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ADSORPTIVE STRIPPING VOLTAMMETRIC PROPERTIES OF FENTANYL AT Hg ELECTRODE

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Summary—Cyclic voltammetry shows that in a supporting electrolyte of NaOH, fentanyl (FENT) has a pair of cathodic and anodic peaks at Hg electrode. The peak potentials, E_{pc} and E_{pa}, are -1.47 and -1.44 V (*vs.* Ag/AgCl), respectively. Fentanyl can be adsorbed on Hg surface, so the cathodic peak shows adsorptive properties. The adsorptive characteristics of fentanyl are explored in detail with various methods. The adsorbed species is considered to be fentanyl neutral molecule. The method for measuring trace amount of fentanyl by adsorptive stripping voltammetry is established. Under the optimised condition, the detection limit may reach $5 \times 10^{-8}M$ with a 10-min preconcentration.

INTRODUCTION

Fentanyl (FENT) is known as a good and effective analgesic drug. Its structure is shown in Fig. 1. It can be easily absorbed by the human body and enters into the blood. Generally, the concentration of fentanyl in urine and blood is low after metabolization. Highly sensitive methods are thus of significance for the determination of fentanyl. Various chromatographic and other procedures have been employed for this purpose.[1] For example, a GC method using nitrogen-selective detection was used for detecting fentanyl in blood plasma[2] and the limit of detection reached 0.07 ng/ml. A HPLC method was employed for determination of fentanyl in a dosage form[3] and the detection limit was 5 μg/ml. However, electrochemistry of fentanyl at Hg electrode has not been reported until now.

The present work reports the electrochemical behaviour, especially the adsorptive properties, of fentanyl at a hanging mercury electrode. Based on the adsorptive accumulation of fentanyl on Hg electrode surface, a sensitive adsorptive stripping voltammetric method for trace measurement of fentanyl was established. Adsorptive stripping voltammetry has been used effectively for trace measurements of numerous compounds of pharmaceutical significance.[4] As illustrated in this paper, this method yielded a detection limit of $5 \times 10^{-8}M$ for fentanyl.

EXPERIMENTAL

Apparatus

A model 370 electrochemistry system (EG&G Princeton Applied Research) was used for cyclic voltammetry and adsorptive stripping voltammetry. The working electrode was a model 303 static dropping mercury electrode (SDME). A medium sized drop (surface area 0.0171 cm^2) was employed. The counter electrode was a platinum wire and the reference electrode was a saturated Ag/AgCl electrode.

Chemicals

Fentanyl was from Hubei Yichang Pharmaceutical Factory. A stock standard solution of fentanyl in water ($1.00 \times 10^{-3}M$) was prepared and stored in the dark; working standard solutions (1.00×10^{-4}, 1.00×10^{-5} and $1.00 \times 10^{-6}M$) were prepared by dilution with water. All other chemicals were of analytical reagent grade. Triply distilled water was used throughout.

Procedure

A 10-ml volume of 0.05M sodium hydroxide containing a specific amount of fentanyl sample solution was added to the cell and purged with purified nitrogen to remove oxygen for 4 min. The SDME was set to hanging mercury electrode mode. The preconcentration potential

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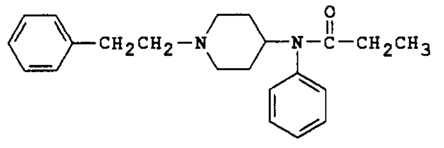

Fig. 1. Structure of fentanyl.

(−1.1 V) was then applied to a new mercury drop for a selected time while the solution was stirred at 400 rpm. The stirring was then stopped, and after 15 sec the voltamperogram was recorded by applying a linear sweep scan. The scan was terminated at −1.6 V.

RESULTS AND DISCUSSION

Reversibility

Figure 2 is a cyclic voltamperogram for $5 \times 10^{-4}M$ fentanyl in sodium hydroxide solution. A pair of well-defined cathodic and anodic peaks was observed. E_{pc} and E_{pa} were −1.47 and −1.44 V, respectively. The existence of the anodic peak suggests that the product of electrode reduction of fentanyl can be oxidized again at the electrode when the scan direction is reversed. Thus, the reduction of fentanyl at a Hg electrode shows some reversibility.

Adsorptive properties

Cathodic normal pulse polarography (NPP) of fentanyl showed a polarogram of peak shape. It is well known that for the diffusion-controlled system the typical shape of NPP is wave-like. However, when the reactant is adsorbed on the surface of Hg cathode, the shape of NPP will become peak-like.[5] The peak-like shape of NPP for fentanyl thus illustrates that fentanyl as a reactant of the electrode reaction is adsorbed on Hg electrode surface.

