Voltammetric Detection of Paracetamol at Cobalt Ferrite Nanoparticles Modified Glassy Carbon Electrode

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A promising electrochemical sensor based on $CoFe_2O_4$ nanoparticle modified glassy carbon electrode (CF/GCE) was developed for the sensitive detection of paracetamol (ACOP). Cobalt ferrite nanoparticles were synthesized via wet chemical method. Techniques like X-ray diffraction (XRD) and transmission electron microscopy (TEM) were employed for the structural and morphological characterization of the nanoparticles. The electrochemical behavior of ACOP on CF/GCE was investigated by cyclic voltammetry. The modified electrode displayed excellent redox activity towards ACOP, with a significant reduction of overpotential compared to bare GCE. The CF/GCE exhibited good stability, reproducibility and sensitivity in the determination of ACOP with a detection limit of 36nM. The sensor effectively resolved the overlapping anodic peaks of dopamine, ascorbic acid and paracetamol.

Keywords: cobalt ferrite, voltammetry, sensor, paracetamol, ascorbic acid.

1. INTRODUCTION

Recently, with the prompt development of science and technology, nano-sized materials gained extensive attention. Materials in its nano regime, their properties are significantly modified in comparison with that of their bulk counterparts. Among the diverse nano-structured materials, magnetic nanoparticles are highly recognized since they are applicable in a variety of areas such as biosensors [1], magnetic recording, drug delivery, pigments, paints [2,3], detection of DNA hybridization [4] etc. Their applicability as sensors in the field of electrochemistry is quite remarkable. Ye and co-workers [5] synthesized a novel electrochemical sensor based on LaNi_{0.5}Ti_{0.5}O₃/CoFe₂O₄ (LNT-CFO) nanoparticles fabricated glassy carbon electrodes for the sensitive determination of paracetamol. Chen and co-workers [6] have reported the synthesis of Fe₃O₄ nanoparticles modified

with electroactive Prussian blue (PB) and further immobilized them on the surface of glassy carbon electrode to develop a new type of biosensor for the reduction of H_2O_2 . Inorder to study the electron transfer reactions of DNA, Wang et al have reported the switching of DNA electron transfer reaction through the attraction and removal of DNA- incorporated magnetic nanoparticles [7, 8].

Considering the family of magnetic nanomaterials, cobalt ferrite nanoparticles play a very prominent role. They are well known for their high cubic magneto crystalline anisotropy, chemical stability, mechanical hardness accompanied by a reasonable saturation magnetization [9,10]. Additionally, the large specific areas of the nanoparticles make them better candidates in absorbing micromolecular pharmaceuticals and possess unique physical as well as chemical properties.

Paracetamol [acetaminophen or N-acetyl amino phenol] is widely used as an antipyretic and analgesic drug. It is highly effective for the release of pain associated with arthralgia, neuralgia, and headache and even to patients suffering from gastric symptoms. In most countries it is used as a substitute for aspirin [acetyl salicylic acid] [11]. Since paracetamol is easily and completely metabolized, normally it doesn't show any harmful side-effects. However, the over dosage causes the accumulation of toxic metabolites leading to kidney damage, liver disorders, skin rashes and inflammation of the pancreas [12, 13]. Hence it is important to develop a simple, fast, sensitive and accurate method for the detection of paracetamol. Many techniques have been developed for the determination of paracetamol like spectrophotometry [14-16], spectrofluorometry [17,18], liquid chromatography [19], FT-IR Raman spectrometry [20], titrimetry [21], automatic sequential injection analysis [22] and chemiluminescence [23]. However, many of these techniques require tedious extraction process, time-consuming analysis, high costs, sophisticated instruments and skilled operators. Electroanalytical techniques have the advantages of simple, fast, time-saving, inexpensive, sensitive, in-situ and trace detection of various analytes and are extensively used in the detection of pharmaceuticals like ACOP. Kang et al. reported [24] the electro catalytic response for the oxidation of ACOP on graphene modified glassy carbon electrodes and Atta and co-workers [25] demonstrated the electro deposition of gold nanoparticles modified carbon paste electrode (CPE-Au_{nano}) used for the simultaneous determination of paracetamol and some neurotransmitters in biological fluids.

