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Preparation and characterization of a new carbon paste electrode based on ketotifen–hexacyanoferrate

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Abstract A new type of carbon paste electrode (CPE) was made using ketotifen fumarate ($C_{23}H_{23}NO_5S$; an antiasthmatic/antianaphylactic drug) and hexacyanoferrate. This electrode was constructed using an acidic solution of ketotifen fumarate and potassium hexacyanoferrate. For this purpose, ketotifen fumarate was dissolved in acidic solution (pH 1) and hexacyanoferrate was added by agitation, resulting in ketotifen–hexacyanoferrate (Ket–HCF) precipitate. The obtained precipitate was separated and introduced into carbon paste. The electrochemical behavior of Ket–HCF CPE was studied by cyclic voltammetry. A modified electrode shows one pair of peaks with surface-confined characteristics, with a 0.1-M phosphate buffer as supporting electrolyte. The effects of pH, alkali metal cations, and anions of supporting electrolytes on the electrochemical characteristics of modified electrodes were studied. The diffusion coefficients of hydrated K^+ in film (D), the transfer coefficient (α), and the transfer rate constant for electrons (k_s) were determined.

Keywords Carbon paste electrode · Ketotifen–hexacyanoferrate · Modified electrode

Introduction

Modified electrodes have received increasing attention for the past two decades because of their applications in electrocatalysis [1, 2], ion selectivity [3, 4], solid-state battery [5], and biosensor systems [6–8]. To date, various inorganic materials [9–11], organometals [12–14], and polynuclear cyanometalate [15, 16] have been used to fabricate modified electrodes. Among the various mediators used for electrode modification, solid metal hexacyanoferrates (MHCFs) have attracted the attention of

electrochemists as excellent electron transfer mediators. Their redox reactions proceed without the dissolution of solid compounds, as ion diffusion maintains charge balance inside the solid compound. Since Neff [17] and Itaya et al. [18] first deposited Prussian Blue (PB) in the form of a film on solid electrodes, interest in this compound has increased, and various transition metal cations have been used with hexacyanoferrate to fabricate MHCF modified electrodes, where M represents cadmium [19], chromium [20], cobalt [21–24], copper [25–28], gallium [29], indium [30, 31], lanthanum [32], manganese [33], molybdenum [34], nickel [35–37], palladium [38], platinum [39], samarium (III) [40], silver [41], titanium dioxide [42], vanadium [43], zinc [44, 45], or zirconium [46].

Ketotifen fumarate (4-(1-methyl-4-piperidylidene)-benzo [4,5]cyclohepta [1,2-*b*]-thiophen-10-(9*H*)-one (Scheme 1) is a benzocycloheptathiophene derivative with multiple pharmacological actions [47]. It is widely accepted as an antiasthmatic/antianaphylactic drug and also alleviates allergic disorders via a combination of several actions. For example, ketotifen is a relatively selective, noncompetitive antagonist of histamine H_1 receptors and is a mast cell stabilizer, inhibiting the release of inflammatory mediators from mast cells [48–51].

This study proposes and examines a novel organic hexacyanoferrate microstructure represented by ketotifen–hexacyanoferrate (Ket–HCF). To the best of our knowledge, there has been no report on the preparation of modified electrodes using Ket–HCF. This paper deals with the preparation of Ket–HCF as a carbon paste electrode (CPE) and presents a detailed study of the electrochemical behavior of the electrode.

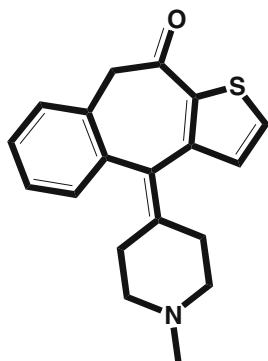
Experimental

Chemicals and instrumentation

$K_3[Fe(CN)_6]$, KNO_3 , and other chemicals (Merck) were of analytical grade and were used without further purification. A solution of 0.1 M phosphate buffer was used as

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Scheme 1 The structure of ketotifen



supporting electrolyte. The buffer was prepared using phosphoric acid, and pH was adjusted with KOH. The working standard of ketotifen was obtained from Modava Pharmaceutical Company (Tehran, Iran). Electrochemical experiments were carried out using a potentiostat/galvanostat (BHP-2063 Electrochemical Analysis System, Behpajoo, Iran). A conventional three-electrode cell was used at 25°C (room temperature). A saturated calomel electrode and a platinum wire were used as reference and auxiliary electrodes, respectively.