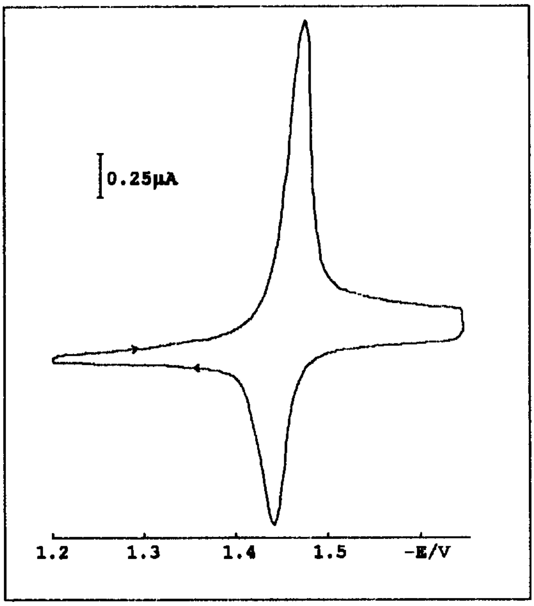

Fig. 2. Cyclic voltamperogram for $5 \times 10^{-4}M$ fentanyl in 0.05*M* NaOH. Scan rate: 100 mV/sec.

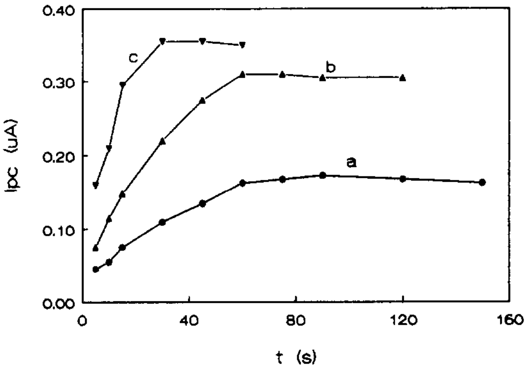

Fig. 3. Effect of preconcentration time on the cathodic peak current. Concentration of fentanyl: (a) $5 \times 10^{-7}M$; (b) $1 \times 10^{-6}M$; (c) $2 \times 10^{-6}M$. Other conditions as for Fig. 2.

Figure 3 shows plots of cathodic peak current (i_{pc}) of linear sweep voltammetry *vs.* preconcentration time (t) for different concentrations of fentanyl. At first, i_{pc} increased rapidly with t at all three levels, indicating that before adsorptive equilibrium was reached, the longer the accumulation time, the more fentanyl was adsorbed, and the larger the peak current. However, after a specific period of accumulation time, the peak current at different concentration levels invariably tended to level off, showing that the adsorptive equilibrium of fentanyl on Hg electrode surface was achieved.

The number of electron transferred, n, thus might be estimated by measuring $\Delta E_{p,1/2}$, the full width at half height of cathodic peak current. According to the formula for the adsorptive system of reversible electroreduction[6]

$$\Delta E_{p,1/2} = 3.53RT/(nF) = 90.6/n \text{ mV } (25°\text{C}).$$

The value of n was estimated as 2. So the function group undergoing reduction might be the carbonyl group of fentanyl, which may gain two electrons from the electrode becoming an alcohol.[7]

System of reactant weakly adsorbed

The effect of square root of scan rate ($v^{1/2}$) on i_{pc} of fentanyl at different proconcentration times showed that when $t = 0$, i_{pc} had a linear relationship with $v^{1/2}$, illustrating the reduction of fentanyl was diffusion-controlled. When $t = 10$ sec, the i_{pc} *vs.* $v^{1/2}$ curve showed an upward bending, indicating that the system began to show some adsorptive characteristics. When $t = 60$ sec, as more fentanyl was adsorbed, the upward turning of the i_{pc}–$v^{1/2}$ curve became more pronounced.

With 60 sec of accumulation, the i_{pc}–v curves were straight lines at lower concentrations, suggesting the electrode process was almost totally adsorption-controlled. However, at higher c_{FENT}, the i_{pc} *vs.* v relationship was not a straight line but a downward bending curve, indicating that the system began to show some diffusion property.

The effect of concentration of fentanyl (c_{FENT}) on i_{pc} at four different accumulation times is shown in Fig. 4. When $t = 0$, the relative peak current expressed as the ratio of i_{pc}/c_{FENT} was small and kept nearly constant with increasing the concentration of fentanyl (curve a). This indicates that the reduction of fentanyl at the Hg electrode was almost totally diffusion-controlled. However, when $t > 0$ sec, the values of i_{pc}/c_{FENT} were much larger than those of curve a at lower c_{FENT} because of the adsorption of fentanyl on Hg surface. At higher c_{FENT}, however, the adsorption of fentanyl reached saturation and its contribution to peak current did not increase further. The ratio then declined rapidly with increasing concentration of fentanyl, and eventually tended toward the constant value of curve a (curves b–d). All of these suggest the gradual transformation of the system from adsorption-controlled to diffusion-controlled when the concentration of fentanyl grows.

