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STUDYING THE ELECTROCHEMICAL REDUCTION OF ANTIBACTERIAL CIPROFLOXACIN IN ITS PURE FORM AND DRUG FORMULATIONS

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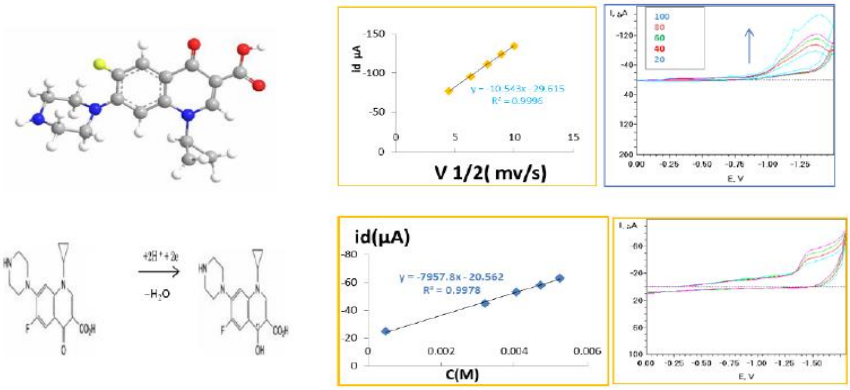
ABSTRACT
In this study, we investigated the electrochemical direction of the antibiotic ciprofloxacin (CIP) using the glassy carbon electrode as the working electrode and Silver/silver chloride**)** Ag/AgCl) electrode as comparative electrode, employing the cyclic voltammetric method. We examined the impact of varying concentrations on the electrochemical direction of CIP, observing a single cathodic wave during scans towards the most negative potentials. No wave was observed during scans in the opposite direction, indicating a one-stage controlled process of CIP direction with supported by a correlation coefficient R2 = 0.9987. To understand the transfer mechanism and kinetics of CIP molecules, we explored the effect of scanning speed on the electrochemical direction behavior of CIP by varying scanning rates (20-40-60-80-and100mV/s) at a constant CIP concentration. Our findings revealed that the movement of ciprofloxacin molecules from the solution to the glassy carbon electrode surface follows diffusional kinetics in a moderate medium. Additionally, we observed a linear increase in peak current with rising reactant concentration, with a correlation coefficient R2 = 0.9996. Continuing with the analytical and practical aspects of our research, we detected ciprofloxacin in pharmaceutical formulations. We examined a pharmaceutical tablet approved by the Syrian Ministry of Health and manufactured by (Medico), revealing that themedication content in the tablet was 98.23%. This percentage falls within the acceptable range as per the American and British Pharmacopoeia standards (90-110%).

KEYWORDS: Electrochemical Behavior, Polarography, Electrochemical Reduction, Carbon Glass Electrod, Ciprofloxacine.

Graphical chart



INTRODUCTION

Polarography is the most widely used electrochemical analysis technique in modern times. It involves recording current-potential (i-E) curves with a mercury electrode (DME) in the presence of an electrolyte. This method was developed by Herowski in 1922, earning him the Nobel Prize in 1959. Herowski also authored his first book "Principles of Polarography," explaining the fundamentals of this technique. Analytical chemistry statistics show that polarography was among the top five analysis methods from 1950 to 1970. Its popularity declined with the introduction of new organic separation methods like high-performance chromatography and advanced spectroscopic techniques. However, in recent years, polarography has regained significance in analytical chemistry due to technological advancements, including the production of electrodes with unique characteristics and the enhancement of electrical sensor technologies capable of detecting minimal current or potential values.

Different electrodes like mercury, gold, platinum, silver, and graphite are used to record potential-current curves. Despite this, the term "polarography" specifically refers to the use of a mercury electrode, as it was the original electrode employed in this technique. Other methods utilizing two electrodes are categorized under voltammetric methods.[1]

An overview of the studied compound

An overview of the studied compound

Ciprofloxacin (CIP) Chemical formula: C17H18FN3O3

Physical properties: It is a white crystalline powder, bitter in taste, and soluble in acetic acid, water, and methanol.

