

SHORT COMMUNICATION

Cyclic voltammetry of bulk and nano manganese sulfate with Doxorubicin using glassy Carbon electrode

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Abstract

The cyclic voltammetry of both bulk manganese sulfate (BMS) and nano manganese sulfate (NMS) were studied using 0.1M KCl supporting electrolyte and glassy carbon working electrode. The redox behavior for both bulk (BMS) and MnSO_4 (NMS) sulfate was studied voltammetrically in presence and absence of Doxorubicin (DR) using three electrodes system, silver-silver chloride (Ag/AgCl), platinum and glassy carbon electrodes. Various scan rates were studied for the redox behaviors for bulk and nano MnSO_4 (NMS) alone or in presence of Doxorubicin (DR). Stability constants for the interaction of manganese ions with Doxorubicin (DR) were evaluated. The redox mechanism was discussed.

Keywords: Cyclic voltammetry; Doxorubicin (DR); Manganese sulfate; Redox mechanism; Glassy carbon electrode.

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INTRODUCTION

Drug doxorubicin (DR) is used for certain types of bladder, breast, lung, stomach, and ovarian cancer; Hodgkin's lymphoma (H. L) and also non-Hodgkin's lymphoma, N. H. L (cancer begins in the cells of the immune system); and also some types of Leukemia, L. K. (cancer of the white blood cells), including acute lymphoblastic Leukemia (LK) besides acute Myeloid Leukemia. Doxorubicin (DR) is used in combination with some other medications for treating certain types of thyroid cancer, certain types of soft tissue and bone sarcomas (cancer that forms in bones and muscles). It is used to treat neuroblastoma (a cancer that begins in some cells like nerve cells and occurs in children) and Wilms' tumor cancer (a type of kidney cancer that occurs in children). Doxorubicin (DR) (Fig. 1) belongs to class of medications called anthracyclines. It works with decreasing the cancer cells growth in the bodies [1, 2].

EXPERIMENTAL

Materials: Manganese sulfate (MnSO_4) and KCl provided from Al Nasr Chemicals Co., while nano

MnSO_4 (NMS) was prepared by ball milling using Retsch MM 2000 swing mill with 10 cm³ stainless double walled tube. Two balls stainless steel with diameter of 12 mm are used. Ball milling was performed at 20225 Hz and shaking was done at room temperature 25° for one hour, temperature did not rise above room temperature.

Instrument:

DY2000, DY2000 EN Multichannel Potentiostat was used for voltammetry measurement Voltammetry analyzer using conventional three - electrode electrochemical cell to perform cyclic voltammetry (CV). Measurements were done by using glassy carbon readymade electrode in our laboratory from pure carbon piece, polished with aluminum oxide in wool piece, as working electrode (WE) with geometrical area of 2 cm², platinum wire electrode as counter electrode and Ag/AgCl (saturated) standard electrode.

Cyclic voltammetry measurements (CV)

Cyclic voltammetry is the most common techniques used to study the electrochemical systems which obtained in undivided glass cell of

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30 ml solution with three electrodes mentioned above. Cyclic voltammetry experiments were carried out using different concentrations of bulk (BMS) and nano MnSO_4 (NMS) solutions in water at 19.3 °C KCl (0.1 M) as supporting electrolyte was used at different scan rates (0.1, 0.05, 0.02 and 0.01 V/sec). After each run, the working electrode was polished with aluminum oxide (α alumina), rinsed with distilled water to obtain reproducible results. The solutions were purged with purified nitrogen gas for (10) min. before each experiment.

RESULTS AND DISCUSSION

TEM Images for nano MnSO_4

The photogram from TEM transmission electron microscope is presented for nano MnSO_4 (NMS) salt. TEM images are sensitive so, it was used to investigate the size and shape of the nano MnSO_4 , (NMS) fluids which found to be spherical in the range 11.1-24.3 nm Fig. 2.

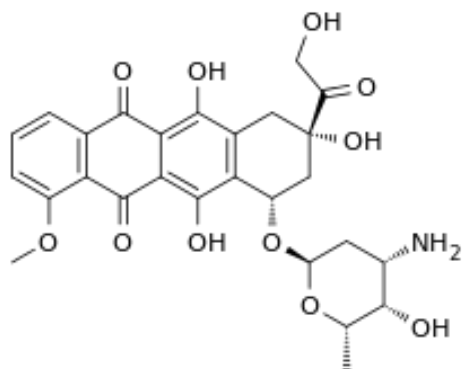


Fig.1: Structure of Doxorubicin.

