Interaction of Mn(II) and Zn(II) with ciprofloxacin antibiotics

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Abstract

The aim of this study is to check the redox behavior of Mn(II) and Zn(II) metals before and after interaction with ciprofloxacin in potassium chloride solution by using cyclic voltammetry, chronoamperomety and chronocoulometry methods. Equimolar solutions of Mn(II) and ciprofloxacin were mixed to a ratio of 1:2 and that of Zn(II) and ciprofloxacin to a 1:1 ratio. The results showed that the redox couple involved in Mn (II) as well as Mn(II)-ciprofloxacin interaction systems are quasi-reversible. However, the Zn(II) systems showed reversibility and the Zn(II)-ciprofloxacin interaction was quasi-reversible. The results obtained from the chronoamperometric study showed that after interaction with ciprofloxacin the rate of electrolysis in the metal systems decreased.

Introduction

Since the ancient times, the world populations rely on the plant based medicine for the cure of human diseases. However, the natural resources are limited and it is not enough to manage the mankind. Recently, the demand of various metals with antibiotics complexes in the field of health sectors as well as the pharmaceutical industries is constantly increasing. The world populations are facing problem with drug-resistant bacteria and it is increasing number tremendously. Therefore, it is urgent to find an alternative new, better sensitivity, cost effective and more acceptable active synthetic drugs. One of the better and most acceptability are to achieve the target through metals-antibiotics complexes. Several authors already reported the preparation of metals-antibiotics complexes and various methods of characterization and their bioactivity (Ketan *et al.,* 2012; Uivarosi V, 2013). Most of the cases, the authors are getting more biologically active metals-antibiotics complexes that could be used as medicines to treat diseases.

Ciprofloxacin belongs to a drug class known as the fluoroquinolone and is classified as second-generation synthetic antibiotic (Nelson *et al*., 2007; Kawahara 1998). It acts on the bacteria that interfere with the enzymes and also stops DNA as well as protein synthesis. A good number of infections are treated by this specific kind of anti-microbial which includes infections of respiratory tract, bones, urinary tract, joints, cellulitis, chancroidetc. (Enzman *et al.,* 1999).

An essential as well as a trace nutrient is manganese in all life forms (Emslay, 2001), has prominent roles in the biological systems and about 12 mg is contained by the human body. It is specifically stored in the tissue as well as in the bones and remains in the liver and kidneys in concentrated forms. Zinc is an essential element present in trace amounts and is distributed all over the body of human in an amount of 2-4 grams (Rink and Gabriel, 2000).

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Semen being a fundamental factor is not only in the function of prostate gland but also the growth of reproductive organ and is particularly rich in zinc. The literature search showed that there are reports available on the metal-ciprofloxacin complexes (Ketan *et al.,* 2012; Uivarosi V, 2013). Therefore, the principle aim of this research is to describe the interaction between ciprofloxacin antibiotics with the above metal ions in solution as the former is extremely important in the disorder treatments and the later in the biological system.

Materials and methods

Reagents and solutions

Various reagents and chemicals such as ciprofloxacin hydrochloride, manganese chloride, zinc chloride and potassium chloride were of reagent grade. Deionized water was used for cleaning as well as other purposes and for purging 99.997% nitrogen was employed.

Equipment

An Epsilon electrochemical work station made by Bioanalytical Systems, Inc. (USA) was employed for the current-voltage measurements. In this work a voltammetric cell made of borosilicate glass in a C3 cell stand (three electrode electrolysis system) was used and GCE (Glassy carbon electrode) was used as working electrode, Ag/AgCl (satd. KCl) as reference electrode as well as a platinum wire was used as counter electrode. An AGE (Velp Scientifica) magnetic stirrer was used for the agitation of all the solutions.

Preparation of metal-antibiotics stock solutions for interactions

Equimolar solutions of Mn(II) and ciprofloxacin were prepared in 0.1M of KCl and mixed to a ratio of 1:2. Then, it was stirred well and settled for 3 hours for successful interaction. After that the solution was taken for the study. Similarly solutions of Zn(II) and ciprofloxacin of same molar concentrations were prepared and mixed to a 1:1 ratio and after interaction, the solution was studied by using different methods.

Results and discussion

The most frequently used electrochemical technique is cyclic voltammetry in the case of collecting electrochemical reaction's qualitative information which specifically provides a rapid location of redox potentials of the electroactive species and suitable assessment on the medium effect on the redox process. It is often considered to be the gateway of electroanalytical study.

