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Electrochemical behaviour of cefdinir at composite polymer membrane electrode

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ABSTRACT

Composite polymer membrane electrode has been fabricated on platinum foil using electrochemical deposition of the pyrrole and aniline as monomers. The electroreductive behavior of cefdinir was investigated and two irreversible well-defined cathodic peaks were observed at composite polymer membrane electrode. From the electrochemical response the main reduction steps were found to be related to the reduction of C=N and C=C group. A fully sensitive and reproducible voltammetric procedure for the trace determination of the pharmaceutical formulation at the composite polymer membrane electrode has been developed.

Key words: Composite polymer membrane electrode, platinum foil, pyrrole, aniline, cefdinir.

INTRODUCTION

In recent years, increased interest in conducting polymers has led to a large number of important applications such as for rechargeable batteries, electrosynthesis, in corrosion to protect films, biosensors, modified electrodes and capacitors[1-3] etc. Conducting polymers containing two components can be prepared as copolymers, bilayers and composites. Some properties of two component conductive polymer systems, such as electrical and physical properties can be improved by copolymerization. The mechanical properties of two component conductive polymeric systems may also be improved by polymerization to two monomers, on platinum foil electrodes.[4-6] Electrolysis of two monomers generally gives a copolymer, as in the case of aniline and thiophene.[7] Pekmez et al[7] reported that the thiophene *I* aniline ratio in the copolymer could easily be adjusted by controlling the polymerization potential.

Cefdinir is a broad-spectrum oral cephalosporin that has been launched in Japan and approved by the U.S. Food and Drug Administration in 1997 for the treatment of mild to moderate bacterial infections. Cefdinir offers enhanced activity against methicillinsensitive *Staphylococcus aureus* and *Staphylococcus epidermis* as well as effective antimicrobial activity against strains of *Staphylococcus* and *Neisseria spp*. and b-*lactamase* producing strains of *Haemophilus* and *Moraxella*.[8-14] Chemically, cefdinir (Scheme-1) is [(6R,7R)-7-[[(2Z)-(2-Amino-4-thiazoyl) (hydroxyl imino) acetyl] amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid][15].

The oximino side chain provides excellent stability against the most common plasmid-encoded β-*lactamase* TEM-1 and TEM-2[11] but not against extended b-*lactamase*, such as TEM-3.[12] It is safe and effective when used in children with infections caused by susceptible bacteria including *Staphylococcus aureus*.[16] Diarrhea was a common adverse reaction associated with cefdinir.[17] A pooled comparison of cefdinir and penicillin in the treatment of group a β-hemolytic streptococcal pharyngotonsillitis was studied and it was found that cefdinir achieved significantly higher clinical cure and microbiological eradication rates compared with penicillin.[18] Cefdinir content in plasma, blister fluid, and urine has been analyzed using a high-

performance liquid chromatography (HPLC)-ultraviolet (UV) detector. The lower limits of detection for this method were 0.015, 0.05, and 0.078 µg mL^{-1} for cefdinir in plasma, blister fluid, and urine, respectively.[19] Cephalosporins in dosage form and body fluid have been determined using various techniques, including derivative spectrophotometric[20-22] and chromatographic[23-26] techniques. The reported methods were time consuming and required a large number of complicated steps to follow for analysis and as well as a sophisticated and expensive instrumentation. Therefore, a rapid, simple, and highly sensitive voltammetric method has been developed in the present study. In the last decades modern voltammetric techniques have been used to realize the determination of organic chemicals in diverse types of samples, especially in the pharmaceutical field.[27-33] Voltammetric techniques were employed for the determination of cephalosporins such as Ceftazidime, Ceftizoxime, Ceftriaxone, Cefazolin, Cefuroxime, Ceftizoxone, Ceftaxime, Cefixime, and Cefpodoxime proxetil.[34-37] Cefdinir is not official in United States Pharmacopeia (USP) or British Pharmacopeia (BP) but a few methods for the analysis of cefdinir in bulk drug by HPLC[20] and in biological fluid by liquid chromatography electrospray ionization tandem mass spectrometry[38] with a detection limit of 5–2000 ng mL^{-1} have been developed. Also, different spectroscopic and reverse-phase HPLC methods[39] have been reported for the determination of cefdinir in pharmaceutical dosages with detection limits of 10–35 and 15– 125 mg mL^{-1}, respectively. HPLC method has been described for the determination of cefdinir in bulk drug substance and its processrelated substances contaminating the bulk drug with a detection limit of 0.01%, and it shows a linearity range between 0.5 and 25 µg mL^{-1}. The cefdinir molecule has electroactive groups but nothing appears to have been published concerning its electrochemical behavior or its voltammetric measurement in particular. Furthermore, there appears to be no electroanalytical method for the determination of cefdinir in pharmaceutical formulation and in biological fluid. The present work demonstrates the voltammetric behavior of cefdinir in aqueous media using composite polymer membrane electrode. This communication also describes validated, simple, rapid, selective, and sensitive cyclic voltammetric procedures for the determination of cefdinir in pharmaceutical.