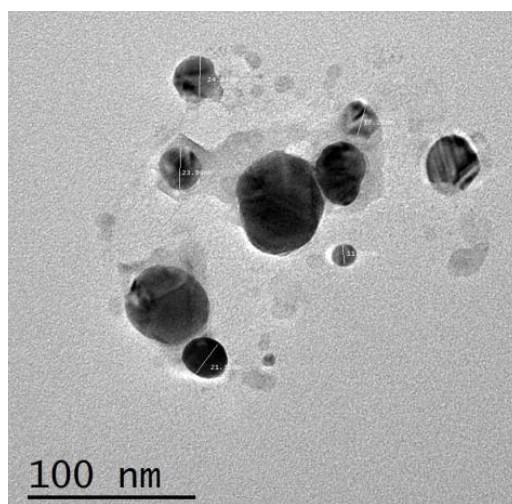


Fig. 2: TEM image of nano MnSO_4 .

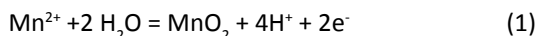
Cyclic voltammetry

The interaction of bulk manganese sulfate (BMS) and nano MnSO_4 (NMS) with doxorubicin (DR) has been studied using cyclic voltammetry technique in the potential range (+2 to -1.5) V at different scan rates in water at 292.15K using KCl (0.1M) as supporting medium and glassy carbon as a working electrode. The study is valuable for evaluating the thermodynamic properties [3, 4].

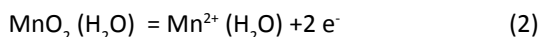
Mechanism of redox reaction

The manganese ions used show two oxidation peaks at +1 V and +0.5 V and two reduction peaks at 0.7 V and 0 V. Oxidation of Mn^{2+} to MnO_2 by two steps and the reduction took place by two steps also at 0.7 and 0 volts consuming two electrons for each process. Each step in the oxidation and reduction consumes one electron. The mechanism can be illustrated as [5]:

Oxidation process:



and reduction process:



The reduction process proceeds by two steps. These two cathodic peaks corresponding to the reduction of Mn (II) to Mn (I) at 0,7 V and the second cathodic peak corresponds to the reduction of Mn (I) to Mn (0).

Adding drug doxorubicin (DR) decrease all the four peaks of manganese sulfate solutions both bulk (BMS) and nano (NMS) indicating complex interaction behaviors between the drug and the manganese a salts as seen in Fig. 3 on the use bulk (BMS) and nano (NMS) .From Fig. 3 for using 1 mmole (1×10^{-3}) bulk (BMS) and Fig. 4 it is observed that the complex is formed due to the anodic and cathodic peak decrease and potential shifts their position to more lower values for using 1mmole bulk manganese sulfate (BMS) with the addition of doxorubicin (DR). Linear sweep voltammetry (LSV) for the cathodic and anodic peaks for 1:3 complexes formed by the interaction of bulk manganese ion (BMS ions) and doxorubicin(DR) in Fig 5 and at different scans for Fig. 6 (0.1 and 0.05 V/sec) were also done and supported the potentials taken from cyclic voltammetry (CV).

The effect of different scan rates for the redox mechanisms were studied for bulk manganese sulfate (BMS) were studied for 1mmole salt as seen in Fig. 7 indicating that both reduction and oxidation processes are diffusion controlled mechanism.

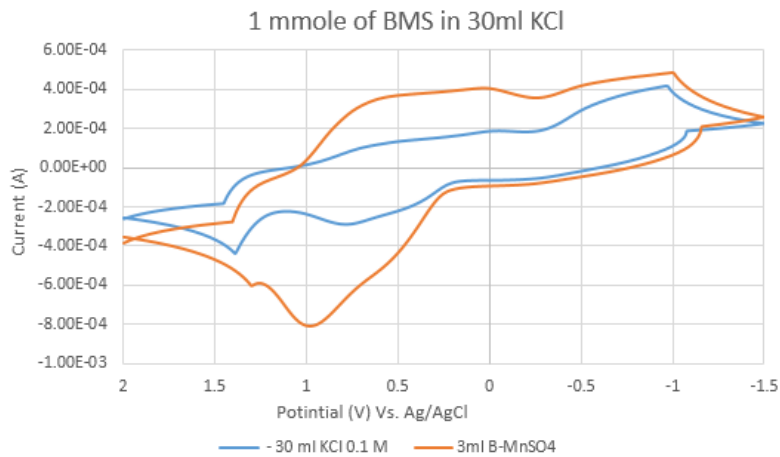


Fig. 3: Cyclic voltammetry for BMS (concentration= 1×10^{-3}) in 30ml KCl (0.1M) at scan rate 0.1 (V/sec), sens (A/V) = 1×10^{-3} .