In the current work, the redox behaviours of Ciprofloxacin, Mn (II) and Zn (II) were studied first, where 0.1M of potassium chloride (KCl) solution was employed as supporting electrolyte. Then the analysis was accomplished for metal-ciprofloxacin interactions, where the ratios for the interactions of Mn (II) and Zn (II) with ciprofloxacin were 1:2 and 1:1 respectively.

Various potential windows employed, as the ranges are dependent on different aspects such as solvent, electrode material, supporting electrolyte and the solution acidity. The windows of potential were from -2.300 V to 2.000 V for ciprofloxacin, -0.900V to 1.500V for Mn(II) and -1.700V to -0.400V for Zn (II). Those were also altered for the studies after interactions. It was from -1.400V to 2.000V for Mn(II)-cirpofloxacin interaction and in case of Zn(II)-cirpofloxacin interaction, it is -1.700V to -0.400V. For all the systems, scan rate variations were also examined and it was done at six different scan rates, which were 0.050 Vs^{-1}, 0.100 Vs^{-1}, 0.150 Vs^{-1}, 0.200 Vs^{-1}, 0.250 Vs^{-1} and 0.300 Vs^{-1}.

Chronoamperometry as well as chronocoulometry were also involved in the present study, as those methods have attained their significance in specifying the rate of electrolysis and adsorption criteria of a system. To accomplish these techniques, at first CV is done and then in relation to the set of peaks found, the chronoamperometry is done and its integrated form, the chronocoulometric response is also acquired from it.

In cyclic voltammetric study, Mn (II) shows two pair of peaks and so for it two sets of chronoamperometric experiments were accomplished but for Zn (II) only one is there. Again after interactions, in all the cases, there is only one set of experiment as the CV responses are of only one pair.

Cyclic voltammetry

Redox behavior of Mn (II) before and after interaction with ciprofloxacin

The redox behaviour of Mn (II) before and after interaction with ciprofloxacin was studied using cyclic voltammetric technique at different scan rates, at room temperature, employing glassy carbon electrode (GCE) and in 0.1M of potassium chloride (KCl).

The CV before interaction shows two cathodic (c_1 and c_2) and two anodic (a_1 and a_2) peaks. But after interaction, there are two cathodic peaks (c_1 and c_2) and one (a) anodic peak. Again after interaction, both c_1 and c_2 shift towards more negative potential. Both the above facts prove that the Mn (II)-ciprofloxacin interaction is successful (Rahman *et al.,* 2007; Islam *et al.,* 2009).

With increasing scan rate (Fig. 1) c_1 and c_2 before interaction and c_1 after interaction moves in the direction of less positive potential. Whereas, a_1 and a_2 before interaction as well as a and c_2 after interaction shifts towards more positive potentials.

Again almost all the peaks both before and after interaction become broader with increasing scan rate which has been assigned to be slower charge propagation, may be as a result of difference in salvation as well as permeability (Akhtar et al., 2008a).

The potential for the peak separation (Fig. 2) escalates with the increasing scan rate both before and after interaction, signifying the iR drop effect (Gosser, 1993; Zhang and Anson, 1992) and also indicates the limitation due to charge transfer kinetic (Bear et al., 1992). Similarly in both the cases, the forward scan peak currents for both forward and backward scan are consistent with the square root of the scan rate, declaring the systems as diffusion controlled (Gosser, 1993; Mascus et al., 1996). The processes are adsorptive controlled (Bear et al., 1992; Bard and Faulkner, 1986: Bockris and Reddy, 1970) which can be concluded by the fact that with an increase in $v^{1/2}$, the peak currents for all the peaks as well as both the pairs have linear increase (Fig. 3).

For the first pair of peaks, the peak current ratio after interaction does not show any traditional character. Same is the case for the Mn(II) system before interaction with the ligand. Hence the conclusion is that exceptional character is shown by the system from the reversible behavior (Gosser, 1993; Mascus et al., 1996; Nicholson and Shain, 1964).

With increasing scan rate, both of the peak current ratio and peak current function ($i_p/v^{1/2}$) increase before interaction (Fig.

4 and 5) and these facts indicate towards the electrochemical process (Akhtar et al., 2009) that does not follow EC mechanism. But after interaction these facts are absolutely opposite indicating that it may follow EC mechanism (Nicholson and Shain, 1964).

A linear relationship is shown by the log i_p versus log v plot both before and after interaction and also the slope is less than unity, which declares diffusion controlled (Fig. 6) process.

