Voltammetric determination of Modecate using Square wave voltammetry (S.W.V.) technique: Application to blood serum and urine of schizophrenic patients

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Abstract:

The direct voltammetric determination of Modecate was studied using square wave Voltammetry. Modecate gives a well defined reduction peak at (-1.23) volt versus the reference electrode (Ag/AgCl/Sat.KCl),calibration curve were constructed in phosphate buffer (pH=7.0), in diluted human serum and normal urine, the plots of peak current versus concentration were linear within the concentration range [(9.99×10^{-8})– (9.90×10^{-7})] M , [(2.98×10^{-7}) – (9.87×10^{-7})] M and [(9.94×10^{-8}) – (1.17×10^{-6})] M. The correlation coefficient were (0.9849) , (0.9965) and (0.9895) respectively. The method was successfully applied to determine Modecate in blood Sera and urine of Schizophrenic patients.

التقدير الفولتامتري للموديكيت باستعمال تقنية فولتامتري الموجة المربعة (S.W.V.)، تم التطبيق على مصل الدم والإدرار لمرضى انفصام الشخصية

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ملخص البحث:

تمت دراسة التقدير الفولتامترية المباشر للموديكيت (Modecate) باستخدام طريقة فولتامتري الموجة المربعة (S.W.V) وقد أظهر الدواء موجة اختزال واضحة عند الجهد (-١.٢٣) فولت ضد قطب المرجع (Ag/AgCl/SatKCl) ، وتمت دراسة المنحنى القياسي

للدواء باستخدام محلول الفوسفات المنظم ذي الرقم الهيدروجيني ($pH=7.0$)، وبوجود مصل الدم البشري، وكذلك بوجود الإدرار وعند رسم العلاقة بين التيار والتركيز أعطت المنحنيات خطوط مستقيمة ضمن مديات التراكيز[(9.90×10^{-7})– (9.99×10^{-8})] مولاري ، [(2.98×10^{-7}) – (9.87×10^{-7})] مولاري و [(1.17×10^{-6}) – (9.94×10^{-8})] مولاري وبمعاملات ارتباط (0.9849) ، (٠.٩٩٦٥) و (٠.٩٨٩٥) بالتعاقب، وطبقت الطريقة بنجاح لتقدير الدواء في مصل الدم والإدرار لمرضى انفصام الشخصية.

Introduction

Modecate , its scientific name is (fluphenazine decanoate), is a chemical compound with the formula ($C_{32}H_{44}F_3N_3O_2S$) , with the structure as shown in Fig.1.

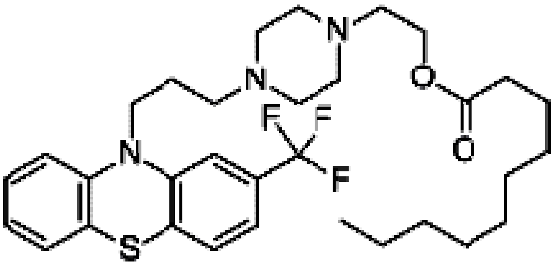

Fig. 1.Chemical structure of Modecate

Modecate is a long-acting piperazine phenothiazine antipsychotic drug which exhibits a more propensity for producing extra pyramidal reactions than the group of phenothiazine antipsychotic drugs, and used via injection sometimes. It may cause less hypertension but less potentiating effect on Central nervous system (CNS) depressants, anesthetics sedating than the group of phenothiazine antipsychotic drugs (1-3).

It helps to correct chemical imbalances in the brain, which may cause mental illness. Modecate is used for the treatment of mental illnesses such as schizophrenia. These mental illnesses may cause disturbances in thinking, feelings and behavior. Modecate is not recommended for use in children under the age of 12; save and effectiveness have not been established in this age group(4).

Modecate should not be used by any one who is allergic to fluphenazine decanoate, other phenothiazine medi-prochlorperazine, perphenazine, chlorpromazine; it shouldn't also be used with a patient who is taking large doses of CNS depressant medications such as lorazepam, diazepam, and with a patient who has blood disorders, brain damage or hardening of the arteries in the brain, liver damage, serious heart disease, brain disease or kidney disease (5,6).

Determination of Modecate :

Several methods have been reported for the determination of fluphenazine hydrochloride in raw material, phamrmaceutical preparations and biological fluids, such as spectrophotometry, spectrofluorometry, HPLC and cyclic voltammetry(7,8).

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). The present work involve the use of Square Wave Voltammetric method for trace determination of modecate in different mediums .