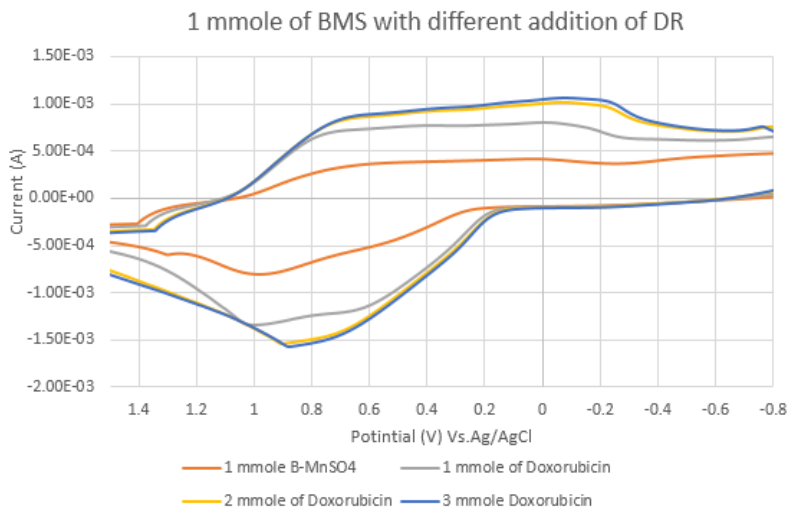


Fig. 4: Cyclic voltammetry for BMS 1 mM and DR with concentration (1×10^{-3} , 2×10^{-3} , 3×10^{-3}) at scan rate 0.1(V/sec), sens(A/V) = 1×10^{-3} .

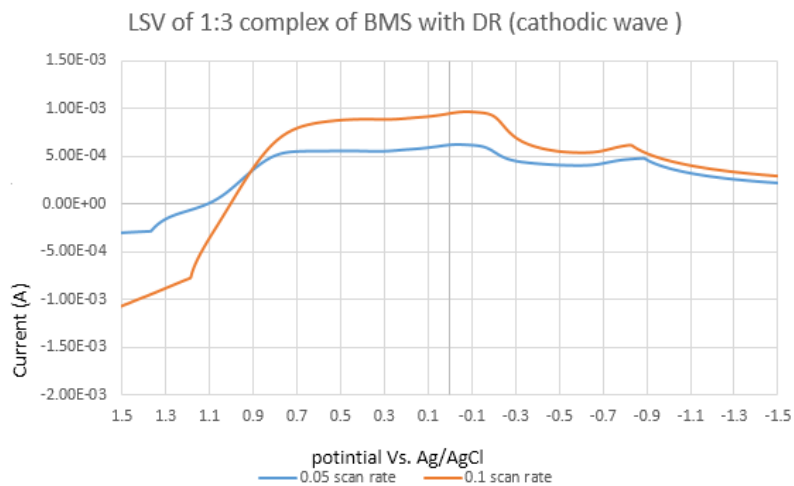


Fig. 5: Linear sweep voltammetry, LSV for cathodic wave of 1:3 complex of BMS with DR at different scan rate 0.1,0.05 (V/sec).

