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STUDY ON THE INTERACTION OF Zn(II) ION WITH METRONIDAZOLE DRUG IN AQUEOUS MEDIUM USING ELECTROCHEMICAL TECHNIQUES

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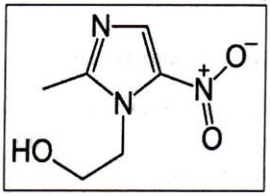
Abstract

This study includes the investigation of redox behavior of Zn^{2+} ion and its electrochemical nature when interacts with pharmaceutical drugs metronidazole. This research was carried out using cyclic voltammetry (CV), chronoamperometric (CA) and chronocoulometric (CC) techniques. The redox process of the Zn ion system in presence and in absence of metronidazole is diffusion controlled as well as adsorption controlled. This fact is supported by both CA and CC. The redox process of Zn ion system is quasireversible but almost irreversible in presence of metronidazole. pH change affects the redox behavior sharply and maximum interaction accurse at pH%.

Key words: Electrochemical properties, Redox processes, Cyclic voltammetry, Chronoamperometric, Chronocoulometric

Introduction

The redox studies of biologically active compounds are gaining importance for various purposes. Such redox phenomena are close to the natural redox processes occurring in human and other living organisms. Chemical reaction occurring in living systems are numerous and complex (Prescher and Bertozzi 2005 and Dube *et al.* 2004), many of them are redox reaction. Introduction of other biologically active compounds such as, medicinal compounds may alter the pathway of the redox reaction mechanism occurring at the biological system. The complexion capacity of biologically active organic compounds with selected metals plays an important role in metabolism of biological systems (Ross *et al.* 2006 and Cox *et al.* 2010). This capacity may be significantly changed with the introduction of the medicinal compounds. They may also form complexes that are non-toxic, soluble in biological system and readily eliminated from body, saving it from toxic effect. Simultaneously, excess use of the drugs also causes drastic changes in charge transfer in the biological system. Therefore, study of metal-medicinal compounds interactions is very important [Sigel and Sigel 2004).



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Zinc is one of the metallic elements which are essential to human health (Prasad 1995). These elements, along with amino and fatty acids as well as vitamins, are required for normal metabolic processes (Sandstead 1994 and Mc Carthy *et al.* 1992). On the other hand metronidazole is a common medicine used by human being (Zar *et al.* 2007, Tally *et al.* 1972 and 1975). Investigation of mechanism of electrochemical interaction between the essential trace element like Zn and metronidazole is extremely important. Among all the techniques, the cyclic voltammetry is extremely popular in electrochemical research, because it can provide useful information about redox systems (Heinze 1984).

Materials and Methods

Chemicals, Reagents and Equipments: Analar grade zinc sulphate (MERCK, Germany), metronidazole (Aldrich Chemical Co. Ltd., England) and potassium chloride (MERCK, Germany) were used in the experiments. The buffers were prepared using sodium acetate (MERCK, Germany) and acetic acid (Sigma-Aldrich Laborchemikaline, GmbH). Cleaning of the electrodes and all the solutions were prepared using de-ionized water. Before electrochemical measurements 99.997 % Nitrogen from Bangladesh Oxygen, Ltd. was used for purging the solution.

This study was carried out using an Epsilon Electroanalyser developed by Bioanalytical System, Inc., USA. A glassy carbon electrode was used as working electrode, which was cleaned by polishing on cloth using alumina powder. Ag/AgCl electrode and Pt wire were used as reference and counter electrodes, respectively. An AGE (Velp Scientifica) magnetic stirrer with a teflon coated magnetic bar was employed for stirring and a pH meter (Mettler, Toledo) was used in measuring of the pH of the solutions. All glasswares used in the preparation of solutions were of borosilicate glass.

