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Research Article

POLAROGRAPHIC REDUCTION OF CURCUMIN AT DROPPING MERCURY ELECTRODE

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ABSTRACT

The polarographic reduction of curcumin has been done in various conditions, at different temperatures, at different solvent and at different concentrations by D. C. Polarography. The electrode processes were irreversible and exhibit diffusion controlled reduction. Single well defined irreversible wave obtained. The polarographic technique was used to determine the kinetic parameters (K^0_{fh}, αn) and thermodynamic parameters such as enthalpy change (ΔH), free energy change (ΔG) and entropy change (ΔS) of curcumin at pH-6 in 0.5M acetate buffer.

Keyword: Curcumin, D.C. Polarography, Kinetic parameters, Thermodynamic parameters.

INTRODUCTION

Curcumin, (1,7-bis(4-hydroxy-3-methoxy phenyl)-1,6-heptadiene-3,5-dione) (Fig. 1) is an active principle of turmeric (Curcuma Longa Linn.) which has a long history of medicinal use in the middle East and India. Extensive scientific research on Curcumin have demonstrated anti-inflammatory,[1-2] anticancer,[3-5] and potent antioxidant[6-10] activities apart from its promising role in variety of disease conditions including AIDS, Alzheimer's disorders.[11] The polyphenolic compound is harmacologically safe even when administered at doses up to 10 g/day[12] and hence has enormous potential in the prevention and therapy of variety of acute diseases and chronic disorders. However, it exhibits low oral bioavailability and undergoes rapid first-pass metabolism and excretion in the bile.[13] Curcumin and its derivatives are free-radical scavengers, interacting with the oxidative cascade by quenching oxygen and chelating and disarming oxidative properties of metal ions. [14-15] Biological activity of curcumin has been attributed to the benzene rings and the diketonic structure. [16] In the hybridization process, curcumin is selected as an indicator.[17]

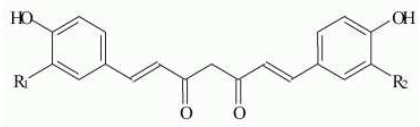

Fig. 1: Structure of Curcumin

1) R1 = R2 = OCH3
2) R1 = OCH3, R2 = H
3) R1 = R2 = H

The electrochemical behaviors and electrode reaction mechanism of curcumin on the glassy carbon electrode were studied by cyclic voltammetry. [18-19] The differential pulse voltammetric method, for curcumin determination has been described.[20] Curcumin in Curcuma longa L, have been determined and the interaction of curcumin, H_2O_2 and OH^- have been studied.[21]

A large number of pharmaceuticals can be reduced or oxidized in the available potential range and their waves can be used in their determination. It seems that often the therapeutical activity is paralleled by electrochemical reactivity. Pharmaceutical companies will use, whenever possible, officially approved methods of analysis. In the past, some polarographic analytical procedures were listed in numerous Pharmacopoeias. It should be a goal of electroanalytical chemists around the world to have them listed again. The lower costs, faster results, and the possibility for quickly detecting mishandlings by technicians, are powerful arguments. To use polarographic methods for analyses of such simple matrices yields results often much faster, with a better accuracy and without using organic solvents.[22] Numerous examples of such applications have been reported earlier.[23]

In this work, the optimum conditions for the determination of reduction of curcumin have been investigated using D.C. Polarography. The method was simple, rapid, sensitive and reliable and the method could be used directly to detect the content of curcumin in medicine. The variation of current and potential of the curcumin as function of pH, temperature, concentration and supporting electrolytes solution were measured by D.C. polarography.

MATERIALS AND METHODS

Apparatus

The D.C. recording polarograph (CL 357) of Elico limited was used for study. The three electrode system was completed using a working electrode (D.M.E.), reference electrode (saturated calomel electrode) and counter electrode (platinum electrode). A polarographic capillary 120 mm long and 0.05 mm in diameter was used. The $m^{2/3}t^{1/6}$ value was 2.376 $mg^{2/3}s^{1/4}$ at 65cm effective height of mercury reservoir. A digital pH meter model 111 E was used for measuring the pH of the analytes.

Reagents

All the solutions were prepared from doubly distilled water and analytical reagent grade chemicals (MERCK). Curcumin solution was prepared freshly every 5 days. 0.5 M Acetate buffer (pH-6) has been used as supporting electrolyte. Triton X-100 (0.001%) was used to suppress polarographic maxima.

