Research article

# Effect of indomethacin on the electrical conductance and electrochemical voltammetry of copper chloride in methanol, ethanol, and their binary mixture with water

AbdulAziz A. Alayyafi [a], Hany A. Nasef [b], Shereen E. Salem [c], Esam A. Gomaa [c], Elsayed M. AbouElleef [b,*,1]

[a] Chemistry Department, Al-Qunfudhah University College, Umm Al-Qura University, Saudi Arabia
[b] Basic Sciences Department, Delta Higher Institute for Engineering and Technology, 35681-Dakhlia, Mansoura, Egypt
[c] Chemistry Department, Faculty of Science, Mansoura University, 35516-Mansoura, Egypt

## A B S T R A C T

This study investigated the physicochemical properties of the interaction of indomethacin and copper chloride using the electrical conductance measurement in methanol, ethanol, and their binary mixture with water at room temperature (298.15 K), to determine the solvation behavior, redox behavior, and kinetics. The association parameters were computed using the Fuoss-Hsia-Fernández-Prini and Fuoss-Shedlovsky models. The standard Gibbs energy for association ($\Delta G_A^o$), Walden product ($\Lambda_o \eta_o$), and hydrodynamic radii ($R_H$) were calculated to study the interaction of indomethacin and copper chloride. On the other hand, cyclic voltammetry examines the electrochemical redox behavior of copper chloride using a gold electrode and its interactions with indomethacin. Results showed changes in peak potentials and currents density in the presence of indomethacin, indicating alterations in redox behavior and reaction rates. Overall, this research can be valuable in understanding the electrochemical properties and potential applications of indomethacin and copper chloride, as well as in developing new drugs or therapeutic agents, which could have has implications in various fields, including drug development, electrochemistry, and materials science.

## 1. Introduction

Indomethacin belongs to a class of drugs known as nonsteroidal anti-inflammatory drugs (NSAIDs) that are widely used to relieve the symptoms of chronic musculoskeletal pain and to close a hemodynamically significant patent ductus arteriosus in premature newborns. Indomethacin is available under the brand names indocin and tivorbex, as well as the generic name indomethacin. Indomethacin, commonly known as indomethacin, is an anti-inflammatory, antipyretic, and analgesic nonsteroidal drug. Indomethacin is an indole-acetic acid derivative with the chemical name [1-(*p*-chlorobenzoyl) 25-methoxy-2-methylindole-3-acetic acid] [1]. Indomethacin has a comparable mode of action to other medications in its class; it inhibits cyclooxygenase enzymes 1 and 2 in a

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nonselective manner, which are involved in the manufacture of prostaglandins from arachidonic acid. Indomethacin reduces pain, heat, and inflammation by decreasing prostaglandin synthesis [2,3]. Indomethacin's mechanism of action was first described in 1971, along with that of numerous other NSAIDs that inhibit cyclooxygenase [4].

Copper chloride is a common metal salt that is often used as a model system in electrochemical studies; it can undergo redox reactions, where it can be oxidized or reduced at different potentials [5]. Conductivity is a measure of a solution's ability to conduct electric current and can provide information about the interactions between ions and solvents. With the aid of various conductivity equations, such as the Fuoss-Shedlovsky [5] and Fuoss-Hsia-Fernández-Prini equations [6,7], conductivity data can be examined to obtain knowledge about the interactions between molecules and the geometrical consequences that these interactions have on the systems. These findings can have applications in various fields [8,9].

The solvent percentage is very important in different applications for surface facilities, pipeline systems, and mass transfer operations. Methanol and ethanol are commonly used as solvents in electrochemical studies due to their high dielectric constants and good solvating properties. The addition of water to these solvents can affect the solvation behavior and conductivity of the system. Information on the viscosity and density of liquid mixtures, as well as their relationships with composition and temperature, is critical in the chemical industry for a variety of applications, such as surface facilities, pipeline systems, and mass transfer activities. The binary mixed solvents (MeOH–H₂O) and (EtOH–H₂O) are the most popular solvents in the chemical industry for researching ion mobility and ion association due to variations in a broad range of chemical and physical properties [10].