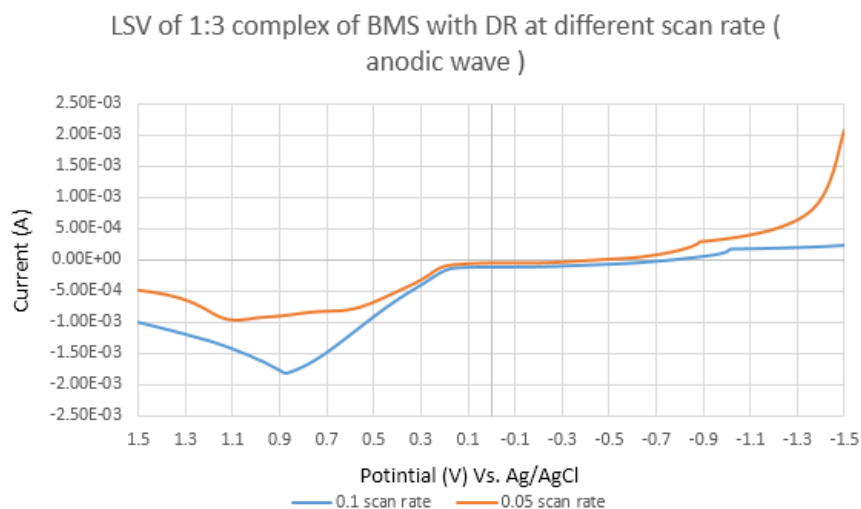


Fig. 6: Linear sweep voltammetry, LSV for anodic wave of 1:3 complex of BMS with DR at different scan rate 0.1,0.05 (V/sec).

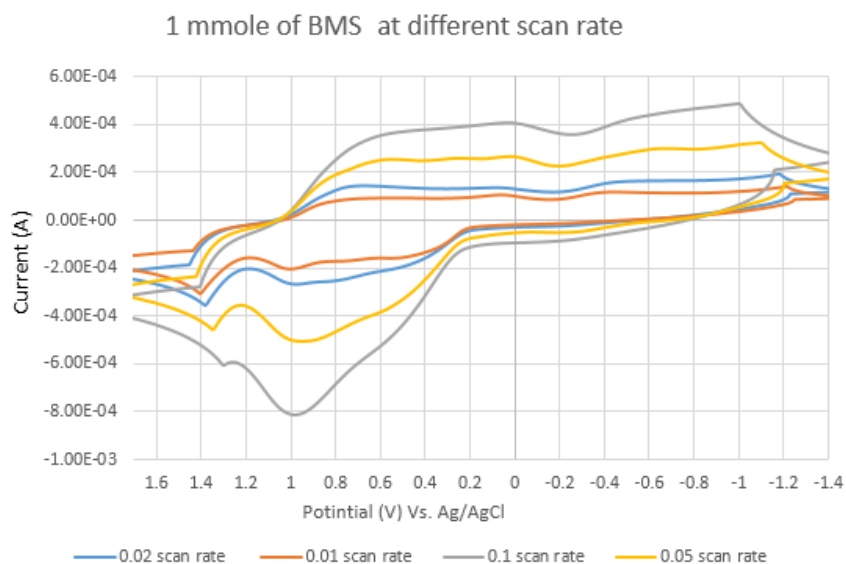


Fig. 7: Effect of different scan rate for BMS at concentration 1mM. the scan rates were maintained at 0.1,0.05, 0.02 and 0.01 (V/sec), sens(A/V) = 1×10^{-3} .

Redox behaviors of nano manganese sulfate (NMS) salt

The redox cyclic voltammetry (CV) for nano manganese sulfate (NMS) were done as shown in Fig. 8 for 1 mmole nano manganese sulfate (NMS) and we can observe that redox solvation behaviors proceed through mainly one step at 0.8 V vs. Ag/AgCl as shown in the corresponding Figure in comparison to that of the supporting electrolyte. The second wave was appeared also better in reduction process at 0.15.

As represented in Fig. 9 the effect of different scan rates on the redox behavior of nano

manganese sulfate (NMS) in KCl medium at 0.1, 0.05, 0.02 and 0.01 (V/sec), sens(A/V) = 1×10^{-3} indicate that both oxidation and reduction processes are diffusion controlled. Aqueous solvent study in this case is interesting other than non aqueous solvents (organic solvents) because in the latter type of solvents small ionization and little amounts of ion produced favouring not seen voltammograms.

Adding doxorubicin to nano manganese sulfate (NMS) shifts the reduction waves to more negative potentials and shift oxidation waves to less negative ones as clear in Fig. 10 indicating the

complex reaction between drug and salt.

Linear sweep voltammetry (LSV) for the cathodic and anodic peaks for 1:1 complexes formed by the interaction of nano manganese sulfate (NMS) with doxorubicin (DR) at two scan rates 0.1 and 0.05 V/sec, were experimentally studied and presented in Figs. 11 and 12 supporting the potentials obtained in aqueous 0.1M KCl solution for further calculation. The analysis of the complex formation was done and the diffusion coefficients were estimated and found to be within the range of diffusion reactions. Due to precipitating the complex during the process, no peak is appeared.