Elemental analysis was performed using a CHNS analyzer (LECO), an atomic absorption spectrometer (Schimadzo AA-670), and a flame photometer (Corning 410).

Electrode preparation

The Ket–HCF CPE was constructed using a Ket–HCF ion pair. For the preparation of ion pairs, 50 ml of 0.1 M ketotifen fumarate acidic solution (pH 1) was slowly added, with agitation, to 50 ml of 0.1 M hexacyanoferrate. The produced Ket–HCF precipitate was filtered, washed, and dried. Then 0.015 g of the obtained precipitate was mixed with 0.3 g of graphite (5:100). After adding a few drops of paraffin oil, the mixture was housed in a polyethylene tube (inner diameter, 2.4 mm) and polished with a weighing paper. Electric contact was made by a copper wire through the back of the electrode.

The Ket–HCF precipitate obtained was a yellow powder. The product was stable in acidic solutions and was dissolved gradually in basic solutions. Table 1 presents the results obtained from elemental analyses by a CHNS analyzer (LECO), an atomic absorption spectrometer (Schimadzo AA-670), and a flame photometer (Corning 410).

On the basis of such results, we conclude that the obtained salt may be $K(Ket)_2Fe(CN)_6$.

Table 1 Elemental analysis results of Ket–HCF by different techniques

C (%)	H (%)	N (%)	S (%)	Fe (%)	K (%)
57.26	5.15	23.76	7.03	6.40	3.90

Results and discussion

Electrochemical behavior of modified electrode

A Ket–HCF modified electrode prepared in optimum conditions was characterized by cyclic voltammetry. Cyclic voltammograms of Ket–HCF in the presence of 0.1 M phosphate buffer, containing indeliberately added electroactive materials, were recorded between 0.3 and 0.9 V vs SCE at various scan rates of 10–100 $mV s^{-1}$ (Fig. 1a). As seen, the voltammograms consisted of a pair of peaks. The anodic and cathodic peak potentials were 0.67 and 0.6, respectively, at a scan rate of 100 $mV s^{-1}$. The formal potential, taken as the average of the anodic and cathodic peak potentials [$E^{\circ}=(E_{pa}+E_{pc})/2$], is about 638 mV and is almost independent of potential scan rate for sweep rates ranging from 10 to 100 $mV s^{-1}$. The I_{pa}/I_{pc} ratio remains almost unity, and peak separation ($\Delta E_p=E_{pa}-E_{pc}$) equals 23 mV at a scan rate of 50 $mV s^{-1}$; at higher scan rates, wider splitting appears, indicating the limitation arising from charge transfer kinetics. Peak currents of the voltammogram are linearly proportional to the scan rate of up to 100 $mV s^{-1}$, which is expected for surface-confined redox processes (Fig. 1b). For scan rates higher than 100 $mV s^{-1}$, the anodic and cathodic peak