EXPERIMENTAL

Instrumentation

The polymer was deposited on the platinum foil electrochemically. The voltammetric experiments were performed using an EG & G Princeton Applied Research Modal 273-A potentiostat controlled by the modal 270/250 Research Electrochemistry Software 4.30. A three-electrode system composed of a platinum foil as working electrode, saturated calomel electrode as reference electrode and a platinum foil as auxiliary electrode was used.

To provide a reproducible active surface and improve the sensitivity, resolution and deposition of the polymer on the working electrode, platinum foil was washed with dilute HNO_3 and acetone before each electrochemical measurement. After that electrodes were thoroughly rinsed with methanol, double distilled water, and gently dried with the help of tissue paper. All solutions used in electrochemical technique were purged for 10 min with purified nitrogen gas. Digital pH meter (Decible DB-1011) fitted with a glass electrode and saturated calomel electrode as reference, was standardized with buffers of known *pH* in acidic and alkaline medium. All reagents used were of AR grade. The solutions were purged with pure nitrogen gas for 10 min and then polarographed at ambient temperature. All the electrochemical experiments were carried out in an H-type cell. The working electrode and auxiliary electrode were platinum foil having a surface area of 1 cm^2. The reference was saturated calomel electrode. Preliminary studies revealed that this platinum foil thickness was suitable to produce a free-standing and durable conductive polymer film. The deposition of pyrrole and aniline in a solution of 0.02 M pyrrole, 0.1 M aniline and 1.0 M camphor sulphonic acid at a potential of -0.6 to 1.8 V was carried out on the Pt electrode using cyclic voltammetric technique. The composite film of polypyrrole and polyaniline coated electrode was washed with water and dried in vacuum at 50°C.

Reagents and materials

Aniline and pyrrole (Himedia) were used

after distillation under vacuum. Camphor sulphonic acid (CSA) (Aldrich chemical) was used as a doping agent. Cefdinir (99% pure) was a gift from the Drug Monitoring Research Institute (DMRI), Mumbai (India). Capsules containing cefdinir (Sefdin) labeled 300 mg were obtained from commercial sources. A stock solution of cefdinir (1×10^{-3} M) was prepared by direct dissolution in 0.02 M phosphate buffer pH 7.0. The diluted solutions were prepared daily by accurate dilution with 0.02 M phosphate buffer of pH 7.0 and supporting electrolyte 1 M KCl. A series of phosphate buffers of pH 2–11 were prepared. The pH of the buffer was checked using a pH meter (Decible DB–1011 digital pH meter) with a combined glass-calomel electrode of sensitivity ±0.02 pH units. All chemicals used were of analytical reagent-grade quality (Merck and Sigma) and were employed without further purification. High-purity water was obtained from Millipore (Milford, MA, USA) Milli-Q Plus system. All solutions were protected from light and used within 24 h to avoid decomposition.

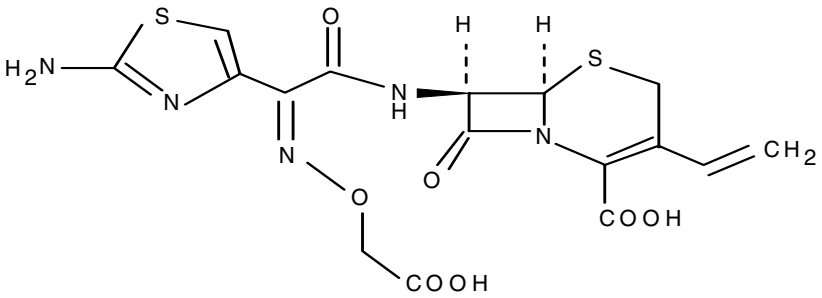
Capsule assay procedure

Cefdinir determination was performed on commercially available capsule dosage form Sefdin. Two capsules were emptied as completely as possible. The combining contents of the capsules were thoroughly ground to a fine powder. A sufficient amount of powder for preparing a stock solution of 1×10^{-3} M was weighed and transferred into a 25 mL calibrated flask and completed to volume with 0.02 M phosphate buffer pH 7.0. The content of the flask was sonicated for 10 min to provide complete dissolution and centrifuged. The sample from the clear supernatant liquor was withdrawn and quantitatively diluted with 0.02 M phosphate buffer pH 7.0 to get the desired concentration. This solution was then transferred to a voltammetric cell along with supporting electrolyte and the desired waveform was recorded.

