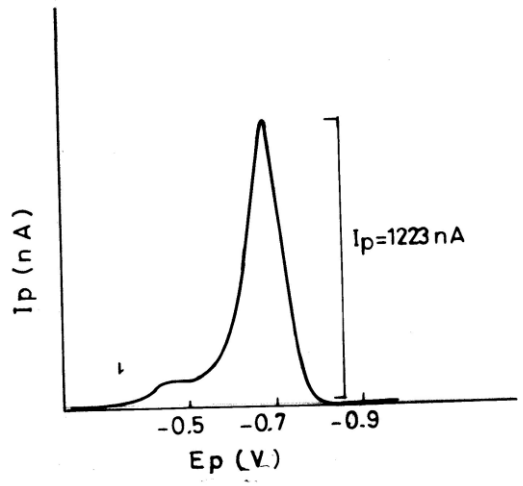

Fig 2 : Square wave voltammogram of ($2.99x10^{-6}$) M SNP.

Fig 2 a well-defined peak appeared at (-0.592 V) versus (Ag /AgCl , Sat KCl) electrode.

Optimum Condition :

The square wave voltammogram of ($2.99x10^{-6}$) M of SNP was investigated in (10ml) phosphate buffer [(pH = 7.0)]. The variations of all parameter that the measurements of the optimum values depend on are tabulated in Table 1.

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

Condition	Value
Initial pot.	**-1.4 V**
Final pot.	**0.02 V**
Deposition time	**10 Sec**
Equilibrium time	**5 Sec**
Frequency	**20 Hz**
Voltage step	**0.001**
Amplitude	**0.03**

Stability time of SNP S.W.V. Peak in aqueous phosphate buffer at (pH = 7.0):

The square wave voltammogram of ($2.99x10^{-6}$) M. of SNP were recorded at different times in phosphate buffer at (pH = 7.0). the results obtained are tabulated in Table 2.

Table 2: Effect of time on SWV peak of ($2.99x10^{-6}$) M of SNP at (pH = 7.0) in aqueous solution.

Time (minute)	Ip (A)	Time (minute)	Ip (A)
3	1.02×10^{-8}	18	1.09×10^{-8}
6	1.04×10^{-8}	21	1.12×10^{-8}
9	1.12×10^{-8}	24	1.15×10^{-8}
12	1.05×10^{-8}	27	1.14×10^{-8}
15	1.18×10^{-8}	30	1.08×10^{-8}

It can be seen from the Table 2 that SNP Peak is stable for more than (30) minute, which is a quite enough for voltammetric measurement.

Analytical Consideration :

Using the optimum condition shown in Table 1, the calibration curve were constructed using a serial dilution of a standared SNP in 10 ml aqueous-phosphate buffer (pH = 7.0). Typical results are listed in Table 3.

Table 3 : Effect of concentration on peak current of [$(0.99*10^{-7}) – (14.77*10^{-7})$] M of SNP at pH=7.0 in aqueous solution at EP = -0.6 V.

Conc. (M) $\times10^{-7}$	Ip (A)
0.99	6.2×10^{-10}
2.99	1.4×10^{-9}
5.96	2.54×10^{-9}
9.9	3.96×10^{-9}
10.88	4.37×10^{-9}
11.85	4.89×10^{-9}
12.83	5.32×10^{-9}
13.8	5.84×10^{-9}
14.77	6.18×10^{-9}
R	0.9985
R^2	0.9971
Slope	0.0040
Intercept	$1.5456\times e^{-10}$

From the Table 3 we can see the values of Ip are increasing with increasing concentration of SNP. A linear correlation between diffusion current Ip with concentration were obtained with a correlation coefficient (R =0.9985) is shown in Fig. 3.