Cyclic voltammetry is a commonly used electrochemical technique that can provide information about the redox behavior and kinetics of a system [11,12]. As the working electrode's potential changes linearly over time during cyclic voltammetry, oxidation and reduction reactions in the system take place. The resulting current is measured, and a cyclic voltammogram is obtained, which plots the current response of an electrochemical system as a function of the applied potential [13–15]. By analyzing the shape and characteristics of the resulting cyclic voltammogram, information about the redox behavior of metal ions can be obtained; this includes the identification of oxidation and reduction peaks, which correspond to specific redox processes. The peak potentials can provide insights into the thermodynamics and kinetics of these processes. In the presence of ligand, the cyclic voltammogram of metal ions may exhibit changes compared to its behavior in the absence of ligand [16–19].

The purpose of this research is to investigate the physicochemical properties of the interaction between indomethacin and copper chloride in binary mixed solvents (MeOH–H₂O and EtOH–H₂O) with different volume fractions, and to investigate the ion-ion and ion-solvent interactions in these solutions using conductivity techniques using the Fuoss-Shedlovsky and Fuoss-Hsia-Fernández-Prini conductivity equations. The research aims to provide insights into the solvation behavior and electrochemical properties of the system. On the other hand, cyclic voltammetry examines the electrochemical redox behavior of copper chloride using a gold electrode and its interactions with indomethacin. This research has implications in various fields, including drug development, electrochemistry, and materials science.

## 2. Experimental

### 2.1. Reagents

The chemicals utilized in this work included analytical reagent grade methanol (99.9 %), ethanol (99.8 %) and copper chloride salt (CuCl₂·2H₂O) were purchased from Sigma-Aldrich, which were used without further purification. Indomethacin has a molecular formula of $C_{19}H_{16}ClNO_4$ (99.5 % purity) was purchased from Sigma-Aldrich (Fig. 1). Deionized water with a specific conductivity <
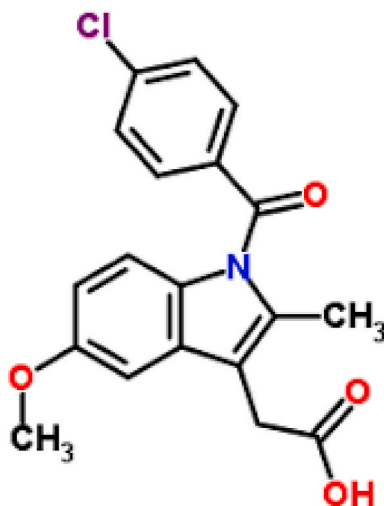


**Fig. 1.** Chemical structure of Indomethacin.

0.5 μS cm$^{-1}$ was distilled and used in this research.

## 2.2. Methods

As the solvent media, (MeOH–H$_2$O) and (EtOH–H$_2$O) binary mixed solvents with organic solvent volume fractions ranging from 0 % to 100 % were utilized. The appropriate volumes of water and methanol or ethanol were combined using equation (1):

$$\text{MeOH or EtOH fraction} = (V_1 d_1)100 \ / \ (V_1 d_1 + V_2 d_2) \tag{1}$$

where $d_1$ and $d_2$ stand for the densities of alcohol and water, respectively. $V_1$ is the volume of ethanol added to $V_2$ of water to make the combination.

Table 1 lists the physical characteristics of pure water and a binary mixed solvent at room temperature, including their dielectric constants, viscosities, and densities [20,21].

## 2.3. Conductance measurements

The conductance of the solution measured using a conductance instrument with the aid of a unity cell constant (Vision plus-EC3175JENCO) was coupled to a 4130 Kottermann ultra thermostat and a deviation of ($\pm$0.1 μS cm$^{-1}$). The conductivity bridge was calibrated with a traditional method [22]. To measure the electrical conductance of solutions, a (20 ml, $1 \times 10^{-3}$ M) concentration of CuCl$_2$ solution was put in a double-jacket glass conductance cell the conductance of the solution measured. The conductance was measured after dilution by di-ionized water with constant stirring at a specific temperature. Take another measurement of the conductance to obtain at least two readings that agree. Each measurement is repeated multiple times to verify the validity of the experimental findings.

## 2.4. Cyclic voltammetry measurements

It was preceded by a DY2000 potentiostat (USA) with a three-electrode system with a potential window of (1 to $-1$) volts. The different electrodes were the auxiliary electrode (Pt electrode), working electrode (gold electrode), and Ag/AgCl/sat KCl, a reference electrode on a cell that contained 30 ml of a supporting electrolyte of 0.1 M KBr at a 0.1 V s$^{-1}$ scan rate and 298.15 K. The composition of gold is 78.85 % Au, 14.80 % Ag, 9.59 % Cu and 0.76 % Zn [23].