Tafel plot which is the plot of peak potential vs log v, of both before and after interaction (Fig. 7) express the slopes not to be zero and provides the conclusion that it is not reversible (Gosser, 1993).

On the whole, it is found that the electrochemical process in Mn-system both before and after the interaction with ciprofloxacin is found quasi-reversible. In addition, the system is diffusion as well as adsorptive controlled.

Redox behavior of Zn(II) before and after interaction with ciprofloxacin

Zn (II) before and after interaction with ciprofloxacin was also studied to have a view of their redox behaviour with the same set up as Mn(II) system. The CV before and after interaction shows same number of peaks but the position of peaks shifted. The cathodic and the anodic peaks move towards more negative and less negative potential values respectively with increasing scan rates.
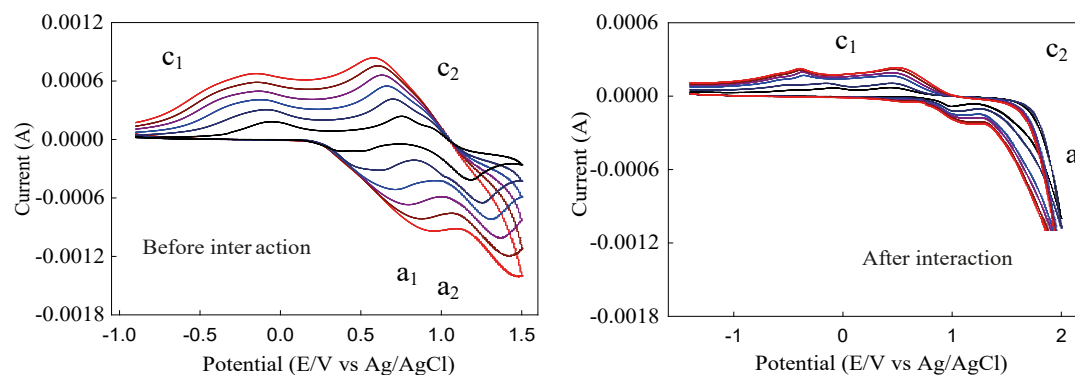

Fig. 1. Cyclic voltammogram of Mn(II) before and after interaction with ciprofloxacin at different rates in 0.1 M of KCl solution.
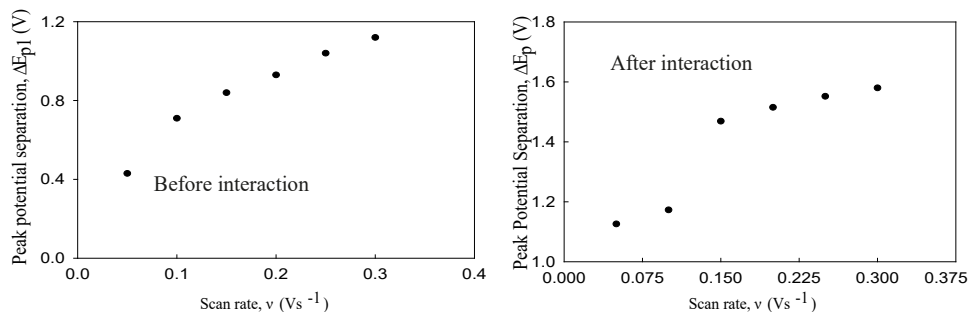
Fig. 2. Peak potential separation variation with scan rate for Mn(II) before and after interaction with ciprofloxacin in 0.1 M of KCl solution (first pair of peaks)
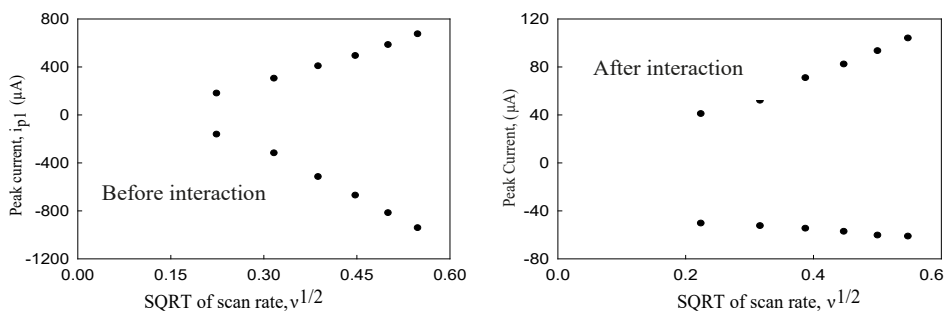