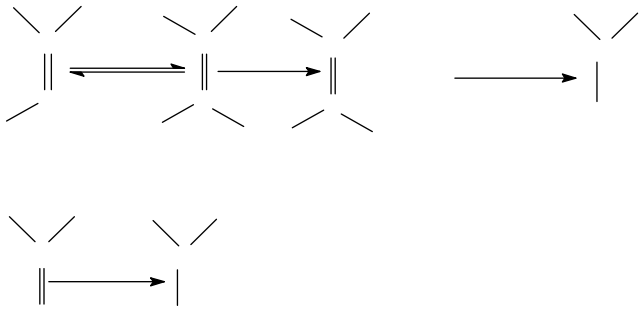
RESULTS AND DISCUSSION

Cyclic voltammetry

The thickness of the polymer film on the electrode surface (here the polymer thickness was 0.02 mm) is of importance because it is thin enough to allow the anion diffusion for the reactions to the electrode. Examination of the film with the optical microscope showed that this technique give



Scheme 1.



Scheme 2.

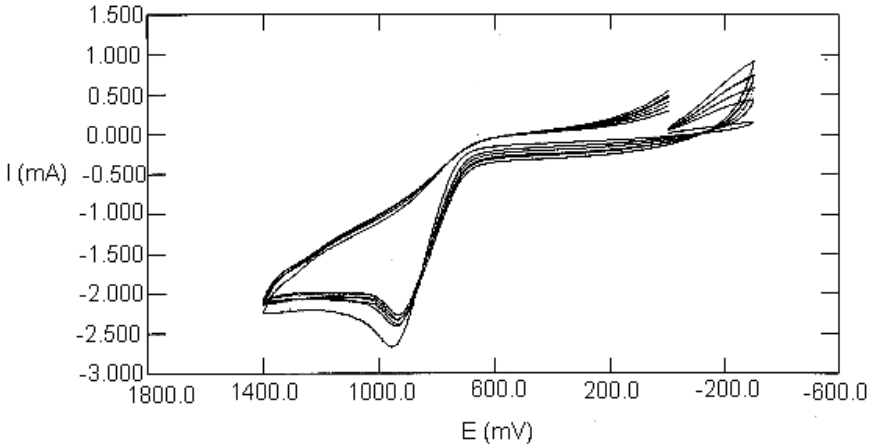


Fig. 1: Multiscan cyclic voltammograms of the Pt electrode in 1.0 M CSA containing 0.02 M pyrrole at a scan rate of 50 mV/ s

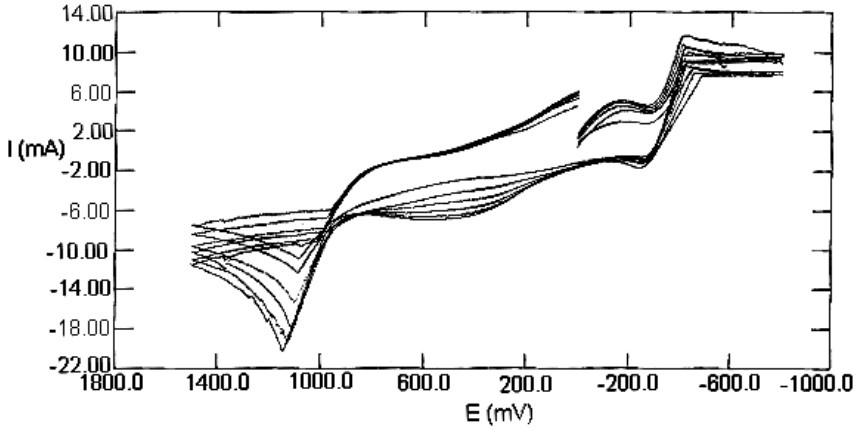


Fig. 2: Multiscan cyclic voltammograms of the Pt electrode in 1.0 M CSA containing 0.1 M aniline at a scan rate of 50 mV/s