Experiment :

Apparatus :

All experiment were performed using the (797 VA computrace) from metrohm company. A three electrode potentiostat was used. The working electrode (HMDE); the reference electrode, (Ag/AgCl/sat.KCl) electrode, and the pt-wire electrode as counter electrode. pH measurements were made using pw 9421- PH-meter.

Reagents :

All chemicals used were analytical reagents grade from Merck and Roth company and used without any further purification, solutions of 1.0×10^{-3} M of modecate was prepared. Benzyl alcohol was used for dilution of solutions required

Phosphate buffer was prepared by mixing 30.5 ml of 0.2 M of K_2HPO_4 and 19.5 ml of 0.2 M of KH_2PO_4 in (100) ml volumetric flask and the volume was completed to the mark by distilled water.

Procedure :

The square wave voltammogram was recorded in (10) ml phosphate buffer (pH =7.0) under the optimum conditions [voltage step (0.002)v/s ; pulse amplitude (0.03) ; deposition time (10) sec ; frequency (25) Hz ; equilibrium time (5) sec] , after passing purified Nitrogen gas for (300) seconds to remove the dissolved oxygen. Then appropriate amounts of modecate stock solution were added to the cell solution and the current-voltage curve was recorded again.

Preparation of Human blood serum:

solution (50) µl of human blood serum were diluted with phosphate buffer (pH=7.0) to (10) ml using volumetric flask, then (25) µl of this solution was added to the cell containing (10) ml of phosphate buffer (pH=7.0) which is nearest to the pH of the human blood serum.

Results and Discussion :

Typical square wave voltammogram of ($5.96x10^{-7}$)M modecate in phosphate buffer at (pH = 7.0) is shown in Fig. 2.

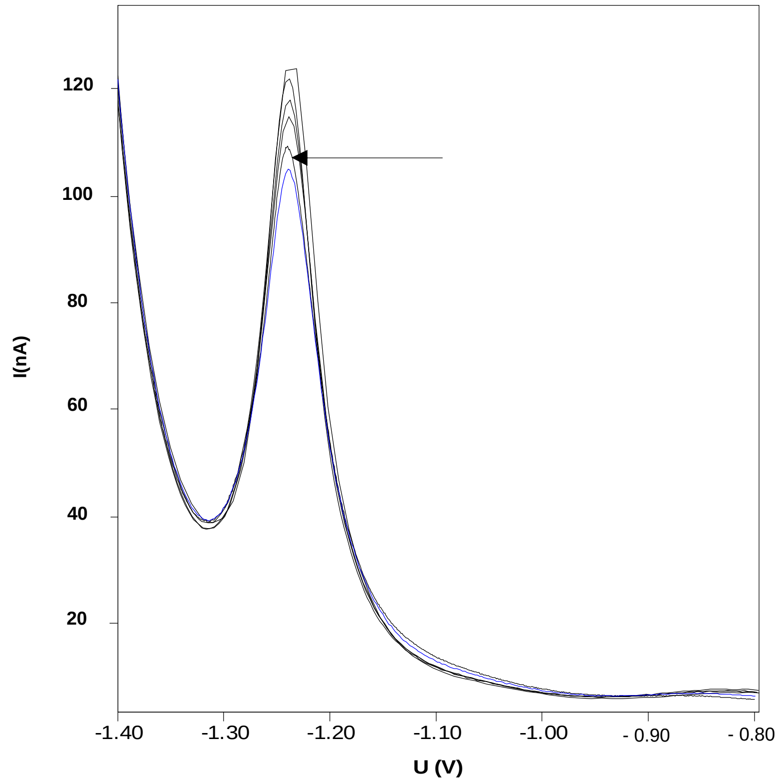

Fig. 2 : Square Wave Voltammogram of ($5.96x10^{-7}$) M Modecate

The Voltamogram (fig.2) shows a well-defined peak appeared at (-1.23)V versus (Ag/AgCl/sat KCl) electrode.

Optimum conditions :

The effect of different parameters such as intial and final potential, deposition time, equilibrium time, Frequency, Voltage step and pulse amplitude were examined using ($5.96x10^{-7}$)M modecate solution, phosphate buffer (pH = 7.0) The results obtained are shown in table 1.

Table 1 : Shows the optimum conditions obtained using S.W.V

Condition	Value	Condition	Value
Initial pot.	-1.4 V	Voltage step	0.002v/s
Final pot.	0.02 V	Pulse amplitude	0.03
Deposition time	10 Sec		
Equilibrium time	5 Sec		
Frequency	25 Hz		

The optimum conditions represent either the highest peak current or the best peak resolution.