A stability constant is a measure of the strength of the interaction between the reagents that come together to form complex.

The stability constant (β_{MX}) for bulk (BMS) and nano $MnSO_4$ (NMS) complexes in 0.1 M KCl at 0.9 and 0.5V potentials for oxidation peaks, current 1mA and scan rate 0.1V/S in water was calculated [6, 7] by applying equation (1).

$$(E_p)_M + (E_p)_C = 2.303 \frac{RT}{nF} \text{Log} \beta_{MX} + 2.303 \frac{RT}{nF} \text{Log} C_X \quad (1)$$

Where $(E_p)_M$ is the peak potential of metal at final adding in absence of ligand, $(E_p)_C$ is the

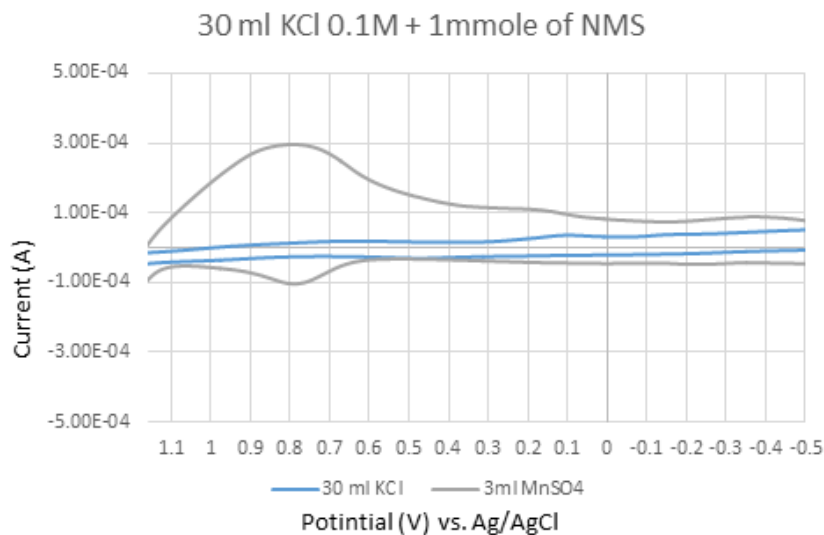


Fig. 8: Cyclic voltammetry for NMS (concentration= 1×10^{-3}) in 30ml KCl (0.1M) at scan rate 0.1 (V/sec), sens (A/V) = 1×10^{-3} .

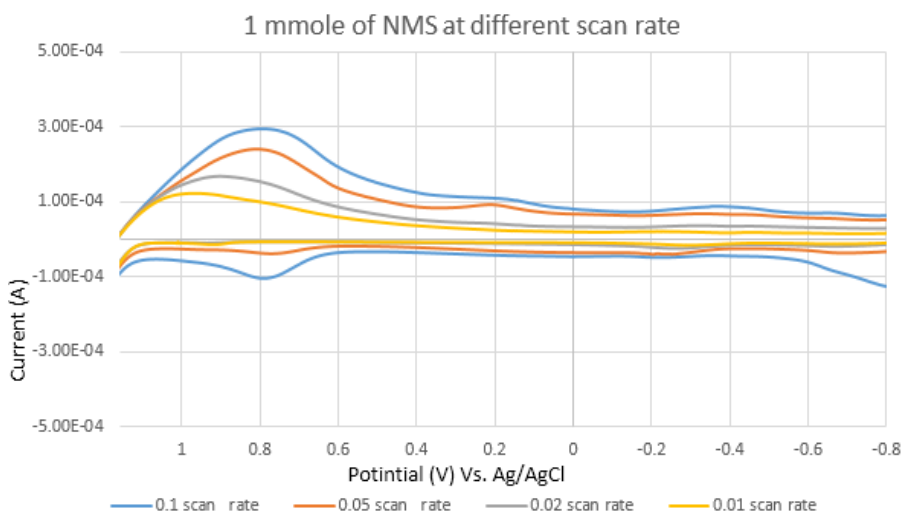


Fig. 9: Effect of different scan rate for NMS at concentration 1mM, the scan rates were maintained at 0.1,0.05, 0.02 and 0.01 (V/sec), sens(A/V) = 1×10^{-3} .