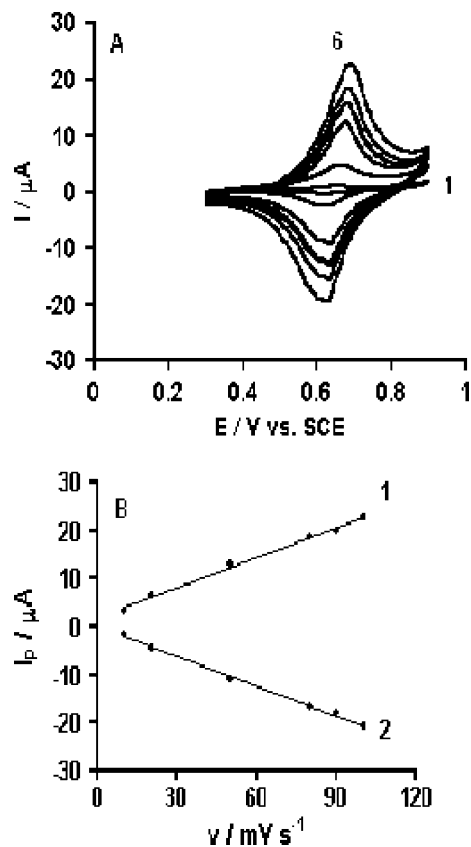


Fig. 1 a Cyclic voltammograms of the Ket–HCF electrode, with a 0.1-M phosphate buffer solution (pH 7) as supporting electrolyte. Potential scan rates: 1 10 $mV s^{-1}$; 2 20 $mV s^{-1}$; 3 50 $mV s^{-1}$; 4 80 $mV s^{-1}$; 5 90 $mV s^{-1}$; 6 100 $mV s^{-1}$. b Plot of anodic 1 and cathodic 2 peak currents vs potential scan rate. The electrode diameter is 2.4 mm

currents are proportional to the square root of the scan rate, which is expected for a diffusion-controlled electrode process.

Effect of pH

Cyclic voltammetry was also used to study the effect of phosphate buffer pH on peak currents. The resulting I_{pa} vs pH (4–8) data are illustrated in Fig. 2. As seen, peak currents increase with increasing pH (up to pH 7) and then decrease at higher pH values. The protonated ketotifen N is a weak base with $pK_a=6.7$ [52]; at pH values lower than about 7, ketotifen is in the protonated form and can be stable as a $K(Ket)_2$ -HCF precipitate, but at higher pH values, the unprotonated form of ketotifen exists and then the precipitate gradually dissolves in alkaline solutions. Thus, a 0.1-M phosphate buffer solution (pH 7) was selected and used for further studies.

Stability of modified electrode

The stability of the Ket-HCF modified electrode was examined by repetitive scans in a 0.1-M phosphate buffer solution. In the first few scans, the peak current increased on continuous scanning. Then, negligible variation in height and separation of cyclic voltammetric peaks were observed. The response of the modified electrode decreased by 8% after 100 cycles. Furthermore, there was no loss of redox activity after storing the modified electrode in air for a month.

Effect of alkali and alkaline-earth metal cations

In order to maintain the electroneutrality of a Ket-HCF film, the motion of a counterion always accompanies electron transfer during the redox process. Thus, cations have a considerable effect on the electrochemical behavior of the Ket-HCF film. The effects of alkali and alkaline-earth metal

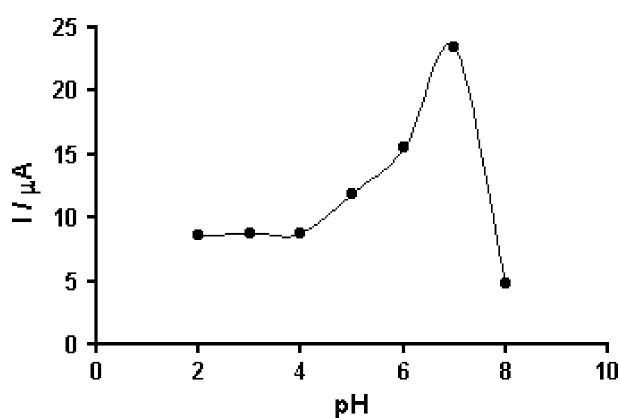


Fig. 2 The effect of pH on the response current of Ket-HCF, with a 0.1-M phosphate buffer solution as supporting electrolyte