Effect of pH :

The effect of pH was investigated using ($5.96x10^{-7}$M) of modecate solution, different pH values (5 – 9) and the voltammograms were recorded under the optimum conditions , the results obtained are shown in table 2.

Table 2 :Effect of pH on the redaction peak current of ($5.96x10^{-7}$)M of modecate.

pH	Ep(V)	Ip(nA)
5	-1.10	9.5
6	-1.15	21.5
7	-1.23	54
8	-1.28	86.9
9	-1.33	180

The peak current Ip is clearly dependant on the pH. Maximum current response were found at pH = 9.0. On the other hand , the peak potential Ep is found to be greatly dependent on pH and shifted to more negative value with increasing pH , As shown in Fig. 3.

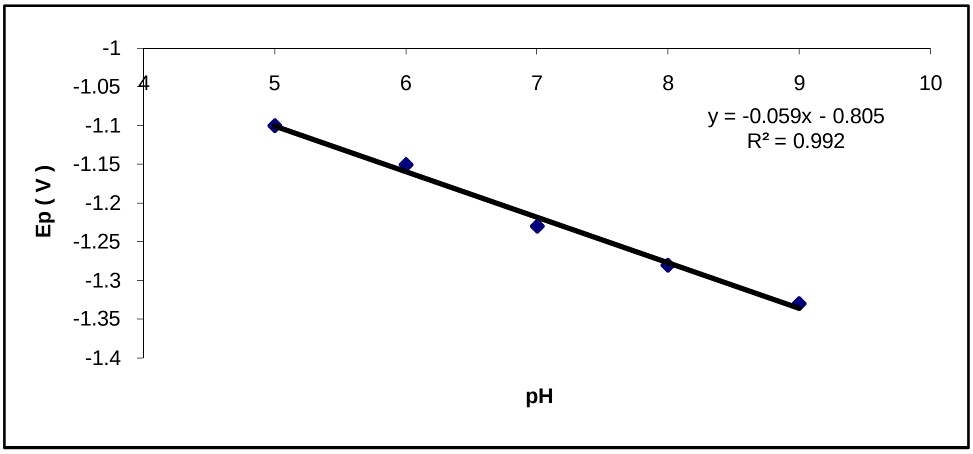

Fig.3. The relation between Ep and pH of ($5.96x10^{-7}$)M of modecate.

The plot of pH versus Ep gives a straight line (Fig.3) with correlation coefficient. (R= 0.9961), the value of slope is very near to theoretical value obtained by Hammett equation which is equal to (-0.059 VpH^{-1}). In this study, we use pH = 7.0 because it is very near to pH of human serum.

Stability of modecate :

The square wave voltamogram of (5.96×10^{-7}) M modecate solution was recorded at different times in phosphate buffer at pH = 7.0. The results obtained are tabulated in Table 3 .

Table 3 : Effect of time on SWV peak of ($5.96x10^{-7}$)M of modecate at pH = 7.0 in aqueous solution.

Time (min)	Ip (nA)	Time (min)	Ip (nA)
1.5	37.2	13.5	37.5
3.0	32.1	15.0	30.5
4.5	30.7	16.5	38.3
6.0	29.5	18.0	36.5
7.5	32.9	19.5	33.8
9.0	32.3	21.0	34.4
10.5	31.6	22.5	33.0
12.0	33.4	24.0	33.8

It can be seen from the Table 3 that modecate is stable for 24 minutes, which is quite enough for carrying the voltammetric measurement.

Analytical consideration :

Using the optimum condition shown in table 1, the calibration curve was constructed using a serial dilution of a standard modecate in aqueous phosphate buffer. Some typical results are listed in Table 4 . These solutions were prepared by adding appropriate aliquots of standard modecate to the voltammetric cell containing 10 ml of phosphate buffer (pH = 7.0) .

Table 4: Effect of concentration on peak current of [(9.9×10^{-8})–(9.9×10^{-7})] M of modecate at pH = 7.0 in aqueous solution at Ep = -1.23 V.

Conc. of comp. 10^{-7} (M)	Ip (nA)
0.9990	2.51
1.9960	27.4
2.9910	37.4
3.9840	48.2
4.9751	79.2
5.9642	106
6.9513	145
7.9365	190
8.9197	219
9.9009	227

The relation of Ip and concentration (Fig.4) is linear with correlation coefficient = 0.9849.