Ciprofloxacin is a well-known anti-inflammatory and antibacterial medication.[2] It is effective in treating respiratory and urinary tract infections.[3] This drug can be administered orally or through intravenous injection.[4] Overdosing on ciprofloxacin can lead to health issues like liver damage, hypersensitivity, and nerve problems.[5] Therefore, ensuring the accuracy of its dosage is crucial. Monitoring the concentration of ciprofloxacin in pharmaceutical preparations has become essential due to its widespread use, prompting researchers to investigate its properties and analytical methods.[6][7][8]

Chemists have turned to identifying ciprofloxacin in various pharmaceutical preparations,[9] either alone or in drug samples, using different methods like spectroscopy and liquid chromatography.[10] which are time-consuming.[11][12] As a result, attention has shifted to utilizing electrolysis techniques known for their high sensitivity and cost-effectiveness, as well as their shorter duration compared to other methods.[13]

The electrochemical oxidation behavior of ciprofloxacin was examined using a glassy carbon electrode as the working electrode and employing the differential pulse voltammetry method in various solutions within the pH range of (0.3-12). Ciprofloxacin undergoes oxidation, generating a single irreversible peak at high positive potentials, with the return process being diffusion-controlled.[14]

Furthermore, the electrochemical oxidation behavior of ciprofloxacin (CIP) was investigated using the differential pulse method and utilizing both a glassy carbon electrode (GC) and DNA-modified carbon (DNA-GC). It was observed that a single non-reversible anodic wave occurred. The modified electrode exhibited an improved shape of the polarographic wave and a wave shift. The oxidation occurred at lower positive potentials, enhancing sensitivity compared to the unmodified electrode.[15]

The compound ciprofloxacin was examined using a modified glassy carbon electrode, CO Fe2O4. A comparison was conducted between the modified and unmodified electrodes. The modified electrode exhibited a linear response for detecting CIP in the ranges of 0.1-1μm and 1-30 μm, with a detection limit of 0.036 μm. The electrode was produced in a pure spherical shape by the sol-gel method and can detect low concentrations of CIP at pH=7.[16]

A high-performance liquid chromatographic (HPLC) method was developed to determine various pharmaceutical compounds in bulk doses or tablets using a chromatographic column. The UV absorption wavelength was λ = 250 nm, and the mobile phase flow rate was 1 ml/min over 22 minutes. The correlation coefficients ranged from 0.9985 to 0.9998, and the percentage of mobile phase flow was 1ml/min over 22 minutes. The relative standard deviations for repeated analyses were below 5%, indicating the accuracy of the method. Thelimits of detection (LOD) and quantification (LOQ) ranged from 0.020-0.27 mg/l and 0.080-0.91 mg/l, respectively. The recoveries for pure compounds were between 86.0% and 102%, while in pharmaceutical tablets, it was -90.9% to 106%.[17]

The electrochemical behavior and characterization of a hybrid drug (ciprofloxacin and tobramycin) were investigated using the differential pulse voltammetry technique, with a bare glassy carbon electrode (GCES), and Ag/AgCl as a reference electrode.[18]

The Significance and Objective of the study

This study concentrated on utilizing electrochemical techniques, known as crucial clean and eco-friendly methods. The study also seeks to investigate the mechanism and kinetics of the electrochemical reduction process of the compound ciprofloxacin in both its pure form and pharmaceutical forms.

Chemicals and Work method

Equipment and tools used

To carry out this task, an amperometric volt-ampere station (AMELE 433) was utilized, along with a selection of external solid electrodes including the glassy carbon electrode and the Hg/Hg2CL2/KCL comparative calomel electrode. Various techniques were employed: Polarography, Voltammetry, Stripping, as well as generating the traditional polarographiccurve (DC), normal pulse (NPP), differential pulse (DPP), and cyclic voltammetry method, by adjusting different parameters like the initial potential and final potential of the voltage curve. Factors such as amperometrics, scan rate, and purging time were considered, along with identifying the peak potentials associated with the mesoscopic processes and their magnitudes.