cations on the voltammetric behavior of the Ket-HCF film were studied by cyclic voltammetry. In this study, cations such as Li^+ , Na^+ , K^+ , Mg^{2+} , and Be^{2+} were examined at the same concentration (0.25 M) (Fig. 3). The results obtained from this study showed that, in the presence of Li^+ cation, no obvious redox peaks can be observed (Fig. 3a) It is feasible that hydrated Li^+ may enter the channels of the Ket-HCF crystal lattice and then become trapped, blocking access to all channels into the lattice. Therefore, even when changing the counterion of the bulk electrolyte, no redox signal is observed, but in the presence of other cations, a pair of peaks is obtained (Fig. 3b–e). The formal potential and the peak separation for all cations are presented in Table 1. As can be seen in Table 2 and Fig. 3, the peak separation for K^+ is lowest and the current is highest. According to these data, we conclude that the Ket-HCF modified electrode exhibits a preference for alkali metal cations in the order $K^+ > Na^+ > Mg^{2+} > Be^{2+} > Li^+$ in an aqueous solution. The results also led us to conclude that alkali metal and alkaline-earth metal cations can freely penetrate into the Ket-HCF crystal lattice.

Effect of anions

Experimental investigations showed that voltammetric characteristics of the Ket-HCF electrode were firmly affected by the nature of anions present in the solution. Therefore, the effects of various anions, such as NO_3^- , Cl^- , and phosphate, were studied. The results obtained showed that well-defined and reproducible cyclic voltammograms were obtained in a 0.1-M phosphate buffer solution.

Effect of surface coverage

The surface coverage of the Ket-HCF modified electrode Γ represents the moles of the Ket-HCF redox site per unit area of electrode surface. The amount of charge Q consumed for anodic peaks recorded at 50 mV s^{-1} was

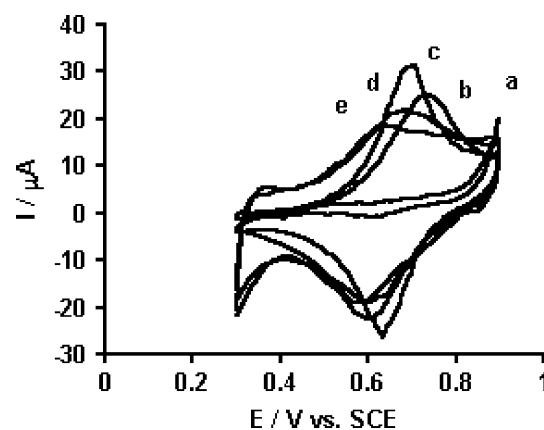


Fig. 3 Cyclic voltammograms of the Ket-HCF electrode in the presence of different alkali metal cations at the same concentration (0.25 M). a LiCl; b NaCl; c KCl; d $MgCl_2$; e $BeCl_2$. Scan rate, 100 mV s^{-1}

Table 2 The peak and formal potential of LiCl, NaCl, KCl, BeCl₂, and MgCl₂ (0.25 M) (scan rate, 100 mV s⁻¹)

Electrolyte	E_{pa} (V vs SCE)	E_{pc} (V vs SCE)	E° (V vs SCE)
LiCl	–	–	–
NaCl	0.85	0.64	0.74
KCl	0.75	0.65	0.70
BeCl ₂	0.67	0.61	0.64
MgCl ₂	0.64	0.59	0.61

measured with respect to baseline and was used to calculate Γ from the following equation:

$$\Gamma = \frac{Q}{nFA} \quad (1)$$

where n , F , and Γ are the number of electrons transferred in the surface redox reaction, the Faraday constant, and the electrode surface coverage, respectively. It should be pointed out that the calculated surface coverage is an efficient attribute (per cross section of the electrode) and does not reflect the actual amount of Ket–HCF per area of CPE. An increase in scan rate, ranging from 50 to 6,000 mV s⁻¹, causes a continuous decrease of apparent coverage from 1.0×10^{-9} to 1.4×10^{-10} mol cm⁻². A decrease of the apparent coverage with increasing scan rate is probably related to charge transfers through a modified electrode layer, which becomes rate-limiting at higher scan rates.