Results and Discussion

Cyclic voltammetric study of aqueous Zn^{2+} ion: The redox behavior of 1 mM solution of uncoordinated Zn^{2+} ion was studied in 0.1M KCl as supporting electrolyte at room temperature (25 °C) using cyclic voltammetry with potential window from 200 mV to -1500 mV at glassy carbon electrode. A series of cyclic voltammograms (Fig. 1) of the uncoordinated Zn^{2+} ion in KCl electrolyte at different scan rates was taken to understand the scan rate effect on the redox behavior. The related parameters listed in Table 1 show that for the anodic peaks, the peak potentials gradually decreased as the scan rate increased and for the cathodic peaks, the peak potentials gradually increased with the increase of scan rate.

In both cases the increasing and decreasing rate of potential was very small. This behavior can be described by slower charge propagation, probably due to difference in salvation or permeability (Bard and Faulkner 2000, Conway 1965 and Nicholson 1965).

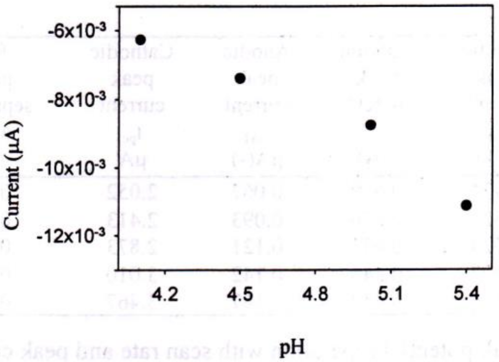

Fig. 6. Peak current *vs* pH plot for the redox behavior of Zn^{2+} ion in absence of ligand.

Interaction of Zn^{2+} ion with Metronidazol: The CV of Zn^{2+} ion was also studied in presence of metronidazol to understand whether there is any interaction between the metal and the drug molecule. CVs of Zn^{2+} ion and metronidazol solutions and CV of Zn^{2+} in presence of the ligand metronidazol are overlayed in Fig 7. From the figure it is seen that the number of peaks and their positions in the CV of Zn^{2+} ion in presence of drug molecule was different from that of the CVs of uncoordinated Zn^{2+} ion and metronidazol, which indicates that the Zn^{2+} ion interact with the drug molecule and make complex compound. The CVs of interactions of Zn^{2+} ion and metronidazol for 1:1 ratio at different scan rates are presented in Fig. 8. The shape of the voltammogram indicates that in presence of metronidazole the redox system of Zn(II) ion becomes almost irreversible. The very small anodic peak was almost negligible. The figure indicates that the peak current increases with scan rates. The interactions for different ratios of metal and ligand, nearly similar CVs wrer obtained. The data obtained from the Fig. 8 are recorded in Table 2.

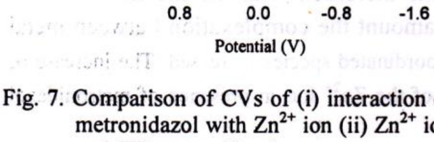

Fig. 7. Comparison of CVs of (i) interaction of metronidazol with Zn^{2+} ion (ii) Zn^{2+} ion and (iii) metronidazol.

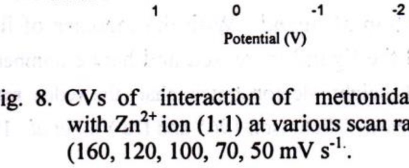

Fig. 8. CVs of interaction of metronidazol with Zn^{2+} ion (1:1) at various scan rates (160, 120, 100, 70, 50 mV s^{-1}.

Table 2. Current-potential data for the interaction of Zinc and Metronidazol (1:1) at different scan rates.

Scan rate (v) Vs^{-1}	SQRT of scan rate $v^{1/2}$	Anodic peak poten^{l} E_{pal} V(-)	Cathodic peak poten^{l} E_{pc} V(-)	Anodic peak current i_{pal} μA(-)	Cathodic peak current i_{pc} μA	Peak poten^{l} separation ΔE V	Peak current Ratio $E_{pc}-E_{pal}$ i_{pal}/i_{pc}
0.050	0.2236	0.475	0.619	0.067	2.052	0.144	0.033
0.070	0.2645	0.521	0.636	0.093	2.413	0.129	0.038
0.100	0.3162	0.524	0.637	0.121	2.873	0.119	0.042
0.120	0.3646	0.527	0.645	0.142	3.010	0.118	0.047
0.160	0.4000	0.541	0.652	0.167	3.467	0.111	0.048