Chemicals used

Ciprofloxacin 99.9% purity from Sigma Aldrich, Ciprofloxacin from Medico, KCL 99.9% purity from BATCH company and Double distilled water.

Method of work

Studying the electrochemical reduction of ciprofloxacin in mild medium

Method of work

Investigating the electrochemical retrieval of ciprofloxacin in a moderate solution

We examined the electrochemical retrieval of ciprofloxacin in a moderate solution with the presence of a supporting electrolyte (0.5 M KCL) using the volt-amperometric terminal on the glassy carbon electrode, employing the cyclic voltammetric technique. Samples were prepared at various concentrations, and the following parameters were identified: the initial return potential (0.00 mV) and the final return potential (-1800 mV), along with a scanning rate of(50 mV/s). Dissolved oxygen was eliminated with nitrogen for twenty minutes, and the appropriate procedure was implemented. The polarogram depicted in (Fig 1) was generated:

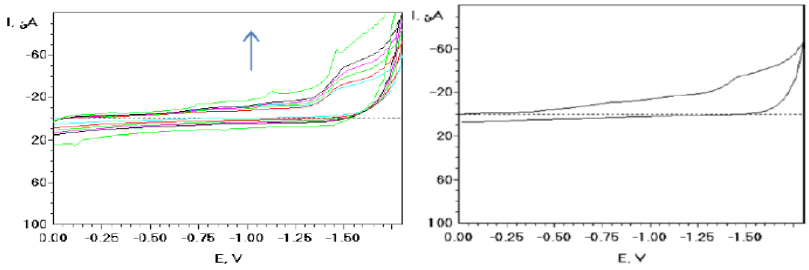


Figure 1: Cyclic voltaic curve of ciprofloxacin on a glassy carbon electrode in mild medium (0.5 M KCL).

From the preceding polarogram, we observe a single cathodic wave emerging when scanning towards the most negative potentials. However, no wave is observed when scanning backtowards the more positive potentials, indicating that the return process occurred in a single stage.

Studying the effect of changing concentration on the electrochemical reduction of ciprofloxacin in moderate medium

In furtherance of the analytical aspect of our research, we investigated the impact of varying the concentration on the electrochemical reduction process of ciprofloxacin in a mild medium on a glassy carbon electrode using the cyclic voltammetric technique. To achieve this, a standard series was prepared with varying ciprofloxacin concentrations: (5×10-4M, 3.214×10-3M, 4.722×10-3M, 5.681×10-3M). The samples were prepared in 25 ml volumetric flasks using 0.5 M KCL. Following parameter determination, the starting potential for the reflux was 0.0 mV, the ending potential was -1800 mV, and the scanning rate was 50 mV/s. The solution's dissolved oxygen was eliminated by bubbling with nitrogen gas for 20 minutes. A polarogram was recorded for each concentration, as depicted in (Fig 2).

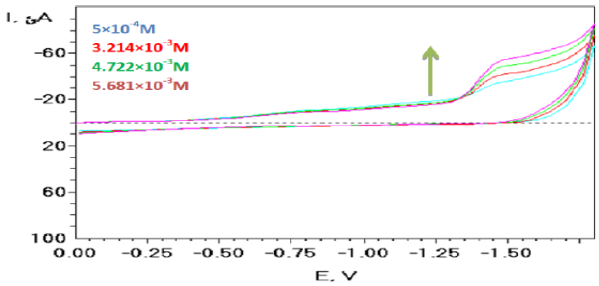


Figure 2: Cyclic voltaic curves of ciprofloxacin on a glassy carbon electrode at different concentrations in the mild medium (0.5 M KCL).

We observed in the previous polarogram that the reflux process occurred in a single stage. Additionally, we observed a rise in the current limit values as the ciprofloxacin concentration in the sample increased. To understand the connection between the current limit values and concentration, we plotted a relationship between Id and C as depicted in (fig3).