Fig. 3. Peak current variation against square root of scan rate for Mn(II) before and after interaction in 0.1M of KCl with ciprofloxacin (first pair of peaks)
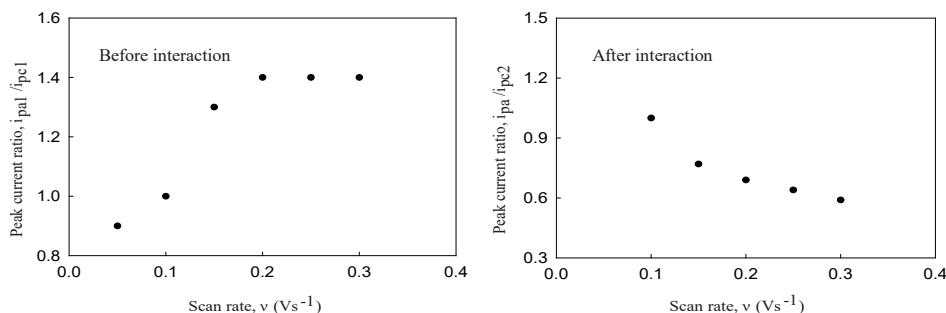

Fig. 4. Peak current ratio variation against scan rate for Mn(II) before and after interaction in 0.1 M of KCl solution with ciprofloxacin (first pair of peaks)
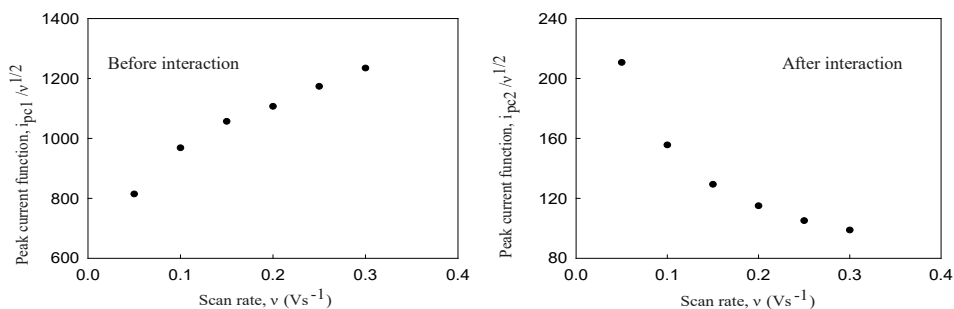

Fig. 5. Peak current function variation against scan rate for Mn(II) before and after interaction with ciprofloxacin in 0.1M of KCl solution (first pair of peaks)
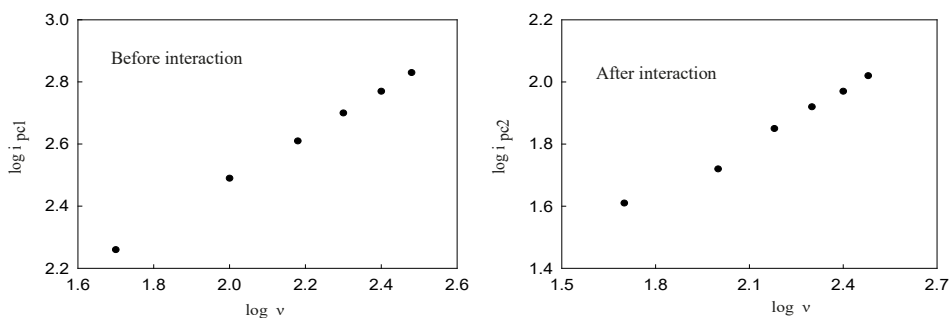
Fig. 6. Plot of log ip versus log ν for Mn(II) before and after interaction with ciprofloxacin in 0.1 M KCl (first pair of peaks)