The aim of the present study is to construct a stable as well as sensitive electrochemical sensor based on cobalt ferrite nanoparticles modified glassy carbon electrodes (CF/GCE), and to extend the same for the simultaneous detection of ACOP and to observe the interference behavior on ascorbic acid (AA) and neurotransmitters like dopamine (DA). The electrochemical behavior was investigated using cyclic voltammetry techniques and the results were compared with other available reports.

2. EXPERIMENTAL

2.1. Chemicals and Reagents

Ferric nitrate [Fe(NO₃)₃. 9H₂O], Cobalt nitrate [Co(NO₃)₂. 6H₂O], and citric acid [C₆H₈O₇) were obtained from Merck. Acetaminophen, dopamine and ascorbic acid were purchased from Aldrich (USA). The buffer solution was made up of 0.1M KH₂PO₄ (Merck) and the pH was adjusted by using

0.1M KOH and 1:1 H₃PO₄. All other reagents were of analytical grade and were used without further purification. All solutions were prepared using double distilled water.

2.2. Apparatus

Electrochemical experiments were done by using an Electrochemical analyzer CHI 604D (CH Instrumental Co. USA) having a three electrode system. A bare glassy carbon electrode [GCE, 3mm diameter] and cobalt ferrite nanoparticles modified glassy carbon electrode [CF/GCE] serves as the working electrode, a saturated calomel electrode as the reference electrode and platinum wire as the counter electrode respectively. Cyclic voltammetric experiments (CV) were carried out in a quiescent solution at 100mVs^{-1} in an electrochemical cell filled with 10ml of buffer solution (supporting electrolyte). Powder X-ray diffraction (XRD) studies of the cobalt ferrite nanoparticles were recorded on a Bruker AXS D8 ADVANCE X-ray diffractometer with Cu/K α radiation (1.5406Ű). Transmission electron microscopic (TEM) was carried out with PHILIPS CM200 having an operation voltage of 20-200Kv. The magnetic characterizations were done on a Lakeshore vibrating sample magnetometer (VSM 7410) at room temperature.

2.3. Synthesis of Cobalt ferrite nanoparticles

A wet chemical method was employed for the synthesis of cobalt ferrite nanoparticles. The materials used were analytical grade cobalt nitrate $[Co(NO_3)_2.6H_2O]$ and ferric nitrate $[Fe(NO_3)_3.9H_2O]$ and citric acid $[C_6H_8O_7]$. 25ml of 0.2M solution of $(CoNO_3)_2.6H_2O$ and 0.1M solution of $Fe(NO_3)_3.9H_2O$ (Fe:Co = 2:1) were mixed and citric acid was added after the addition of 10 ml of HNO₃ (68%). The resulting solution was stirred vigorously at 60°C until the formation of a gel fluffy deposit. The ratio of citric acid added to that of the nitrate solution is 1:1. Further, the gel deposit was dried overnight in a hot air oven and is subjected to calcination at 600°C for 3hours. The thus obtained deposit was thoroughly powdered and employed for the modification.

2.4. Preparation of the CF/GCE

Cobalt ferrite nanoparticles (2mg) were dispersed in 1mL N,N dimethyl formamide and the resulting solution was agitated in an ultrasonic bath for an hour to achieve a well dispersed suspension. Prior to use, the bare GCE was polished to mirror finish surface using 0.5 or $0.05\mu m \alpha$ -Al₂O₃, then rinsed ultrasonically with water, absolute ethanol and sonicated in double distilled water respectively. To modify the GCE with CF, $5\mu L$ of CF suspension was cast on the surface of the pre-treated GCE and allowed to dry at room temperature. The cobalt ferrite nanoparticles modified glassy carbon electrodes were thus prepared.

3. RESULTS AND DISCUSSION

3.1. Characterization of Cobalt ferrite nanoparticles



Figure 1. XRD patterns of CoFe₂O₄ nanoparticles



Figure 2. TEM image of CoFe₂O₄ nanoparticle

Figure 1 illustrates the XRD patterns of $CoFe_2O_4$ calcined at 600°C. The typical reflection planes of the sample are shown at a 20 angles of 30.09°, 35.38°, 36.99°, 43.05°, 57.54° and 62.75° corresponding to the (2 2 0), (3 1 1), (2 2 2), (4 0 0), (5 1 1) and (4 4 0) (JCPDS file 22-1086) lattice planes, respectively, revealing the formation of standard structure of $CoFe_2O_4$ having a cubic spinel structure (Fd3m) [9]. The particle size was determined from the full width at half maximum (FWHM) of the XRD patterns using Scherrer formula and was found to be 23nm. The transmission electron micrograph of the cobalt ferrite nanoparticles indicate (Figure 2) that the morphology of the particles are weakly agglomerated, spherical and regular in shape and are uniformly distributed. The particle size was 23nm which agrees well with the value estimated from the X-ray powder diffraction peaks. Moreover, the sample exhibited a saturation magnetization of 20emu/g and coercivity 822G.