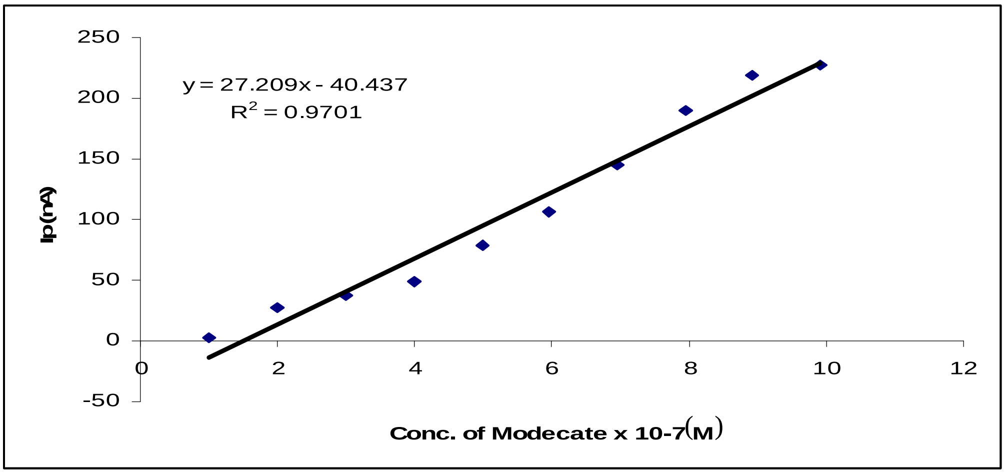

Fig. 4: The relation between peak current IP and concentration of $[(9.9\times10^{-8})–(9.9\times10^{-7})]$ M of modecate at pH = 7.0 phosphate buffer in aqueous solution.

Regression analysis of standards indicated a straight line and lowest experimental detections limit was (9.9×10^{-8}).

Calibration curve of moderate in human serum :

Using the optimum condition shown in table 1, the calibration curve was constructed using phosphate buffer pH = 7.0 and a serial dilution of a standard modecate in the presence of diluted human serum (25)µl. Some typical results are shown in table 5. one redaction peak was observed at Ep = -1.26V.

Table5: Effect of concentration on peak current of $[(2.98\times10^{-7})–(9.87\times10^{-7})]$M of modecate at pH =7.0 in human serum at Ep=-1.26 V

Conc of comp.x10^{-7}	Ip (nA)
2.9835	24.2
3.9741	55.5
4.9627	126
7.9168	340
8.8976	413
9.8765	448

The relation of Ip and concentration (Fig 5) is liner with correlation coefficient (0.9965).

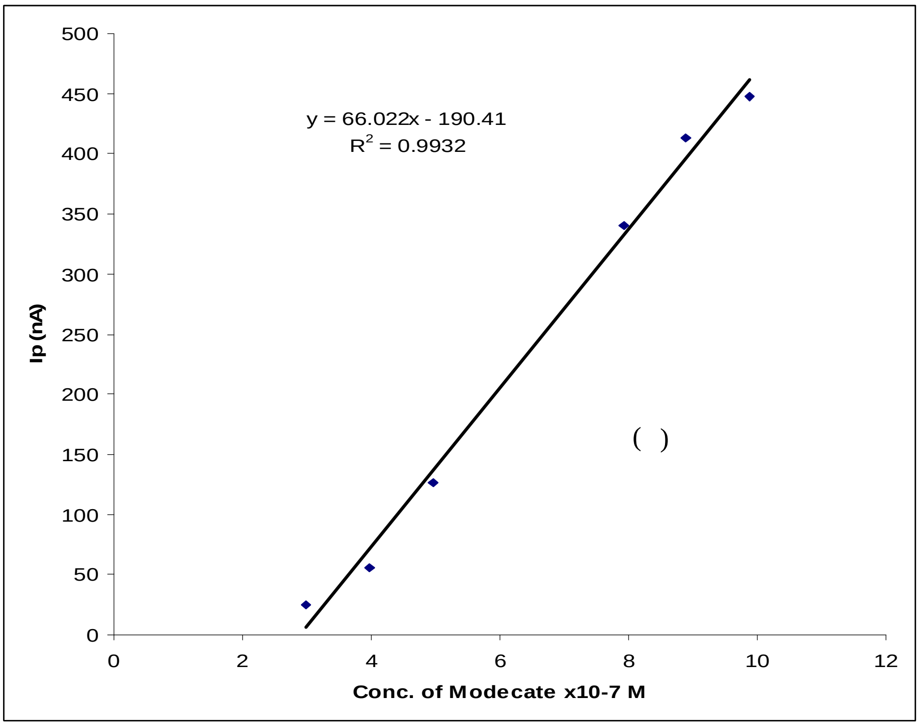

Fig. 5 : The relation between peak current Ip and concentration of [(2.98 × 10^{-7})–(9.87 × 10^{-7})]M modecate at pH=7.0 of phosphate buffer with human serum.