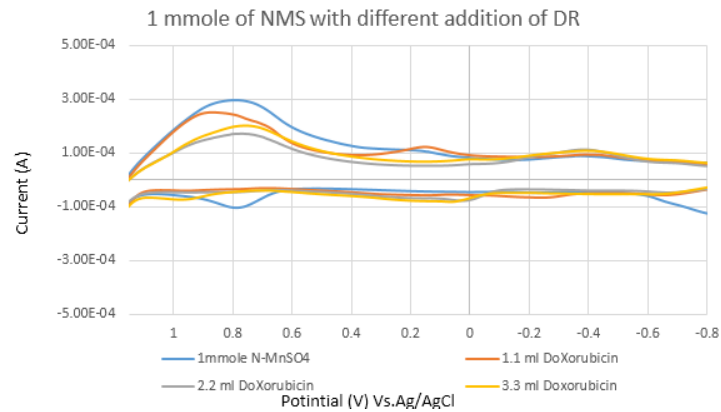


Fig. 10: Cyclic voltammetry for (NMS) 1 mM and DR with concentration (1×10^{-3} , 2×10^{-3} , 3×10^{-3}) at scan rate 0.1 (V/sec), sens(A/V) = 1×10^{-3} .

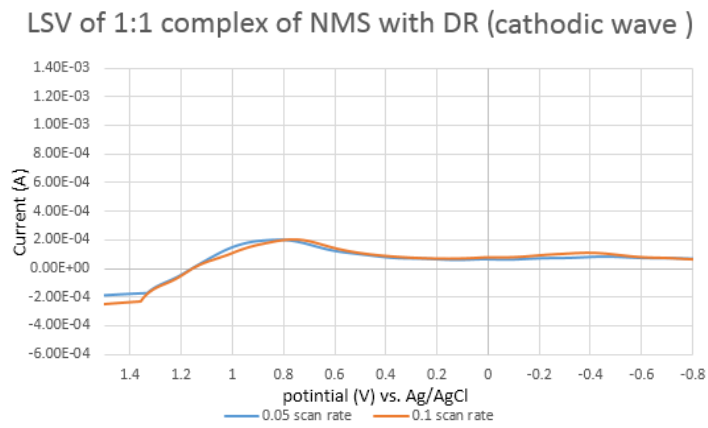


Fig. 11: Linear sweep voltammetry LSV for cathodic wave of 1:1 complex of NMS with DR at different scan rate 0.1 and 0.05 (v/sec).

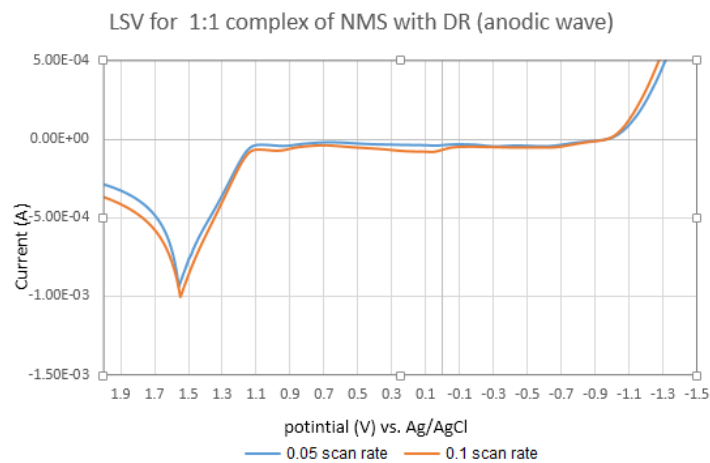


Fig. 12: Linear sweep voltammetry, LSV for anodic wave of 1:1 complex of NMS with DR at different scan rate 0.1 and 0.05 (v/sec).

Table 1: Solvation parameters of BMS and NMS in presence of DR.

[M] × 10 ³	[L] × 10 ³	log γ±		ΔE _{1/2}		D _c	
		Bulk	Nano	Bulk	Nano	Bulk	Nano
1	0.333	-0.0219	-0.0219	1.967	1.664	9.92E-10	1.34E-14
1	0.667	-0.0178	-0.0179	1.974	1.614	3.17E-08	9.88E-13
1	1	-0.0219	-0.0219	1.981	1.572	3.53E-08	3.06E-12
1	1.333	-0.025	-0.0253	1.897	1.554	8.05E-07	2.29E-12
1	1.667	-0.0282	-0.0283	1.896	1.554	4.29E-10	1.86E-12
1	2	-0.0309	-0.0310	1.884	1.544	2.84E-10	1.65E-12

Table 2: Stability constant and Gibbs free energy of BMS and NMS with DR using cathodic wave.