Procedure

The general procedure for Direct current Polarography is as follows-

A 10 ml of experimental solution was placed in a polarographic cell and deoxygenated with nitrogen for 13 min. The cell was placed in the thermostat and the capillary was inserted in solution. The current voltage curves were measured manually. Polarographic experiments were carried out with Elico D.C. recording polarograph CL 357. The current voltage measurements were performed with three electrode assembly, a dropping mercury electrode as working electrode, calomel as reference electrode and platinum electrode as counter electrode. A digital pH meter model 111 E was used for measuring the pH of the analytes. The potential was applied to the working electrode with 150 mV/min span rate and 100 nA/div. sensitivity of current measurement.

RESULT AND DISCUSSION

Electrochemical reduction of curcumin has been studies in 0.5M acetate buffer in alcoholic medium. Reduction of carbonyl group in this media gave one well- defined wave. The reduction was found to be diffusion controlled as the plot of i_d versus concentration was found to be linear and also the temperature coefficient was found to be greater than 3 mv per degree. Linear plots were obtained for log $(i/i_d\text{-}i)$ versus $E_{d.e.}$ with slope 0.0591/αn and zero intercept on y-axis gave the value of $E_{1/2}$. Hence for irreversible wave kinetic

parameters were calculated from Meites-Israil method as well as by Gaur-Bhargava's method. Results by both methods are in agreement with each other.

The value of diffusion coefficient ($D^{1/2}$) has been determined by Ilkovic equation[24]

$$I_d = 607\ n\ D^{1/2} m^{2/3} t^{1/6}\ C$$

Where n = number of electrons transferred in the process,
m = rate of mercury flow in mg/sec,
D = diffusion constant of depolarizer in cm^2/s,
t = drop time in s,
C = depolarizer concentration in millimoles/litre,
I_d = diffusion current in micro amperes.

The value of heterogeneous rate constant ($K^o_{f,h}$) has been evaluated by Meites-Israel equation[25]

$$-E_{1/2} = \frac{0.05915}{\alpha n} \log \frac{1.349\ K^o_{f,h}\ t^{1/2}}{D^{1/2}}$$

Where αn = product of transfer coefficient (α) and number of electrons transferred in the rate determining step.

Meites Israel has extended the Koutecky's graphical method into comparatively more precise mathematical form. Further, Gaur-Bhargava has also extended the Koutecky's treatment for irreversible wave, since according to them the diffusion to the electrode surface (mercury drop) is spherical and not a linear one as assumed by Meites and Israel.

Gaur Bhargava's modification[26]

$$-E1/2 = \frac{0.05915}{\alpha n} \log \frac{1.349\ Kof,h\ t1/2}{(\text{antilog } c) D^{1/2}}$$

A well defined irreversible and diffusion controlled wave for curcumin was observed in 0.5M acetate buffer at pH 6. The value of $E_{1/2}^{irreversible}$ for curcumin was found to be -1.2134 to -1.2183 volts (at various concentrations) vs. SCE.

With increase in concentration of curcumin, $E_{1/2}$ shifted to more negative potential confirmed the irreversible nature of wave.[27] As the curcumin concentration increases the irreversibility of the electrode reaction increases because the formal rate constant was decreases gradually. The value of I_d is linear with concentration.

Table 1: Electrochemical reduction of curcumin in acetate buffer

S. No.	Drug Concentration (M)	$E_{½}$ (V)	I_d (µA)	$D^{1/2}$ (cm^2/s)	$K^o_{f,h}$ (ME Method) (cm/s)	$K^o_{f,h}$ (GB Method) (cm/s)
1.	0.000543	-1.2250	1.5	1.3195	7.72366×10^{-09}	1.04322×10^{-08}
2.	0.000814	-1.1850	1.9	1.1143	1.42587×10^{-09}	1.92711×10^{-09}
3.	0.001086	-1.2183	2.4	1.0556	3.62513×10^{-10}	4.90255×10^{-10}