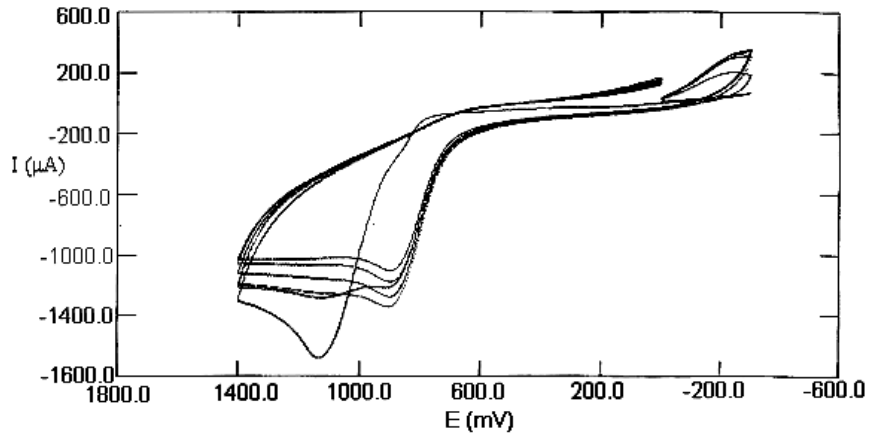


Fig. 3: Multiscan cyclic voltammogram of the Pt electrode in 1.0 M CSA containing 0.02 M pyrrole and 0.1 M aniline at a scan rate of 50 mV/s

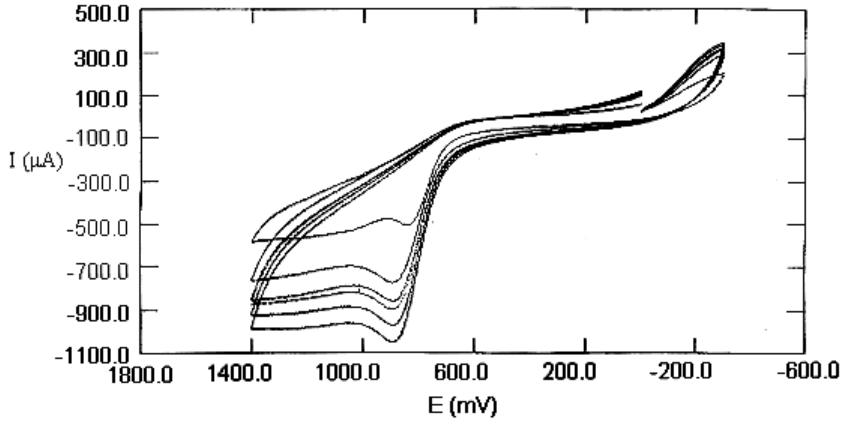


Fig. 4: Multiscan cyclic voltammograms of the Pt electrode in 1.0 M CSA containing 0.02 M pyrrole at a different scan rate