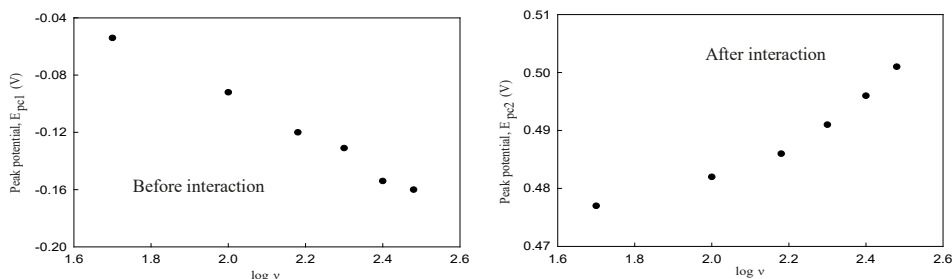**Fig. 7. Peak potential variation against log ν for Mn(II) before and after interaction with ciprofloxacin in 0.1 M KCl solution (first pair of peaks)**
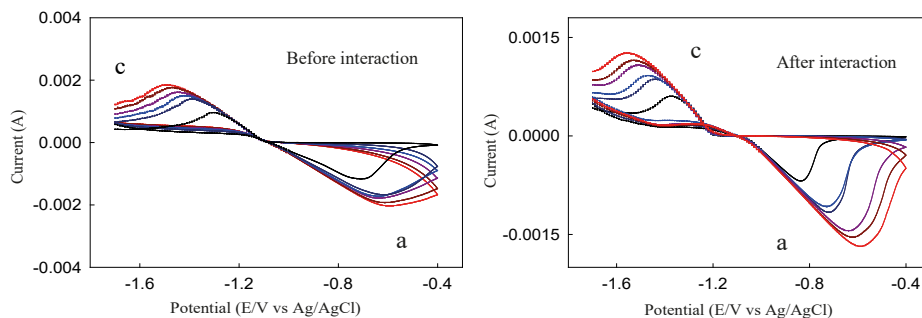

Fig. 8. Cyclic voltammogram of Zn(II) before and after interaction with ciprofloxacin in 0.1 M KCl solution at different scan rates

At different scan rates (Fig. 8) voltammograms of Zn(II) before and after interaction shows similar character. Moreover, all the signals are becoming broader which are assigned to slower charge propagation, may be as a result of difference in permeability as well as salvation.

The peak potential separation before and after interaction increases with the increases in scan rate due to the result of iR drop which indicates the limitation as a result of charge transfer kinetics.

The (i_{pc}) vesus $\nu^{1/2}$ plot indicates the system to be diffusion controlled before and after interaction. The process is proved to be adsorptive controlled.

A strong evidence for reversibility is that at all the scan rates, the peak current ratio before interaction is very much nearest to unity. But after interaction, are very much higher than unity showing almost exceptional character from reversibility.

After interaction it does not show any explicit decision about electrochemical process, which is found from the facts that both

of peak current ratio as well as peak current function ($i_p/v^{1/2}$) increases and decreases respectively with increasing scan rate.

The graph of log i_p versus log v exhibits a linear connection and slope less than unity both for before and after interaction, showing the process to be accompanied by diffusion. The slope before interaction is not zero but is about to zero for the Tafel plot indicating the electrochemical process to be reversible. While after interaction it is not zero which signifies exception from reversible character.

All the above findings give the conclusion that the electrochemical process involved in Zn(II) before and after interaction is near to reversible and quasi-reversible respectively. Also the systems are diffusion and adsorptive controlled as well.

Chronoamperometric and chronocoulometric study

Chronoamperometric (CA) and chronocoulometric (CC) techniques were also involved to study the interaction of all the above metals before as well as after interaction with ciprofloxacin.

The CA study of Mn(II) before interaction was done corresponding to two pairs of peaks found in CV. But after interaction, the study was done corresponding to one pair of peaks as there was one anodic peak after interaction. It was found that after interaction with ciprofloxacin the spike heights are decreased (Fig. 9). Again as the rate of electrolysis (Akhtar *et al.*, 2008b) is proportional to the spike height, it can be concluded that after interaction rate of electrolysis is decreased. This also gives a clear indication towards successful interaction between metal and ligand. Similar type of observations are found for Zn (II) system.

CC study shows that after interaction, the charges are decreased at τ for all the systems (Table II) which indicate that the metals interact with the ligand in solution.

In addition to that CC shows some characteristics. If on the same graph, Q value acquired from time less than τ is plotted against $t^{1/2}$ and also $-Q_r$ is plotted versus $\theta = [\tau^{1/2} + (t-\tau)^{1/2} - t^{1/2}]$ for all the systems, there appears two straight lines not intersecting each other at Q=0 axis (Fig. 10) and not have