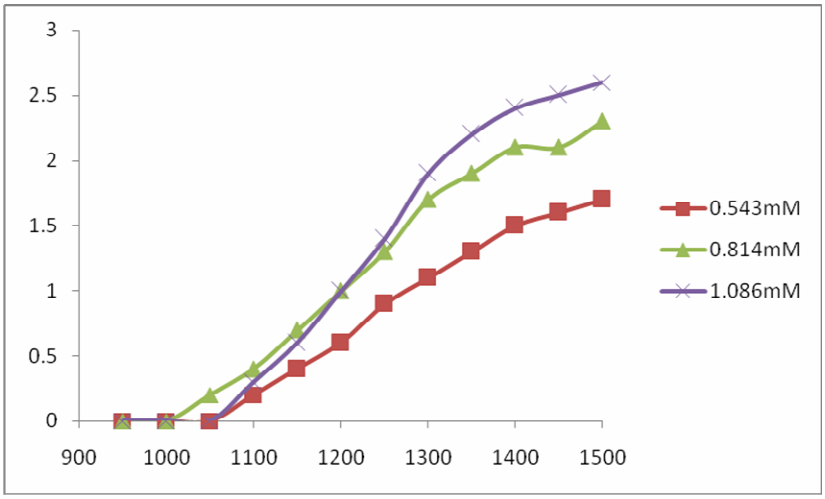

Fig. 1: Polarogram of curcumin (various concentrations) in acetate buffer (pH 6)

Changes in the nature and concentration of the supporting electrolytes may affect half wave potential. Acetate buffer was selected as the optimum because it gave the highest response and good reproducibility.

The half wave potential and diffusion current of curcumin strongly depends on the pH of the solution. It means the H^+ ion involves in reaction mechanism. The best wave was observed in pH 6 so this pH was selected in subsequent work.

Effect of temperature

A gradual change in diffusion current and half wave potential was observed when the solution temperature was increased from 25°C to 40°C (Table-4). When we increase the temperature of solution the half wave potential of system becomes more positive. In this system the temperature coefficient is greater than 3 mv per degree so that the system is irreversible.[28]The value of K^0_{fh} at various experimental conditions comes out to be of the order of $10^{-11\pm2}$which indicates irreversible nature of reaction. The value of αn decreases with increase in temperature (Table- 4). A decrease in value of αn implies that transfer of electrons becomes difficult as temperature was elevated.[29] Further the values of K^0_{fh} increases with increase in temperature which suggests that irreversibility decrease with increase in temperature; this implies that reduction products of drug are stable at lower temperature.

Table 2: Electrochemical Reduction of curcumin at DME in acetate buffer (pH-6.0) at various Temperatures:

S. No.	Temp (K)	Drug Concentration (M)	E ½ (V)	I_d (µA)	αn	$D^{1/2}$ (cm^2/s)	$K^o_{f,h}$ (ME Method) (cm/s)	$K^o_{f,h}$ (GB Method) (cm/s)
1.	298.0	0.00081432	-1.2700	1.2	0.5523	0.7037	3.61659×10^{-13}	4.88794×10^{-13}
2.	303.0	0.00081432	-1.2530	1.6	0.4987	0.9383	9.47088×10^{-12}	1.28002×10^{-11}
3.	308.0	0.00081432	-1.2220	2.0	0.3997	1.1729	2.40695×10^{-09}	3.25307×10^{-09}
4.	313.0	0.00081432	-1.2020	2.1	0.3775	1.2316	9.74329×10^{-09}	1.31684×10^{-08}

Where
K^0_{fh} = Formal Rate Constant obtained from Meites & Israel's method
D = Diffusion coefficient.
αn = Transfer coefficient.

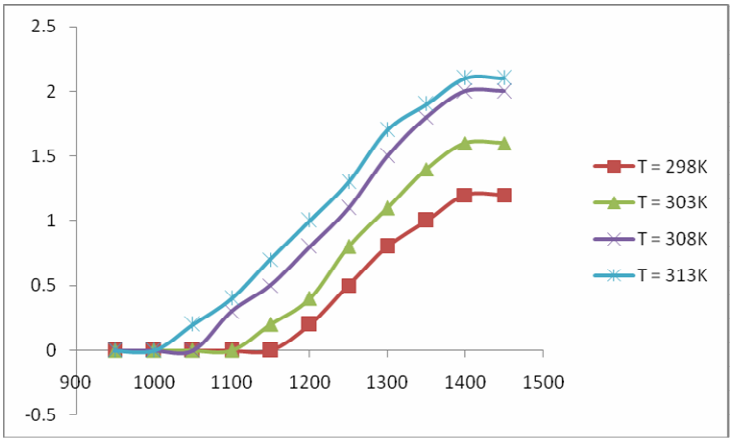

Fig. 2: Polarogram of curcumin at various temperatures in acetate buffer (pH 6)