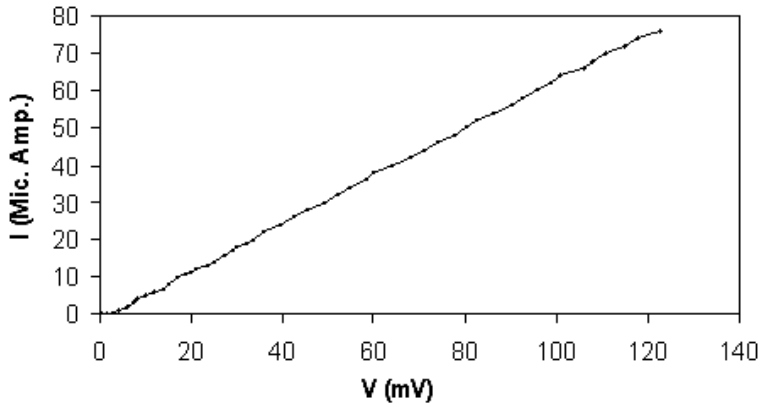


Fig. 5: Current-voltage characteristics of the composite polymer film

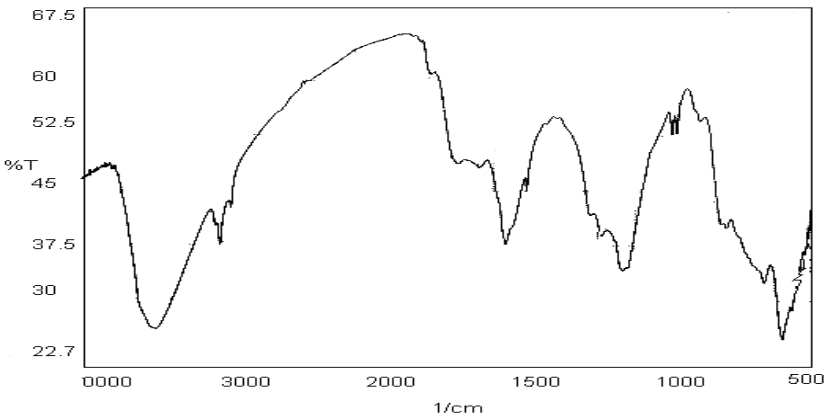


Fig. 6: FT-IR spectrum of the composite polymer film

homogenous polymer film. Thicker coating did not allow and the diffusion of the anion and due to this examination of organic compound becomes difficult. Fig. 1 shows the electrochemical deposition of polypyrrole on a platinum electrode, 0.02 M pyrrole and 1.0 M camphor sulphonic acid, peak at 942.0 mV, corresponding to the oxidation peak[19-24]. As the minima shifts upward, this indicates the polymer deposition. The peak at -382.0 mV corresponds to the reduction. The peak current decreases with the deposition of the polypyrrole. Fig. 2 shows the cyclic voltammetric curve of 0.1 M aniline on a Pt electrode in 1.0 M camphor sulphonic acid. In this case, a pronounced dip in the current was observed at the oxidation peak. This minimum reduces with the deposition of the polymer. Here pronounced peak was seen at 1144.0 mV. For polyaniline deposition both oxidation and reduction peaks are pronounced and are clearly seen. Fig. 3 displays the cyclic voltammetric curve on Pt electrode with 0.02 M pyrrole and 0.1 M aniline in 1.0 M camphor sulphonic acid with 50 mV/s scan rate. In Fig. 3 a unique graph was obtained, which is believed to be due to the initiation of polyaniline deposition on the platinum

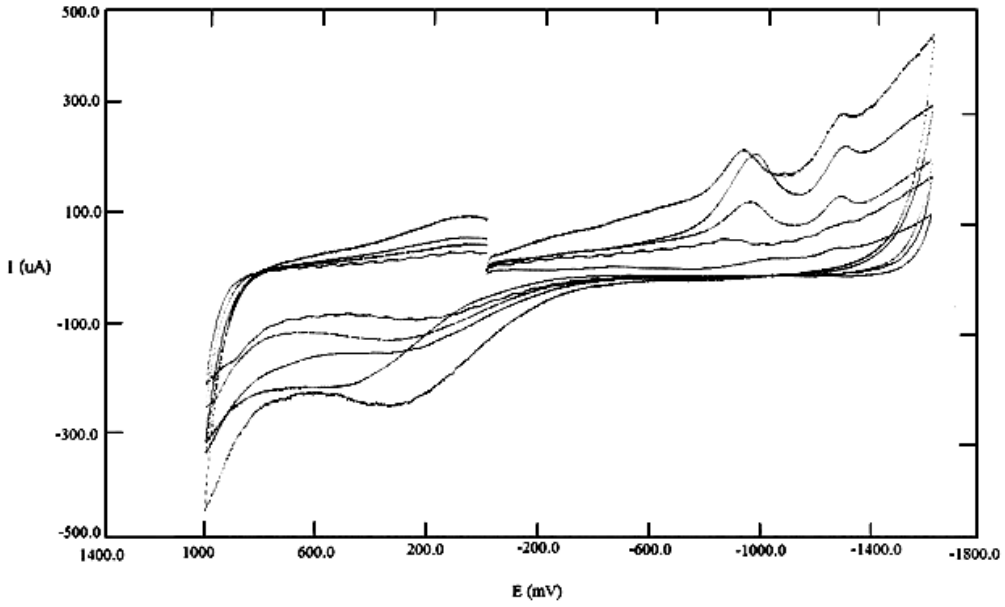


Fig. 7: Cyclic voltammograms of cefdinir at composite polymer as working electrode, at 50 mV/s scan rate