3.2. Voltammetric behavior of ACOP on CF/GCE



Figure 3: Cyclic voltammograms of $2x10^{-4}$ mol L⁻¹ ACOP in 0.1M PBS (pH=2.5) on b) on a bare electrode c) CF/GCE a) absence of ACOP in solution on a bare electrode, scan rate: $0.1Vs^{-1}$.

The electrochemical behavior of CF-modified GCE towards ACOP was investigated using cyclic voltammetry. Figure 3 shows the CVs of bare glassy carbon and cobalt ferrite modified glassy carbon electrode in the potential range from 0.1 to 0.8V in the phosphate buffer solution (PBS) at a pH of 2.5. No significant peak currents were observed for the bare GCE. The CV response is observed only after the addition of ACOP. A small anodic current was observed in the potential range of 0.1 to 0.8, $E_{pa} = 0.647V$. However, the CV of CF/GCE showed a pair of well-defined redox peaks: $E_{pa} = 0.532V$ and $E_{pc} = 0.455V$, $i_{pa}/i_{pc} \sim 1$ and is a quasi-reversible process. This is due to the reason that the cobalt ferrite nanoparticles accelerate the electrochemical reaction and the oxidation overpotential was lowered at the modified electrode in comparison with the bare GCE.

It was reported by Ye et al. [5] that in case of heterogeneous reactions which occurs with electron transfer on pervoskite type oxides, the active sites are mainly the transition metal ions having partially filled d orbitals. In the present case, the cobalt ferrite nanoparticles act as catalyst where the transition metals which can exist in the mixed oxidation state and some of the Co^{2+} or Fe^{3+} ions are expected to be the active sites for the oxidation of ACOP and the main product in the electro oxidation of ACOP in aqueous solution containing 0.1M PBS (pH=2.5) is attributed to the formation of N-acetyl-p-benzoquinone-imine (NAPQI),2 under protonation changed to structure 3 further undergo additional chemical reactions leading to the formation of p-benzoquinone 5,[26] {scheme 1}



Scheme 1:

3.3. Effect of scan rate and pH:



Figure 4. (a) Cyclic voltammograms acquired on CF/GCE with $2x10^{-4}$ mol L⁻¹ in 0.1M PBS (pH=2.5) at different scan rates from 50 to 210mVs^{-1} . (b) . Linear relationship of paracetamol Vs scan rate.

The influence of scan rate on the electrochemical behavior of ACOP was investigated in the range from 50-210 mVs⁻¹(Figure 4(a)). The peak current increased with an increase in the scan rate followed by a positive shift in the peak potential. The redox peak current increases linearly with the square root of scan rate (Figure 4(b)) indicating a diffusion controlled process of ACOP on CF/GCE.



Figure 5. (a) Cyclic voltammograms of 2.0×10^{-4} mol L⁻¹ ACOP on 0.1M PBS at different pH values (a-g): 2.0, 2.5, 3.0, 3.5, 4.0, 4.5 and 5.0. (b) Linear relationship of E_{pa} Vs pH.

The effect of pH in the range of pH 2.0 to 5.0 on the redox of ACOP was studied and is shown in Figure 5 (a). From the figure, it is found that the anodic peak potential shifted negatively with an increase in pH. The shifting is mainly because of the participation of proton(s) in the oxidation reaction of 1 to N-acetyl-p-benzoquinone-imine (NAPQI), {(2), scheme 1}. The relationships between the potential and pH were linear with a correlation of 0.99 (Figure 5(b)). The oxidation of paracetamol is a two-electron two-proton process having a theoretical slope of 59mVpH⁻¹. The present value of 50mV is in agreement with the theoretical slope having m=2, m is the number of protons involved in the reaction. It can also be shown that the peak current reached maximum at a pH of 2.5 and is chosen for further investigations.