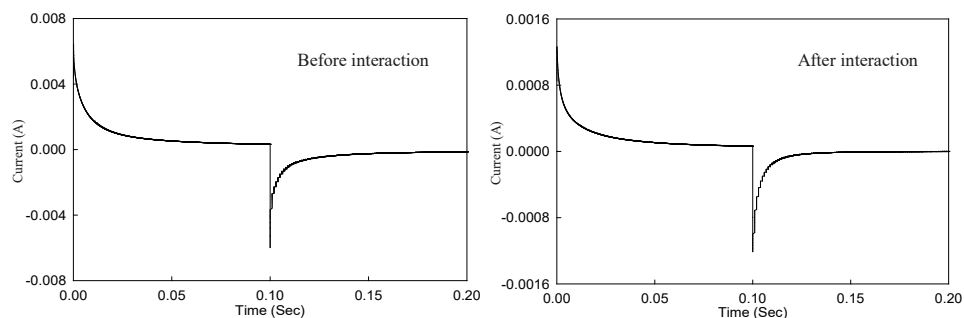**Fig. 9. Current responses for Mn(II) before and after interaction with ciprofloxacin in 0.1 M KCl solution**

Fig. 10. Plots of Q vs t1/2 and –Qr vs θ for Mn(II) before and after inaction with ciprofloxacin in 0.1M of KCl solution
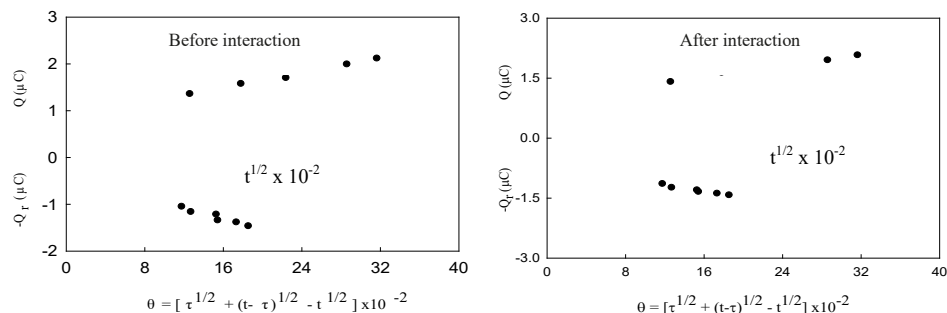
Table I. Current-potential data for the interaction between Mn(II) and ciprofloxacin at different scan rates in 0.1M of KCl solution

Scan rate	SQRT of scan rate	Cathodic potential	peak	Anodic peak potential	Cathodic current	peak	Anodic peak current	Peak potential separation	Peak current ratio
v (Vs^{-1})		E_{pc1} (V)[-]	E_{pc2} (V)	E_{pa} (V)	i_{pc1} (μA)	i_{pc2} (μA)	i_{pa} (μA)[-]	$\Delta E_p = E_{pa}-E_{pc2}$(V)	i_{pa}/i_{pc2}
0.050	0.2236	0.075	0.477	1.051	60.25	41.11	50.21	1.126	1.22
0.100	0.3162	0.089	0.482	1.084	86.22	52.21	52.32	1.173	1.00
0.150	0.3872	0.358	0.486	1.111	111.84	71.08	54.47	1.469	0.77
0.200	0.4472	0.362	0.491	1.153	137.35	82.45	57.04	1.515	0.69
0.250	0.5000	0.365	0.496	1.187	163.71	93.55	60.22	1.552	0.64
0.300	0.5477	0.369	0.501	1.211	180.25	104.15	61.04	1.580	0.59

Table II. Charge at τ derived from CC study of different systems for both pair of peaks

Systems	Charge at τ (μC)			
	Before interaction		After interaction	
	First pair	Second pair	First pair	Second pair
Mn(II)	2.211	2.483		1.745
Zn(II)	4.659		1.362	

equal slopes (Bard and Faulkner, 1986; Kambara, 1954) as well, which indicates that on the electrode adsorption of reactant or products occur (Barcley and Anson, 1969). Therefore the CA and CC study give the ideas (i) in the solution interaction occurs between the metals and ciprofloxacin (ii) both before and after interaction for all the systems on the electrode, adsorption of reactant or products occur (Akhtar and Ehsan, 2020).

Conclusion

The fundamental aspect found in the above cyclic voltammetric study indicates towards successful interaction. Mn(II)-ciprofloxacin as well as Zn(II)-ciprofloxacin interactions are quasi-reversible. In addition to that almost all the systems are diffusion controlled and adsorptive controlled too. Chronoamperometric study shows that after interaction there is decrease in the electrolysis rate. And the chronocoulometric study provides the observation that in all the cases there are deceases of the charge at τ. A successful interaction between metal and ligand is indicated by both of these facts combindly. The findings from the plots Q vs t$^{1/2}$ and -Q$_r$ vs θ gives the idea of adsorption of reactant or products after interaction on the electrode.

Acknowledgement

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