Effect of solvent concentration

The effect of the ethyl alcohol concentration in the supporting electrolyte on the height and shape of the wave was studied simultaneously. Polarogram were run of solutions containing curcumin in concentrations of solvent ranging from 40 to 60 % ethyl alcohol in 0.5M Acetate buffer (pH=6). The results indicate that the reaction is irreversible. The half-wave potential shifts towards more negative value with increasing the concentration of ethyl alcohol. Further, the height of the wave was found to vary directly with the concentration indicating the electrode reaction to be diffusion controlled. The values of K^0_{fh} indicate that the electrode reaction is more irreversible at high concentrations of ethyl alcohol. The diffusion coefficient decrease with the increase in concentration of the ethyl alcohol. This can be explained, suggested by Van uitert *et al.*[30] that with the increase of dielectric constant of solvent, ion-dipole interaction between drug and solvent molecules increases. The results are shown in table 3.

Table 3: Electrochemical Reduction of curcumin in acetate buffer (pH-6.0) at various percentage of ethyl alcohol

S. No.	Alcohol	Drug Concentration (M)	E ½ (V)	I_d (µA)	αn	$D^{1/2}$ (cm^2/s)	$K^o_{f,h}$ (ME Method) (cm/s)	$K^o_{f,h}$ (GB Method) (cm/s)
1.	40%	0.00081432	-1.2020	2.1	0.3775	1.2316	9.74329×10^{-09}	1.31684×10^{-08}
2.	50%	0.00081432	-1.2130	1.4	0.3734	0.8210	6.69105×10^{-09}	9.04317×10^{-09}
3.	60%	0.00081432	-1.2250	1.0	0.4698	0.5865	4.04809×10^{-11}	5.47112×10^{-11}

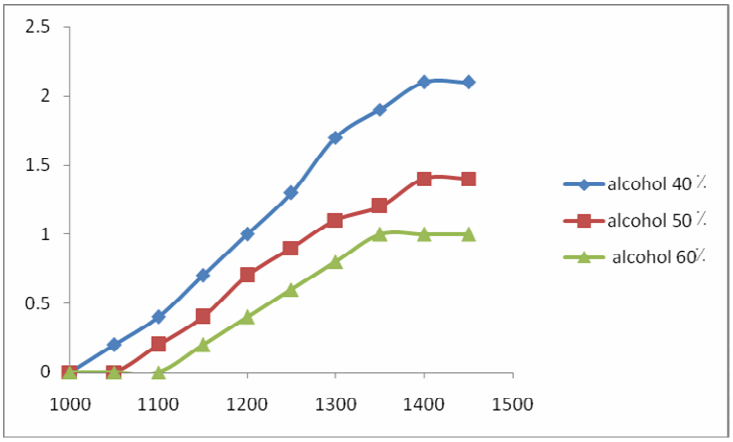

Fig. 3: Polarogram of curcumin at various % of ethyl alcohol in acetate buffer (pH 6)

Effect of buffer concentration

Electrochemical behavior of curcumin has been studied as a function of buffer concentration in acetate buffer (Table 3).The diffusion currents decrease with the increase in concentration of the buffer solution. Since the diffusion current (I_d) depends on the diffusion coefficient of the electroactive species, which in turn depends on the viscosity of the solution, increase in the viscosity causes I_d to decrease.[31] Further, the half wave potential of the drug shifts to the more negative direction on increasing the concentration of the buffer solution. This increase in potential is due to the alteration in the rate of electron transfer step for an irreversible electrode reaction.[32] The values of K^0_{fh} indicate that the electrode reaction is more irreversible at high concentrations of acetate buffer.

Table 4: Electrochemical Reduction of curcumin at various concentrations of acetate buffer (pH-6.0)

S. No.	Acetate buffer conc.(M)	Drug Concentration (M)	$E_{½}$ (V)	I_d (µA)	αn	$D^{1/2}$ (cm^2/s)	$K^o_{f,h}$ (ME Method) (cm/s)	$K^o_{f,h}$ (GB Method) (cm/s)
1.	0.10	0.00081432	-1.2029	2.1	0.3773	1.2316	9.69147×10^{-09}	1.30983×10^{-08}
2.	0.15	0.00081432	-1.2114	1.5	0.4232	0.8797	7.02765×10^{-10}	9.49809×10^{-10}
3.	0.20	0.00081432	-1.2000	1.4	0.4624	0.8210	1.26608×10^{-10}	1.71114×10^{-10}