[M] × 10 ³	[L] × 10 ³	(E _{p,c}) _M		(E _{p,c}) _C		β _{MX}		ΔG(kJ mol ⁻¹)-	
		Bulk	Nano	Bulk	Nano	Bulk	Nano	Bulk	Nano
1	0.333	0.034	0.982	-0.024	0.87	4861.905	1.31E+32	-20.694	-180.281
1	0.667	0.034	0.982	0.379	0.82	2.06E+10	9.08E+30	-57.8879	-173.767
1	1	0.034	0.982	0.385	0.778	1.74E+10	1.15E+30	-57.4784	-168.726
1	1.333	0.034	0.982	-0.74	0.76	5.98E-10	4.22E+29	51.7688	-166.288
1	1.667	0.034	0.982	-0.06	0.76	233.8883	3.38E+29	-13.2972	-165.744
1	2	0.034	0.982	-0.068	0.75	142.0071	1.89E+29	-12.0809	-164.335

Table 3: Stability constant and free energy of BMS and NMS with DR using anodic wave.

[M] × 10 ³	[L] × 10 ³	(E _{p,a}) _M		(E _{p,a}) _C		β _{MX}		ΔG(kJ mol ⁻¹)-	
		Bulk	Nano	Bulk	Nano	Bulk × 10 ⁻³⁷	Nano	Bulk	Nano
1	0.333	0.982	0.78	0.985	1	2.12	1.3E+34	-209.516	-191.473
1	0.667	0.982	0.78	0.992	0.01	1.40	6.22E+16	-208.502	-94.2629
1	1	0.982	0.78	0.999	0.09	1.23	9.84E+17	-208.189	-100.993
1	1.333	0.982	0.78	0.915	0.99	0.0332	2.18E+33	-199.382	-187.129
1	1.667	0.982	0.78	0.914	0.998	0.0256	2.39E+33	-198.742	-187.357
1	2	0.982	0.78	0.902	0.999	0.0132	2.08E+33	-197.140	-187.009

peak potential of metal complex, R is a gas constant (8.314 J.mol⁻¹.degree⁻¹), T is the absolute temperature, C_x is the concentration of metal in the presence of ligand, F, Farady constant, n number of electrons and β_{MX} is the stability constant.

The Gibbs free energy ΔG of interaction for bulk MnSO₄ (BMS) and nano MnSO₄ (NMS) with doxorubicin (DR) were calculated [8-24] from stability constant (β_{MX}) using equation (2), where R is gas constant and T is the absolute temperature for our experiment.

$$\Delta G = -2.303RT \log \beta_{MX} \quad (2)$$

The total stability constants for the interaction of both bulk and nano MnSO₄ with doxorubicin were calculated by applying DeFord-Hume equation [6, 7] and their data are given in Table 1. From the activity coefficients, γ±, half wave potential, E_{1/2}, the diffusion coefficients, D_c were calculated and tabulated in Table 1. From the stability constants obtained we change their values into Gibbs free energies of complex parameters [10-24] and the obtained value are listed in Table 2 and Table 3 for the cathodic and anodic waves for both BMS and NMS.

The total Gibbs free energy of interaction for bulk and nano MnSO₄ + doxorubicin given in Tables 2 and 3 were found to be in the range of -164 to -180 kJ/mole on using cathodic wave for nano salt (NMS) and from -12 to -20 kJ/mole for bulk salt (BMS) on applying the cathodic wave. In case of using anodic waves both bulk salt (BMS) and nano manganese sulfate (NMS) gave approximately same values in the range between -190 to -209 kJ/mole. The total stability constants are greater for the interaction of doxorubicin with nano MnSO₄ (NMS) than that of bulk MnSO₄ (BMS), especially on using the cathodic peak giving greater values for the mean Gibbs free energy of interaction.

CONCLUSION

From cyclic voltammetry measurements it is noticed that addition of doxorubicin (DR) to manganese ions decreased the amount of deposited manganese during the cathodic reaction. The redox mechanism was presented. The stability constant and Gibbs free energy of interaction between both B-MnSO₄ and N-MnSO₄ with doxorubicin (DR) for complexes formed were evaluated.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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