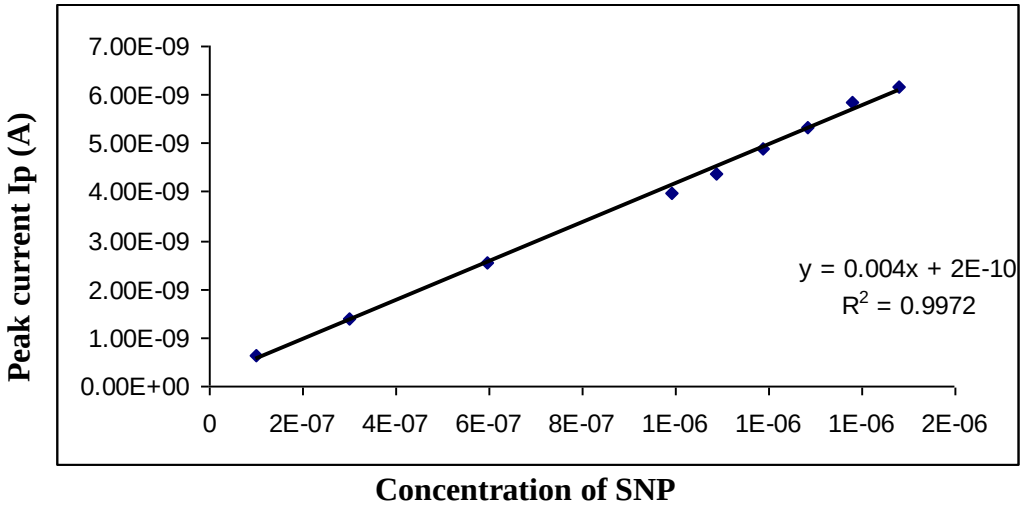

Fig. 3: Calibration curve for SNP in phosphate buffer (pH=7.0)(10ml)

The regression analysis shown on fig.3 indicates a straight line. The lowest experimental Concentration limit is (0.99×10^{-7})M..

Indirect determination of Modecate with SNP:

Using the optimum condition listed in Table 4, the calibration curve was constructed using a serial dilutions of standared Modecate in aqueous-phosphate buffer (pH = 7.0; 10 ml) in the presence (14.77×10^{-6}) M of SNP. Typical result are listed in Table 5.

Table 4 : The optimum values obtained which are either the highest peak current or the best resolution of the Modecate peak.

Condition	Value
Initial pot.	**-1.4 V**
Final pot.	**0.02 V**
Deposition time	**10 Sec**
Equilibrium time	**5 Sec**
Frequency	**25 Hz**
Voltage step	**0.002**
Amplitude	**0.03**

Table 5 : The peak current of (9.84×10^{-11}) - (1.168×10^{-9}) M of Modecate in the presence of (14.77×10^{-6}) M of SNP

Conc. (M)	Ip (A) of Modecate	Ip (A) of SNP
9.84252E-11	2.22E-09	6.67E-08
1.96657E-10	1.97E-08	6.64E-08
2.94695E-10	2.31E-08	6.62E-08
3.92542E-10	3.85E-08	6.59E-08
5.87659E-10	4.33E-08	6.36E-08
7.82014E-10	7.50E-08	6.18E-08
9.7561E-10	1.10E-07	5.49E-08
1.16845E-09	1.41E-07	4.80E-08
1.36054E-09	1.78E-07	4.00E-08
9.84252E-11	2.22E-09	6.67E-08
1.96657E-10	1.97E-08	6.64E-08
2.94695E-10	2.31E-08	6.62E-08
3.92542E-10	3.85E-08	6.59E-08
5.87659E-10	4.33E-08	6.36E-08
7.82014E-10	7.50E-08	6.18E-08
9.7561E-10	1.10E-07	5.49E-08
1.16845E-09	1.41E-07	4.80E-08
1.36054E-09	1.78E-07	4.00E-08

It can be seen from the results in table (5) the increase of diffusion current (Ip) with increasing concentration of modecate with a decreases of diffusion current of SNP which indicates that there is a binding between the two drugs. The relation of diffusion current (Ip) and concentration of modecate and SNP are shown in figures (4,5).