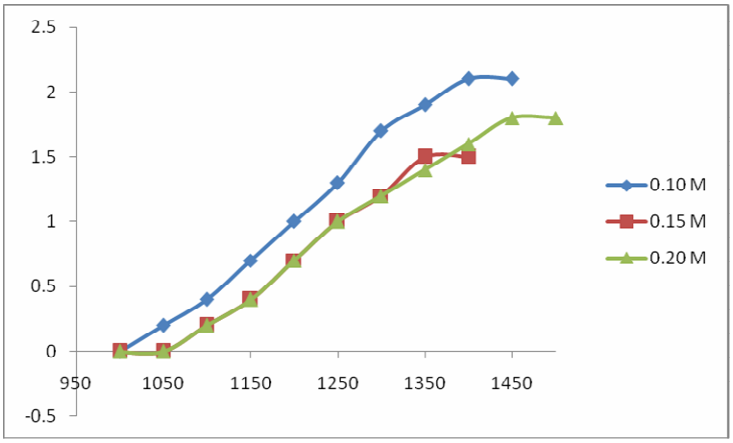

Fig. 4: Reduction of curcumin at various concentration of acetate buffer (pH 6)

Thermodynamic Parameter

Thermodynamic parameter ($\Delta H^{\#}_p$, $\Delta H^{\#}_v$, $\Delta G^{\#}$, $\Delta S^{\#}$) have been reported in table - 6. The enthalpy of activation at constant pressure ($\Delta H^{\#}_p$) has been calculated by substituting the value of slope of the plot (log K^0_{fh} vs. -1/T) in the Vant Hoff equation.

$$\Delta H^{\#}_p = 2.303R \times \text{Slope}$$

Where R= Gas constant.

The value of slope comes out to be 17549.

$$\Delta H^{\#}_p = \Delta H^{\#}_v + RT$$

From this relation $\Delta H^{\#}_v$(enthalpy of activation at constant volume) was evaluated, the activation free energy change ($\Delta G^{\#}$) was determined by relationship.

$$K^0_{fh} = (KT/h)r_o\exp^{-\Delta G^{\#}/RT}$$

Where K = Boltzmann constant,

h = Plank's constant,

r_0 = mean distance between depolarized ions in the bulk solution,

R = Gas constant,

T = absolute temperature.

In general value of r_0 is taken as 2×10^{-8} cm.[9] The entropy of activation ($\Delta S^{\#}$) was calculated using following equation;

$$\Delta S^{\#} = (\Delta H^{\#}_v - \Delta G^{\#})/T$$

The plot of log K^0_{fh} vs. -1/T is found to be linear from the slope of which the values of $\Delta H^{\#}_p$, $\Delta H^{\#}_v$, $\Delta G^{\#}$ and $\Delta S^{\#}$ have been evaluated and presented in table- 6.

A perusal of the values of various quantities presents in table – 6 shows that activation free energy change ($\Delta G^{\#}$) is positive at all the temperatures suggesting the non spontaneous nature of electrode process. Negative value of $\Delta S^{\#}$ suggests that formation of activated state is accompanied by decrease of entropy.[33]

Table 5: Thermodynamic parameters at different temperatures

S. No.	T K	$\Delta H^{\#}_p$ jule/mole	$\Delta H^{\#}_v$ jule/mole	$\Delta G^{\#}$ jule/mole	$\Delta S^{\#}$ jule/kelvin
1	293	336029.3611	336029.33	8.98×10^{-04}	-306.60
2	298	336029.3611	336029.33	1.00×10^{-05}	-335.71
3	303	336029.3611	336029.33	9.35×10^{-04}	-308.70
4	308	336029.3611	336029.33	8.09×10^{-04}	-262.79
5	313	336029.3611	336029.33	7.87×10^{-04}	-251.30

CONCLUSION

A simple and sensitive method was developed for the qualitative determination of curcumin. The wave given by curcumin was found to be diffusion controlled. Its height is proportional to concentration, varies with concentration of buffer solution and nature of the solvent and its temperature coefficient was found to be greater than 3 mv per degree. The value of K^0_{fh} at various experimental conditions comes out to be of the order of $10^{-11\pm2}$ which indicates irreversible nature of reaction. The value of αn decreases with increase in temperature. Further the values of K^0_{fh} increases with increase in temperature which suggests that irrereversibility decrease with increase in temperature, this implies that reduction products of drug are stable at lower temperature. In other words the electrode reaction was rendered more irreversible at higher temperature. It proper attention is given to the effect of factors pH, concentration, temperature, etc. on the half-wave potential, the wave could be of value for qualitative identification.

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