The variations of peak potential separation with scan rate and peak current with SQRT of scan rate are presented in Figs. 9 and 10 respectively. Peak potential separation decreased with the increase of scan rate which is of opposite trend to that of Zn^{2+} ion in absence of the metronidazole. The peak current of both cathodic and anodic peaks increased as the scan rate increased, but the increase rate for anodic peak current was very small. Table 2 indicates that as the scan rate increases the peak current ratios (i_{pal}/i_{pc}) also increase. The values of the ratios were lower than unity. So the charge transfer system is not reversible (Irving and Nicholas 1964 and Bond and Stephan 1998).

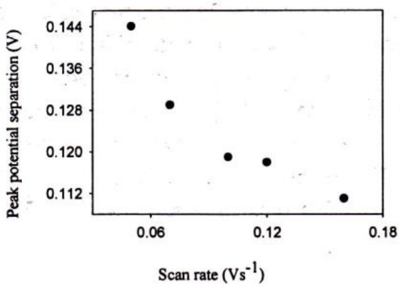

Fig. 9. Variation of peak potential separation against scan rate for the interaction of Zn^{2+} solution and metronidazol.

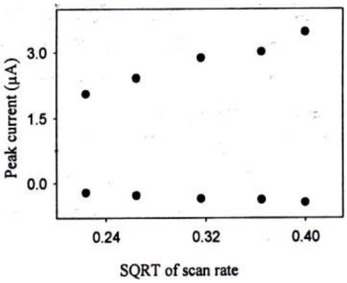

Fig. 10. Variation of peak current against SQRT of scan rate for the interaction of Zn^{2+} solution and metronidazol.

Effect of Concentration: The CVs of the Zn^{2+} ion with different concentration of ligand are presented in Fig. 11 and the peak current data are listed in Table 3. The Table shows that both the anodic and cathodic peak currents increased with the increase of mole fraction of ligand. With the increase of ligand amount the complexation between metal and the ligand increased and hence number of coordinated species increased. The increase of peak height demonstrates that the redox reaction of the Zn^{2+} ion in presence of metronidazol increases (Nicholson 1965 and Du Vall *et al.* 1999).

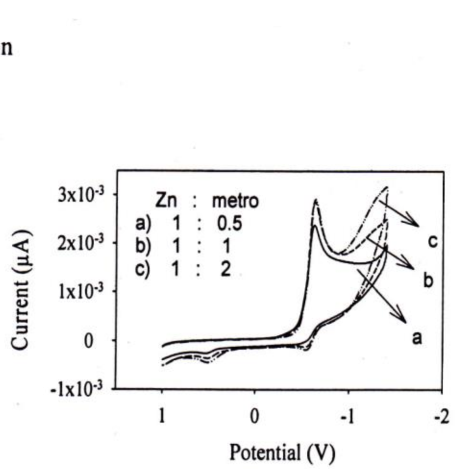

Fig 11. CVs of interaction of metronidazol with Zn^{2+} ion with different concentration of the ligand.

Table 3. Current and peak current ratio of the voltammogram of the interaction of Zn^{2+} with metronidazol at different ratio at 160 mVs^{-1} scan rate at GCE.

Zn^{2+}: Metronidazol	Molefraction of Metronidazol	Anodipeak current (i_{pa1}) μA (-)	Cathodic peak current (i_{pc}) μA	Peakcurrent ratio ($i_{pa1/ipc}$)
1:0.5	0.33	0.306	2.6981	0.1134
1:1	0.50	0.383	3.0049	0.1275
1:2	0.66	0.498	3.1711	0.1570

Chronoamperometric and chronocoulometric study of Zn^{2+} ion: Chronoamperometric study of aqueous Zn^{2+} ion in the presence and in absence of metronidazol were performed. Fig. 12 shows that the spike height for Zn^{2+} ion after interaction with metronidazol decreased compared to that of Zn^{2+} ion in the absence of metronidazol.