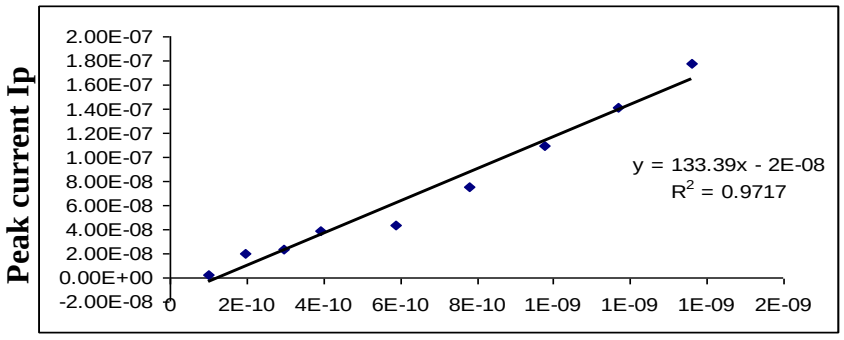

Fig. 4 : Calibration curve using peak current Ip of modecate and concentration of modecate at (pH=7.0) phosphate buffer in aqueous solution

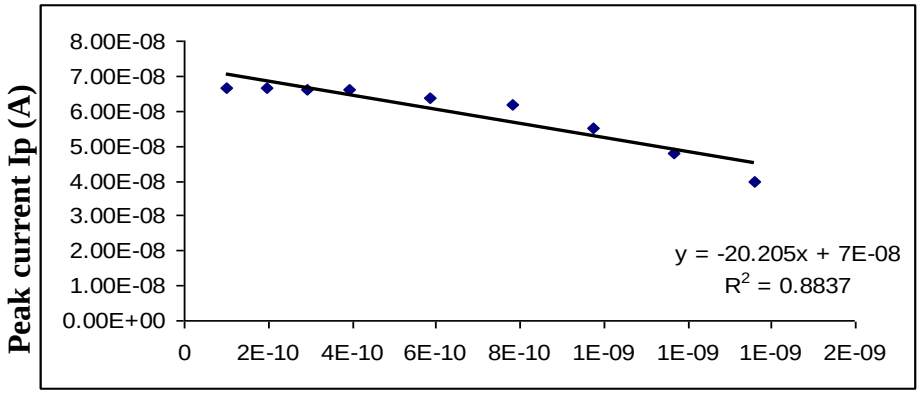

Fig. 5 : Calibration curve using peak current Ip of SNP and concentration of modecate at (pH=7.0) phosphate buffer in aqueous solution

Indirect determination of Tegretol with SNP:

Using the optimum condition listed in Table 6, the calibration curve was constructed using a serial dilutions of a standard tegretol in aqueous-phosphate buffer (pH = 7.0; 10 ml) in the presence (9.9×10^{-6}) M of SNP. Typical results are listed in Table 7.

Table 6 : The optimum values obtained which give either the highest peak current or the best resolution of the Tegretol peak.

Condition	Value
Initial pot.	**-1.4 V**
Final pot.	**0.02 V**
Deposition time	**60 Sec**
Equilibrium time	**5 Sec**
Frequency	**50 Hz**
Voltage step	**0.006**
Amplitude	**0.02**

Table 7 : The peak current of [(9.89×10^{-11})-(9.8×10^{-10})] M of Tegretol in the presence of (9.9×10^{-6}) M of SNP.

Conc (M)	Ip (A) of Tegretol	Ip (A) of SNP
9.8912E-11	9.93E-08	1.44E-07
1.97628E-10	1.44E-07	1.19E-07
2.9615E-10	3.98E-07	9.29E-08
3.94477E-10	7.11E-07	9.12E-08
4.92611E-10	1.28E-06	5.04E-08
5.90551E-10	1.74E-06	3.75E-08
6.88299E-10	2.00E-06	2.61E-08
7.85855E-10	2.32E-06	2.41E-08
9.80392E-10	3.34E-06	9.50E-09
9.8912E-11	9.93E-08	1.44E-07
1.97628E-10	1.44E-07	1.19E-07

2.9615E-10	3.98E-07	9.29E-08
3.94477E-10	7.11E-07	9.12E-08
4.92611E-10	1.28E-06	5.04E-08
5.90551E-10	1.74E-06	3.75E-08
6.88299E-10	2.00E-06	2.61E-08
7.85855E-10	2.32E-06	2.41E-08
9.80392E-10	3.34E-06	9.50E-09

It can be seen from the results in table (7) the increase of diffusion current (Ip) of tegretol with increasing concentration of Tegretol with decreases of diffusion current of SNP which indicate that there is a binding between the two drugs. The relation of diffusion current (Ip) of tergetol and SNP concentration are shown in figures (6,7).