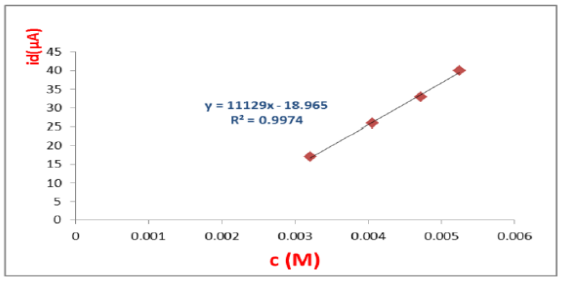


Figure 3: Relationship between polarographic wave Intensity and Concentration.

We observe from the figure that the correlation between concentration and current intensity is linear, with the correlation coefficient reaching (R2=0.9974).

Calculate the number of electrons transferred in the electrochemical reaction process

To determine the number of electrons during the reaction process, we calculated the transfer coefficient (α) by graphing the relationship between log io in terms of log c as shown in (Fig4):

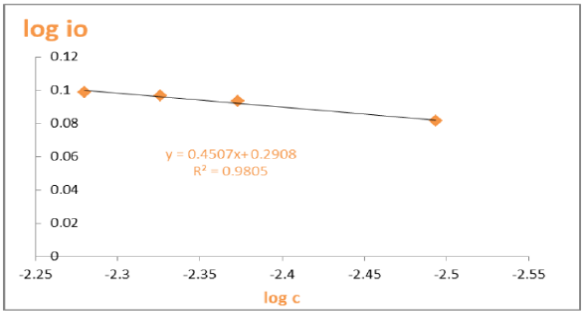


Figure 4: The relationship between log io and log c of the polarogram of the return of ciprofloxacin in the moderate medium.

By deducing the value of α, we find that α = 0.5493 By calculating the number of electrons using the graphic curve between E, log id-i/i for one of the polarographic curves, as shown in (Fig 5)

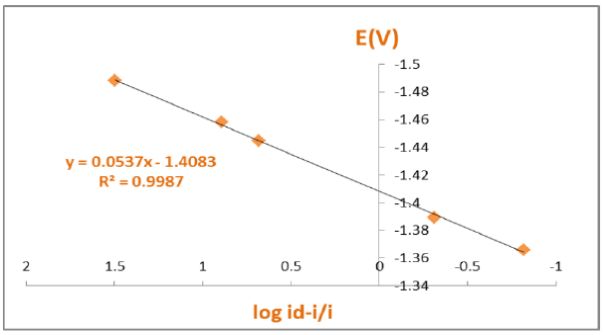
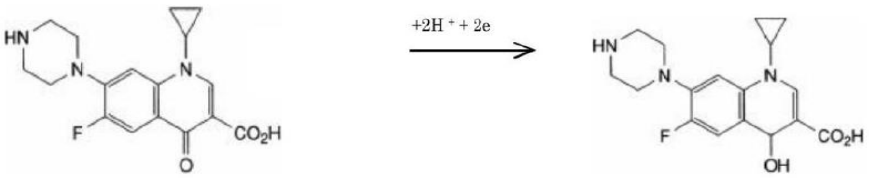


Figure 5: The relationship between E and log id-i/i of the polarogram of the return of ciprofloxacin on a glassy carbon electrode in moderate medium.

We observe that the slope of the line is m = 0.0537. By utilizing the relationship m = 0.059/αn, we deduce that n = 2.

Proposed mechanism of reaction:



It is compatible with Reference[19]

Studying the impact of scanning speed on the electrochemical reduction of ciprofloxacin in moderate medium

The electrochemical reduction of ciprofloxacin was investigated in a mild medium (0.5 M KCL) as a supporting electrolyte, at various scan rates (20, 40, 60, 80, and 100 mV/s), to elucidate the mechanism of ciprofloxacin molecule transfer from the solution depth to the glassy carbon electrode surface using cyclic voltammetry. The study aimed to determine if the electrochemical return process follows diffusional kinetics by analyzing changes in peak current intensity with varying scan rates, as depicted in Fig. 6.