In summary, the reduction of fentanyl at Hg electrode is contributed to by the reduction of both surface species adsorbed on the electrode surface and solution species diffusing to the electrode surface. However, because the adsorption of fentanyl is not strong enough, both of the adsorbed and solution species are reduced at the same potential. The cathodic peak current is thus made up of two parts—adsorption current and diffusion current. The preconcentration time, scan rate and fentanyl concentration have different effects on them. Generally, in the condition of smaller c_{FENT}, faster v and longer t, the system manifests itself mainly with adsorptive properties, but in the condition of larger c_{FENT}, slower v and shorter t, the system basically exhibits diffusion properties. This is characteristic of a system with weakly adsorbed reactant.[8]

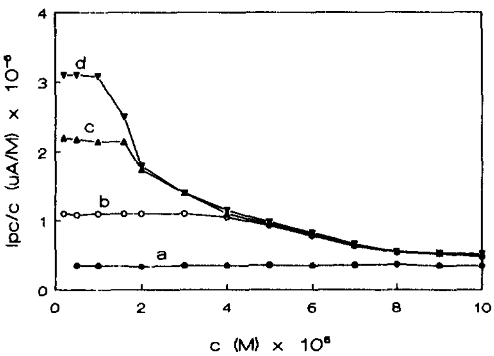

Fig. 4. Effect of fentanyl concentration on relative peak current as the ratio of cathodic peak current to fentanyl concentration. Preconcentration time: (a) 0 sec; (b) 10 sec; (c) 30 sec; (d) 60 sec. Other conditions as for Fig. 2.

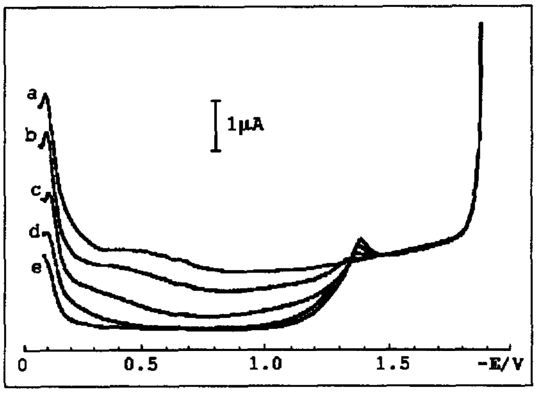

Fig. 5. Tensammetric curve of fentanyl system in 0.05*M* NaOH. Fentanyl concentration: (a) 0*M*; (b) $1 \times 10^{-6}M$; (c) $2 \times 10^{-6}M$; (d) $5 \times 10^{-6}M$; (e) $1 \times 10^{-5}M$. Frequency: 40.5 Hz; amplitude: 25 mV; scan rate: 10 mV/sec. A small-sized drop of SDME was used (surface area 0.0112 cm^2).

Adsorbed species

Figure 5 shows phase-selective AC voltamperograms of the fentanyl system. Ideally, the faradaic and capacitive components of total AC can be separated with the aid of phase-selective technique. The curve of capacitive AC *vs.* DC potential is also called a tensammetric curve, which is similar to differential capacitance curve.[9] After adding fentanyl of different concentrations, the tensammetric curves all decreased over the potential range of -0.2 to -1.3 V as compared to NaOH solution without fentanyl. The larger the concentration of fentanyl, the lower the tensammetric curve until the adsorption saturation was reached. This is clear evidence of the adsorption of uncharged surface-active substances.[9] So the species adsorbed on Hg surface is most probably the neutral molecule of fentanyl, which is in keeping with the fact that fentanyl in alkaline solution exists mainly as the neutral molecular, not positively charged protonized species.

Measurement of fentanyl by adsorptive stripping voltammetry

The adsorptive property of fentanyl can be used as an effective preconcentration step before the voltammetric measurement. In this way, highly sensitive adsorptive stripping measurements of the drug can be achieved.

In order to choose the optimized experimental conditions for the determination of fentanyl by adsorptive stripping voltammetry, a series of experiments was done. Various supporting electrolytes, such as HCl, KCl, HOAc–NaOAc, NH_3–NH_4Cl, KH_2PO_4–K_2HPO_4, $Na_2B_4O_7$, NaOH and Britton–Robinson buffer solution were tested by the method, and NaOH was found to be the best because of the fairly well-defined voltamperogram and reasonably high sensitivity.

Under the optimized condition of $0.05M$ NaOH, preconcentration potential of -1.1 V and scan rate of 200 mV/sec, the peak current had a linear relationship with c_{FENT} over the range from 1.0×10^{-7} to $1.0 \times 10^{-6}M$ when the accumulation time was 60 sec (correlation coefficient 0.9992). The detection limit could reach $5.0 \times 10^{-8}M$ when the preconcentration time was set to 10 min ($S/N = 3$). The precision was estimated by 12 successive measurements of $5 \times 10^{-7}M$ fentanyl under the same conditions as above with an accumulation of 60 sec. The average peak current was 0.175 μA, range 0.163–0.190 μA and relative standard deviation 3.6%.

Table 1. Analytical results of fentanyl in injection samples

Sample	*n*	Mean value (*mg/injection*)	*S*	Range of recovery for added fentanyl (%)
1	4	0.0996	0.0025	97.6–102
2	4	0.101	0.0017	95.5–102

Measurements of fentanyl in injection samples were accomplished by this method. No sample preparation was used other than dilution with the supporting electrolyte. The determination was performed by the standard addition method and the results of a few analyses are given in Table 1.

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