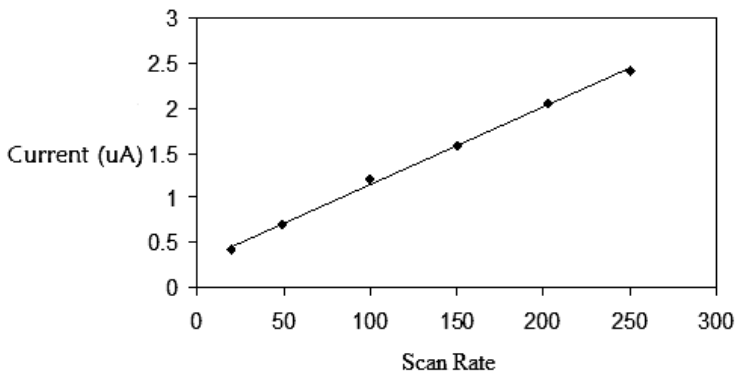


Fig. 8: Plot of different scan rate versus current for cefdinir at composite polymer electrode

electrode. After wends polypyrrole dominates the deposition process. Fig. 4 shows the cyclic voltammetric curve on Pt electrode with 0.02 M pyrrole, 0.1 M aniline in 1.0 M camphor sulphonic acid at different scan rate.

Current-voltage characteristics of composite polymer film

The thickness of the polymer coating at the electrode surface is very important because it limits the diffusion of the reactants towards the electrode surface. The thickness of the deposited polymer was around 0.02 mm. The prepared polymer composite was doped with camphor sulphonic acid which makes it batter conducting. The conductivity was measured by making silver contact at the surface of polymer. The observed Fig. 5 is a straight line and the slope of the line gives the resistance of the film, which is 1.5 KΩ. It shows ohmic behavior and resembled semiconductor like behaviour.

Infrared Spectra

Fig. 6 shows the FT-IR spectrum of the composite polymer film. The broad peak at 3358.07 cm^{-1} corresponds to N-H stretching. The peaks at 2922.16 and 2850.79 cm^{-1}, assigned to aliphatic CH_3 and CH_2, related to the alkyl chain attached to the benzene ring.

The peak at 1735.93 cm^{-1} corresponds to camphore (C=O), at 1454.33 cm^{-1} and 1300 cm^{-1} corresponds to C=C, and C-N stretching respectively. The C=N stretching bands of a quinoid structure at 1631.78 and 1554.63 cm^{-1} are from polyaniline. Further evidence of the presence of sulphonate anion in the polymer film is revealed by peaks at 1037.70 cm^{-1} and 1022.27 cm^{-1} respectively. An interesting feature is the presence of a strong C-H peak at 775.38 cm^{-1} characteristics of the pyrrole spectrum, but this was absent in the composite polymer spectrum.

Analysis of cefdinir at composite polymer membrane electrode

The shape and characteristics of cyclic voltammograms were strongly dependent on the pH of the medium. Peak potential shifted toward more negative potential with increased pH, indicating the involvement of protons in the electrode process.

The cyclic voltammogram of cefdinir 1.0×10^{-3} M in phosphate buffers (pH 2–11) at composite polymer membrane electrode exhibits two cathodic peaks due to the reduction of the C=N and C=C groups (Fig. 7). No peak was observed in the anodic direction, indicating the irreversible nature of the electrode process. For finding the adsorptive character of the drug at composite polymer membrane electrode on cyclic voltammogram. A maximum developed peak current (i_p) was achieved after preconcentration of the drug onto the electrode surface for 15 s, whereas the second cycle exhibited a smaller peak response that may be due to desorption of the drug species out of the composite polymer membrane electrode.

Millicoulometry was employed to find the number of electrons involved in the electrode process using the method and the number was found to be four for C=N (wave I) and two electron process for C=C (wave II) (Scheme 2) grouping for cefdinir.

On the basis of cyclic voltammetry (CV), differential pulse voltammetry (DPV), controlled pulse voltammetry (C_{pe}), coulometry, and spectral studies, the following mechanism may be postulated for the reduction of cefdinir.

CONCLUSION

The electroactivity of cefdinir on composite polymer membrane electrode was established and studied for the first time. The electrochemical reduction of cefdinir under the conditions described in this work is an irreversible process controlled by adsorption. The proposed cyclic voltammetric procedure can be used successfully to determine cefdinir in pharmaceutical formulation. Electrochemically deposited composite polymer membrane electrode on the platinum foil indicates good catalytic current response for the voltammetric determination of cefdinir drug. The current-voltage characteristic of the composite film was found to be linear which indicates a semiconducting behaviour. This composite polymer electrode also shows good stability with the solvent.

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