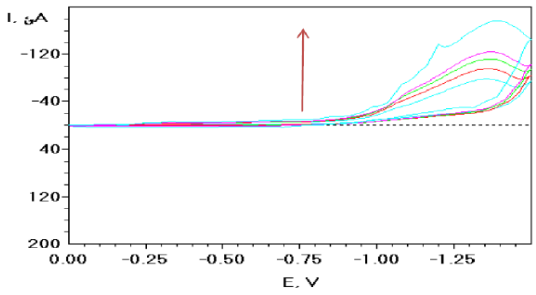


Figure 6: Effect of scanning speed on the electrochemical reduction process of ciprofloxacin on a glassy carbon electrode in mild medium.

We observe from the figure that the current limit values rise as the potential scanning speed increases, and to elucidate the connection between the change in the current limit values and the change in the applied scanning rates, the relationship between the current and the square root of the applied scanning speed rates was depicted as in (Fig 7).

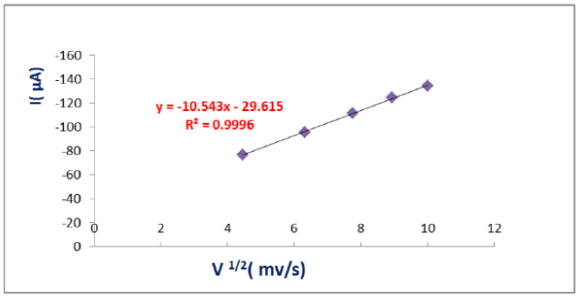


Figure 7: The relationship between the limiting current (id) and the square root of the scanning speed (v 1/2) in the electrochemical reflux process of cebrofloxacin on a glassy carbon electrode in a moderate medium.

The figure illustrates a linear relationship between the limit values of the current and the square root of the applied scanning rates, with a correlation coefficient R2 = 0.9996. This indicates that the transfer mechanism of ciprofloxacin molecules in the moderate mediumfrom the solution depth to the surface of the glassy carbon electrode follows diffusion kinetics.

Analysis of drug samples

In this phase, we examined the practical implications of our findings by applying them to the analysis of pharmaceutical samples approved by the Syrian Ministry of Health. We selected five medicinal tablets from the (Medico) preparation, crushed them, took the equivalent weight of one tablet, and dissolved it in a 25 ml volumetric flask with 5 ml of methanol. The volume was then adjusted to 25 ml using a 0.5 M KCL solution. The contents were stirred until fully dissolved. Subsequently,

the solution was filtered, and the cyclic voltammetric curve shown in (Fig 8) was obtained.

The limit current for the sample was determined, followed by the calculation of the concentration value corresponding to the current. Based on this, the percentage of the active substance in the medicinal preparation was determined to be 98.23%, falling within the acceptable range as per the American and British Pharmacopoeia (90-110%)[20] for commercial preparations. This sample meets the required criteria.

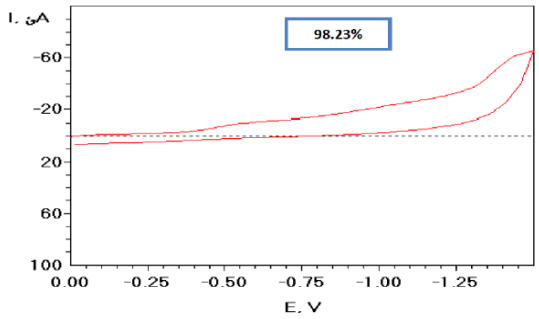


Figure 8: Cyclic voltammetric curve for analysis of a pharmaceutical tablet containing ciprofloxacin in mild medium and on a glassy carbon electrode.

SUMMARY AND CONCLUSIONS

- ✓ In this study, we investigated the electrochemical reduction behavior of the antibiotic ciprofloxacin on a glassy carbon electrode in a mild medium, both in its pure form and pharmaceutical forms.
- ✓ Our research yielded insights into the kinetics governing the reaction and the mechanism of reactions occurring in a moderate medium involving only two electrons.
- ✓ The reflux process in the moderate medium (0.5 M KCL) is subject to diffusional kinetics.
- ✓ Analysis revealed that the active ingredient's percentage in the sample is 98.23%, falling within the acceptable range according to the American and British Pharmacopoeia (90-110%).

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