## 3. Results and discussion

### 3.1. Conductometric measurements

#### 3.1.1. Fuoss-Shedlovsky equation application

The electrical conductance of (20 ml, $10^{-3}$ M) CuCl$_2$·2H$_2$O solution in water and in the (MeOH–H2O) and (EtOH–H2O) binary mixed solvents were recorded at room temperature (298.15 K). To investigate how indomethacin affects the association characteristics of CuCl2·2H$_2$O, (20 ml, $10^{-3}$ M) indomethacin was added dropwise using a micropipette with stirring at room temperature, and the conductance was recorded after each addition.

Using Equation (2), ($\Lambda_m$) the molar conductance was determined [24,25]:

$$\Lambda_m = \frac{(K_s - K_{solv}).K_{cell}.1000}{C} \tag{2}$$

$K_{solv}$ is the specific conductance of the solvent, $K_s$ is the specific conductance of the solution, and C is the concentration of the solution.

The Fuoss-Shedlovsky extrapolation technique was used to examine the experimental conductance data according to equations (3)–(9). Plotting the molar conductance ($\Lambda_m$) vs. (C)$^{1/2}$ yielded the limited molar conductance ($\Lambda_o$) for CuCl$_2$·2H$_2$O, as illustrated in Figs. 2 and 3 [26].

**Table 1**
The mass fraction, dielectric constant, viscosity, and density of the utilized solvents at room temperature at 101.3 kPa.

| V% of MeOH | mass fraction of MeOH, $X_e$ | dielectric constant ($\varepsilon$) | Viscosity ($\eta$)/mPa s | density g.cm$^{-3}$ | V% of EtOH | mass fraction of EtOH, $X_e$ | dielectric constant ($\varepsilon$) | viscosity ($\eta$)/mPa s | density g.cm$^{-3}$ |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 0.0000 | 78.30 | 0.8903 | 0.9970 | 0 | 0.0000 | 78.30 | 0.8903 | 0.9970 |
| 20 | 0.0999 | 73.74 | 0.8558 | 0.9650 | 20 | 0.0717 | 74.44 | 0.9045 | 0.9755 |
| 40 | 0.2284 | 67.89 | 0.8113 | 0.9319 | 40 | 0.1708 | 69.1 | 0.9242 | 0.9452 |
| 60 | 0.3997 | 60.07 | 0.7521 | 0.8915 | 60 | 0.3166 | 61.23 | 0.9532 | 0.9065 |
| 80 | 0.6397 | 49.13 | 0.6691 | 0.8440 | 80 | 0.5527 | 48.44 | 1.0001 | 0.8505 |
| 100 | 1.0000 | 32.70 | 0.5445 | 0.7871 | 100 | 1.0000 | 24.30 | 1.0890 | 0.7873 |

$$\frac{1}{\Lambda S(z)} = \frac{1}{\Lambda_o} + \left(\frac{K_A}{\Lambda_o^2}\right) \left(C \Lambda \gamma_\pm^2 S(z)\right) \tag{3}$$

$$S(Z) = 1 + Z + Z^2/2 + Z^3/8 + \ldots \ldots \text{etc.} \tag{4}$$

$$\text{And } Z = \frac{S(\Lambda C)^{1/2}}{\Lambda_o^{3/2}} \tag{5}$$

$$S = a\Lambda_o + b \tag{6}$$

where

$$a = 8.2 \times 10^5 \big/ (\varepsilon T)^{3/2} \tag{7}$$

$$b = 82.4 \big/ \eta \left((\varepsilon T)^{1/2}\right) \tag{8}$$

$$\text{Degree of dissociation } \alpha = \frac{\Lambda_m S(Z)}{\Lambda_o} \tag{9}$$

The mean activity coefficients ($\gamma\pm$) were evaluated from the Debye-Hückel Equations 10 and 11 [27].

$$\log \gamma_\pm = \frac{Z_+ Z_- A\sqrt{I}}{1 + Br^o \sqrt{I}} \tag{10}$$

$$\text{Debye} - \text{Hückel constant } A = 1.824 \times 10^6 \ (\varepsilon T)^{-3/2} \ ; \ B = 50.29 \times 10^8 \ (\varepsilon T)^{-1/2} \tag{11}$$