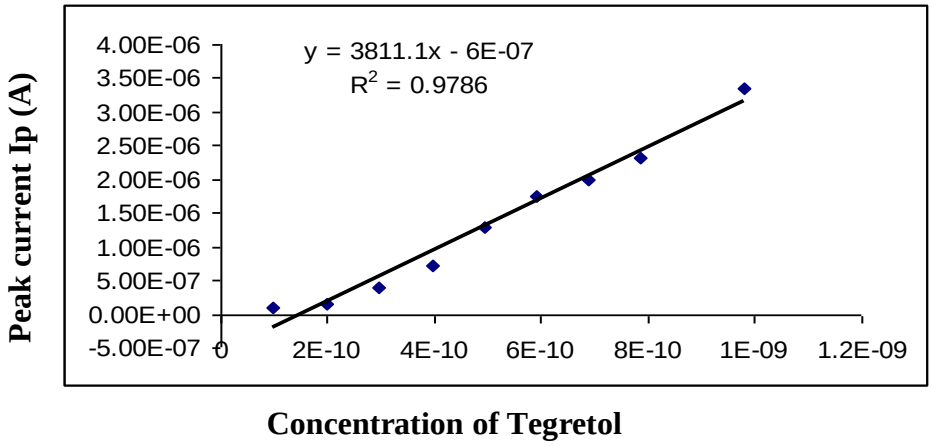

Fig. 6 : Calibration curve using peak current Ip and concentration of Tegretol at [(pH=7.0) (10ml)] phosphate buffer in aqueous solution.

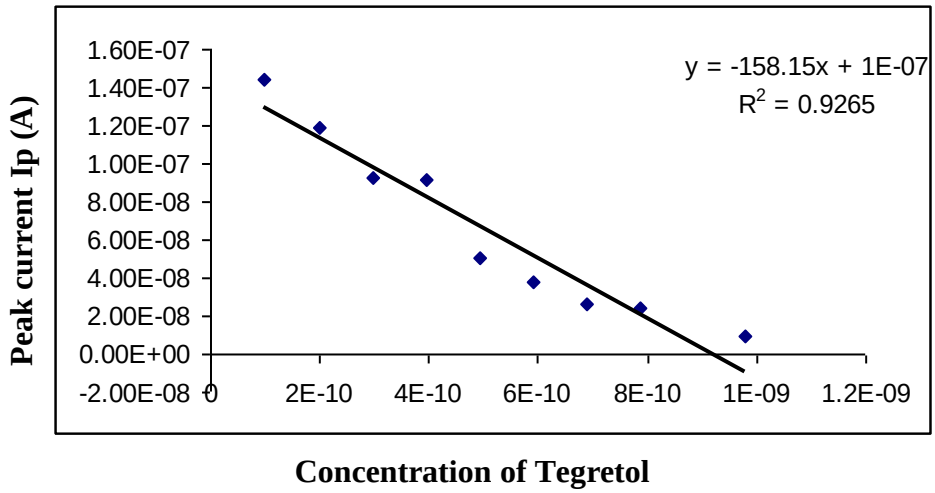

Fig. 7 : Calibration curve using peak current of SNP and concentration of Tegretol at [(pH=7.0) (10ml)] phosphate buffer in aqueous solution

Concussion

It is concluded that the S.W.V. technique can be used as indirect method for determination of drugs via the interaction between the drugs so from the decrease in the (Ip) of the drug which interact with the drug under test. The concentration of the drug under test can be determined.

From the advantages of the methode is the:

1. High speed and
2. The good sensitivity of the methode

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