Charge transfer rate in the film

The peak separation is close to zero when electron transfer rate is fast relative to the scan rate and increases when the electron transfer rate is slow. Using the treatment proposed by Laviron [53] from the variation of peak potentials with the logarithm of scan rate, the heterogeneous electron transfer rate constant (k_s ; s⁻¹) was estimated. For the Ket–HCF modified electrode surface coverage of about 2×10^{-9} mol cm⁻² (for 20 mV s⁻¹), the peak-to-peak sep-

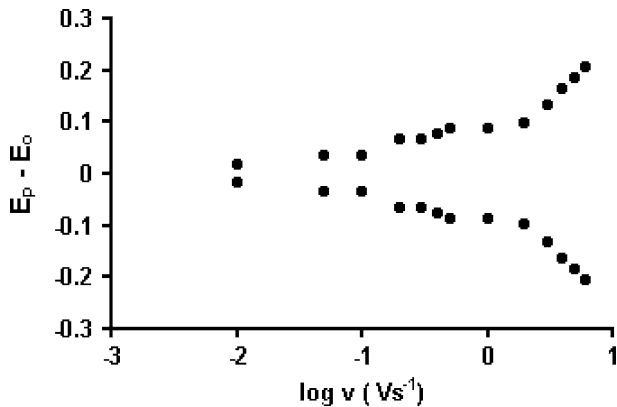


Fig. 4 Plot of $E_p - E^\circ$ vs $\log V$ for cyclic voltammograms recorded for the Ket–HCF electrode in a 0.1-M phosphate buffer solution at scan rates V between 0.01 and 1 V s⁻¹ for anodic and cathodic peaks

aration potential ($\Delta E_p = E_{pa} - E_{pc}$) observed for scan rates of up to 50 mV s⁻¹ was less than 40 mV in the presence of a 0.1-M phosphate buffer solution as supporting electrolyte. At higher scan rates, this value is increased (134 mV for 1 V s⁻¹), indicating the limitation arising from charge transfer kinetics.

Laviron [53] derived general expressions for the linear potential sweep voltammetric response to the case of surface-confined electroactive species. These expressions are as follows:

$$E_{pa} = E_o + A \ln \left[\frac{(1 - \alpha)}{m} \right] \quad (2)$$

$$E_{pc} = E_o + B \ln \left[\frac{\alpha}{m} \right] \quad (3)$$

$\log k_s$

$$= \alpha \log (1 - \alpha) + (1 - \alpha) \log \alpha - \log \left(\frac{RT}{nFV} \right) - \alpha(1 - \alpha) \left(\frac{nF \Delta E_p}{2.3RT} \right) \quad (4)$$

$$\text{where: } A = \frac{RT}{(1 - \alpha)nF}, B = \frac{RT}{\alpha nF}, m = \left(\frac{RT}{F} \right) \left(\frac{K_s}{nV} \right)$$

From these expressions, it is possible to determine the transfer rate constant (α) by measuring the variation of the peak potentials with scan rate V as well as the apparent charge transfer rate constant (k_s) for electron transfer between the electrode and the surface-deposited layer. According to relations 2 and 3, the plot of $E_p - E^\circ = f(\log V)$ yields two straight lines with a slope equal to $2.3RT/\alpha nF$ for the cathodic peak and a slope equal to $2.3RT/(1 - \alpha)nF$