3.4. Analytical application

3.4.1. Detection limit and relative standard deviation

Figure 6 (a) shows the cyclic voltammograms recorded for the addition of varying concentrations of ACOP at CF-nanoparticles modified GCE in PBS. The oxidative peak current increases linearly from a concentration range of 0.1×10^{-6} to 2×10^{-4} mol L⁻¹ of ACOP (Figure 6 (b)) exhibiting an excellent correlation of 0.998. The detection limit was calculated using the formula 3σ /slope, where σ is the standard deviation of the blank [27]. The detection limit obtained by this method is 36nM. A comparison of the response characteristics of different modified electrodes towards the detection of paracetamol is tabulated in table 1.

The relative standard deviation was found to be 0.18% for a solution containing 10μ M ACOP in 0.1M PBS (pH 2.5; n = 15) and repetitive cycling was done to determine the stability of the modified electrode at a scan rate of 100mVs⁻¹ for 2 hours. No significant reduction in electroactivity

and peak current was observed. The results presented excellent stability and reproducibility of the cobalt ferrite modified glassy carbon electrodes for the sensitive detection of paracetamol.



Figure 6. (a) Cyclic voltammogram of ACOP on CF/GCE at different ACOP concentration (pH = 2.5) (a-o;µM) a) 0.1 b) 0.5 c) 2 d) 4 e) 16 f) 20 g) 30 h) 46 i) 65 j) 84 K) 103 l) 138 m) 172 n) 232 o) 322.;(b) . Linear relationship of current Vs concentration of paracetamol.

Table 1	1. Comparison	of electroanalytical	data for	determination	of paracetamol	using different
1	modified electro	odes				

Sl. No.	Modified electrode	Electrochemical technique employed	Linear range (µM)	Detection limit (µM)	Reference
1	MCPE/PR	Differential pulse voltammetry	0.7 - 100	0.53	[28]
2	PolyDAN-RB4/GCE	Differential pulse voltammetry	0.2 - 164	0.083±0.003	[29]
3	Bi ₂ O ₃ /GCE	Cyclic voltammetry	0.5 - 1500	0.2	[30]
4	f-MWCNTs/GCE	Differential pulse voltammetry	0.074 - 230	0.039	[31]
5	PEDOT/GCE	Differential pulse voltammetry	2.5 - 150	1.13	[32]
6	CF/GCE	Cyclic voltammetry	0.1 - 200	0.036	Present work

3.4.2. Simultaneous determination of Paracetamol, dopamine and ascorbic acid

Simultaneous determination of ACOP with common interfering agents like AA and DA were studied by using cyclic voltammetry in the potential range from 0.1V to 0.8V in 0.1M PBS solution. As shown in Figure 7 a single peak was obtained for the bare glassy carbon electrode when placed in a mixture containing millimolar amounts of AA and micro molar levels of DA and ACOP. However, well resolved oxidation peaks were obtained with CF/GCE at peak potentials of 0.569V, 0.223V and 0.111V for ACOP, DA and AA respectively. The enhancement in peak current is a clear indication of the catalytic behavior of the modified electrode towards the oxidation of ACOP, DA and AA respectively. Additionally, the difference between the oxidation potentials facilitated the sensitive and accurate detection of the three compounds simultaneously even for AA at a higher concentration.



Figure 7. Cyclic voltammogram recorded at a) bare GCE b) and the CF/GCE with ACOP (10 μ M), AA (10 μ M), DA (10 μ M) in 0.1M PBS (pH = 2.5) at a scan rate of 0.1Vs⁻¹.

4. CONCLUSIONS

Nanoparticles of cobalt ferrite have been successively synthesized by a wet chemical method. This cobalt ferrite nanoparticles was used to modify the glassy carbon electrode and was subsequently applied for the voltammetric detection of paracetamol. The modified electrode offered excellent sensitivity in the simultaneous detection of ACOP, DA and AA with good separation of the oxidation peaks. Based on the significant electrocatalytic activity of cobalt ferrite nanoparticles the modified electrode showed excellent reproducibility, stability as well as anti-interference performance with a detection limit of 36nM. The proposed method is simple and cost-effective and can be applied to the detection of real samples with satisfactory results.

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