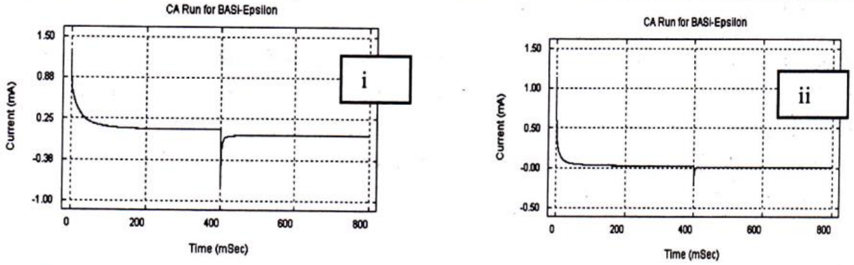

Fig 12. Current responses for (i) uncoordinated Zn^{2+} and (ii) coordinated with metronidazol.

This means that after interaction the rate of electrolysis decreased, which support the result of CV experiment. Chronocoulometric study also shows that the charge at τ decreased after interaction with metronidazol. It was 67.21 μC in the absence of metronidazol, whereas it became 52.14 μC in presence of metronidazol, as shown in Fig. 13.

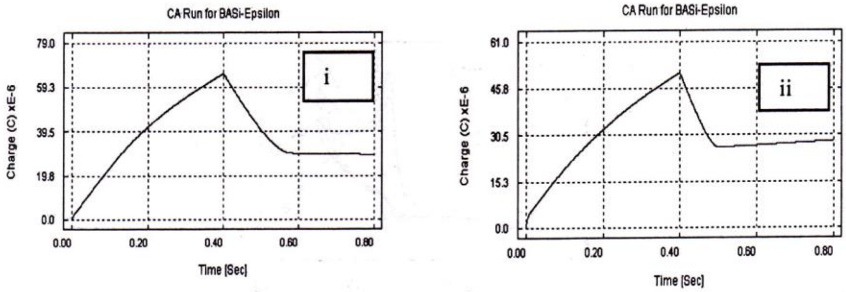

Fig. 13. Charge responses for (i) uncoordinated Zn^{2+} and (ii) coordinated with metronidazol.

Fig. 14 represents the plots of Q vs $t^{1/2}$ and $-Q_r$vs θ on the same graph for the uncoordinated and coordinated Zn^{2+} with metronidazol. The two plots did not intersect at $Q = 0$ axis as well as they do not have equal slope. Therefore it may be said that in both cases adsorption occurs (Conway 1965 and Nicholson 1965).

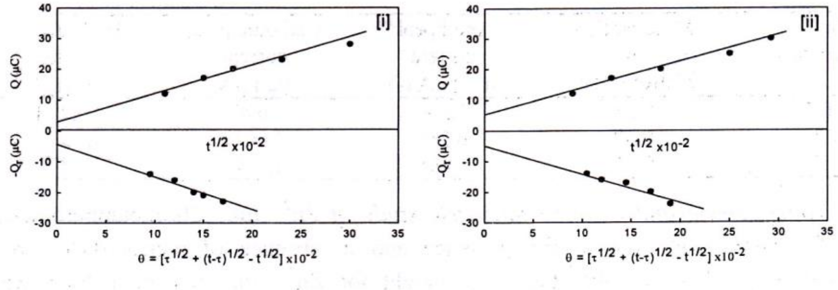

Fig. 14. Plots of Q vs $t^{1/2}$ and $-Q_r$vs θ for (i) uncoordinated Zn^{2+} ion and (ii) coordinated Zn^{2+} ion with metronidazol

Chronoamperometric and chronocoulometric study of uncoordinated and coordinated Zn^{2+} in buffer system was also studied. All the CA and CC experiments support the CV experiments. The plots of Q vs $t^{1/2}$ and $-Q_r$vs θ on the same graph for every experiment also confirmed that the all redox system in this experiment occurs by adsorption (Conway 1965 and Nicholson 1965).

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