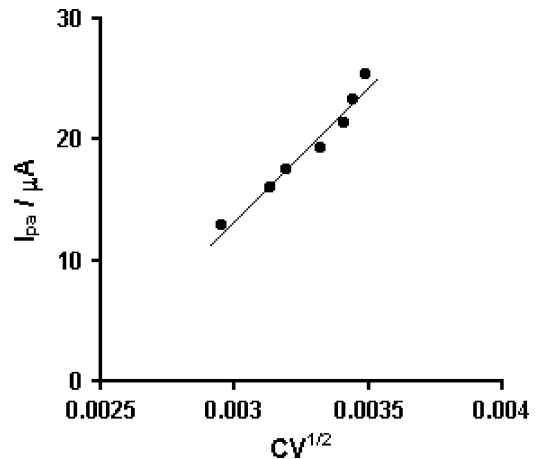


Fig. 5 Plot of I_p vs $CV^{1/2}$ for cyclic voltammograms recorded for the Ket–HCF electrode ($A=0.045$ cm²) in a 0.1-M phosphate buffer solution at scan rates between 500 and 2,000 mV s⁻¹ for anodic peaks

for the anodic peak. A typical example of this plot is shown in Fig. 3 for Ket–HCF films at scan rates of 0.01–1 V s⁻¹, in the presence of a 0.1 M phosphate buffer. Using such a plot and Eq. 4, the values of α and k_s were found to be 0.6 and 2.4±0.2 s⁻¹, respectively. Note that the surface coverage Γ evaluated from the relation $\Gamma=Q_H/nFA$ was $\sim 1.38 \times 10^{-9}$ mol cm⁻². Further experiments showed that the values obtained for α and k_s remained almost unchanged for Γ values in the range 10⁻⁹–10⁻¹⁰ mol cm⁻². Figure 4 shows a typical curve: E_p-E° vs $\log V$.

Diffusion coefficient of K⁺ in the film

The height of cyclic voltammogram peaks obtained for scan rates >500 mV s⁻¹ is an important criterion, which can be related to the facility of cation diffusion in the modified film [54]. The peak current of cyclic voltammograms obtained for scan rates higher than 500 mV s⁻¹, in the presence of potassium cation, is proportional to the square root of scan rate $V^{1/2}$, indicating its diffusion nature. We can calculate the diffusion coefficient of the cations in the modifier film by exhibiting a quasi-reversible behavior at high scan rates, according to Eq. 5 [55]. Using the following equation:

$$i_p = 2.99 \times 10^5 n^{3/2} \alpha^{1/2} A D^{1/2} C V^{1/2} \quad (5)$$

where D is the diffusion coefficient of cation in the film (cm² s⁻¹), A is the electrode area (0.045 cm²), V is the potential scan rate (V s⁻¹), and i_p is the peak current (A). Since, at high scan rates, all redox sites, including mixed valance iron in the film, are not electroactive due to the presence of insufficient amounts of counterions in the film, in Eq. 5, C presents the concentration of alkali metal cations in the film (mol cm⁻³). The value of C that varies with the scan rate was calculated by means of the total moles of cations in the film obtained from Q_H (the area under cyclic voltammograms recorded at scan rates higher than 500 mV s⁻¹) and the total volume of the film obtained from Q_L (the area under cyclic voltammograms recorded at a scan rate of 50 mV s⁻¹). Using peak current i_p measured from baseline and using C for each scan rate higher than 500 mV s⁻¹ (C and the plot of i_p vs $CV^{1/2}$), the diffusion coefficient was calculated [(3.34±0.15)×10⁻¹⁰ cm² s⁻¹]. A typical example of these plots is shown in Fig. 5 for the cyclic voltammogram peaks recorded in the presence of K⁺. The value of D , which may lie in the rigid microstructure of the formed Ket–HCF interface, is relatively small; presumably a low-porous interface would reduce ion diffusion rates through the layer.

Conclusion

We demonstrate the preparation of a new type of modified electrode using an organic compound and hexacyanoferrate. The preparation of a modified electrode is easy, fast,

and reproducible. This modified electrode shows satisfactory stability toward potential recycling. The pH of a solution has considerable effect on the stability and electrochemical behavior of the film, but the alkali and alkaline-earth metal cations and the nature of anions of the supporting electrolyte have significant effects on the stability and electrochemical behavior of the film. K⁺ can freely enter the Ket–HCF crystal lattice. The prepared modified electrode is stable for several weeks in air, as well as in a 0.1-M phosphate buffer solution.

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