Calibration curve of modecate in urine :

Using the optimum condition shown in Table 1, the calibration curve was constructed using a serial dilution of a standard modecate in urine. Some typical results are listed in Table 6, these solutions were prepared by adding appropriate aliquots of standard modecate to the phosphate buffer 10 ml at pH = 7.0, containing 40 µl urine.

Table 6 : Effect of concentration on peak current of [(9.94 ×10^{-8}) – (1.17 × 10^{-6})] M of modecate at pH = 7.0 in human urine.

Conc of comp.x10^{-7}	Ip (nA)
0.9940	1.49
1.9861	14.5
2.9761	26.6
3.9643	61.4
4.9505	85.5
5.9347	99.0
7.8973	125
9.8522	165
11.7994	179

The relation between diffusion current Ip with concentration (Fig.6) shows straight line with R = 0.9895.

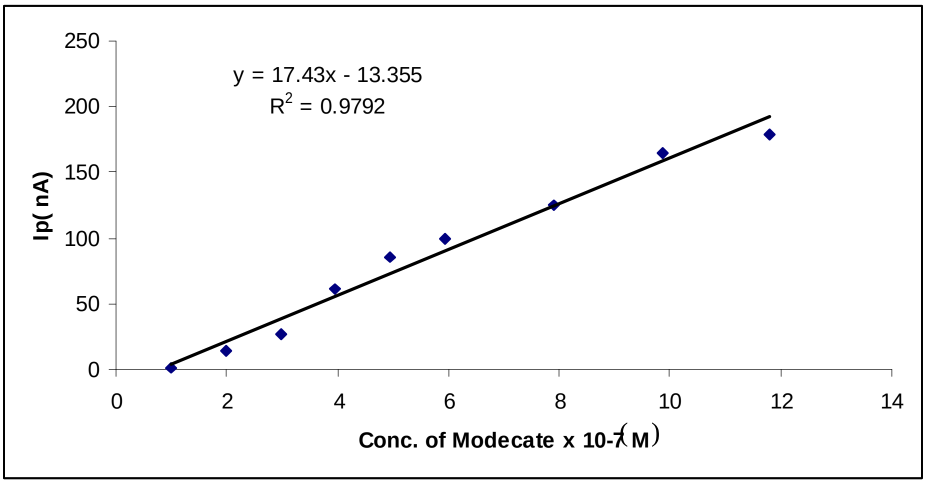

Fig. 6 : The relation between peak current Ip and concentration of [(9.94 × 10^{-8})–(1.17 × 10^{-6})] M of modecate at pH = 7.0 phosphate buffer in human urine.

Applications of proposed method:

a) Determination of Modecate conc. in human serum:

Using the optimum condition in Table 1, the method was successfully applied for determining the drug in diluted human serum. The S.W. voltammogram was recorded using phosphate buffer (pH = 7.0) addition of 10 µl diluted human serum. A standard addition method was used to calculate the concentration of drug in human serum. The results are shown in Table 7.

Table 7 : The results of modecate in human serum.

Sample number	Ip(nA)	Conc.(M)x10^{-8}	Conc. mg/l
1	15.9	0.57	0.003373
2	18.6	0.26	0.001538
3	15.5	0.578	0.003420
4	19.8	0.75	0.004438
5	18.8	0.64	0.003787

b) Determination of modecate concentration in human urine :

Using the optimum condition in Table 1, the method was successfully applied to determine the drug concentration in human urine. The S.W. voltammogram was recorded using phosphate buffer (pH = 7.0) with the addition of 40 µl human urine. A standard addition method was also used to determine the concentration of drug in human urine. The results are tabulated in Table 8.

Table 8 : The results of modecate in human urine.

Number	Ip(nA)	Conc.x10^{-8}(M)	Conc. mg/l
1	13.4	0.805	0.004763
2	26.3	0.490	0.002409
3	16.7	0.847	0.005012

Conclusion

Building on the results, it is concluded that this method can be used successfully to determine the modecate conc. in both human sera and urine of schizophrenic patients. Moreover, the advantages of the proposed method are : simple, fast , and sensitive.

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