### 3.1.2. Fuoss-Hsia-Fernández-Prini equation application

Fuoss-Hsia-Fernández-Prini application can be done by using Equation (12):

$$\Lambda = \alpha \left[ \Lambda_o - S(\alpha C)^{1/2} + E \alpha C \ln(\alpha C) - J_1 \alpha C + J_2 \alpha C^{3/2} \right] \tag{12}$$

where the formulas for the parameters E, $J_1$ and $J_2$ are provided by Fernández-Prini [28,29]. Eq. (13) was used to obtain the association constant ($K_A$).

$$K_A = (1 - \alpha) \big/ \left(\alpha^2 C \gamma \pm^2\right) \tag{13}$$

### 3.1.3. Ion-pair association parameters

Tables 2–5 show the values of the association constant ($K_A$). The trends were found to be identical when the Fuoss-Shedlovsky and Fuoss-Hsia-Fernández-Prini equations were applied. As the alcohol content increased, the values of the association constant increased, indicating that ion-pair formation was more likely. In addition, conductometric data analysis for CuCl$_2$·2H$_2$O revealed that adding
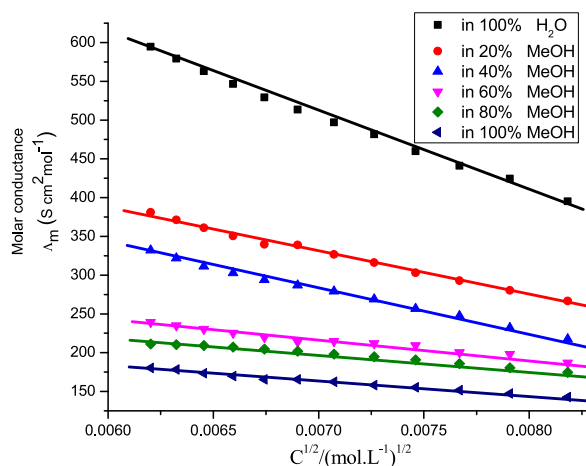


**Fig. 2.** Molar conductivities ($\Lambda_m$) of CuCl$_2$ vs. the square of the concentration ($C^{1/2}$) in binary mixtures (MeOH–H$_2$O) in the absence of indomethacin at room temperature.
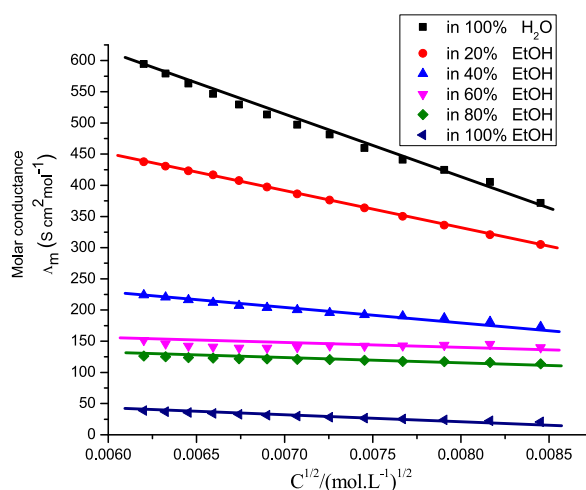
**Fig. 3.** Molar conductivities ($\Lambda_m$) of $CuCl_2$ vs. the square of the concentration ($C^{1/2}$) in the binary mixture (EtOH–$H_2O$) in the absence of indomethacin at room temperature.

**Table 2**
Different association parameters for $CuCl_2$ in binary mixtures (MeOH–$H_2O$) in the absence of indomethacin at 298.15 K using the Fuoss-Shedlovsky equation.

| V% of MeOH | $\Lambda_0$ S.cm$^2$. Mol$^{-1}$ | $\Lambda_m$ S.cm$^2$. Mol$^{-1}$ | S | $\Lambda_0\eta$ S.cm$^2$.mPa. s. Mol$^{-1}$ | $10^{-3}R_H$ A$^o$ | $R_x$ | $\alpha$ | $\gamma\pm$ | $K_A$ dm$^3$·mol$^{-1}$ | $10^{-3}K_D$ mol.dm$^{-3}$ | $10^{-3}K_3$ (dm$^3$·mol$^{-1}$)$^2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 1182.37 | 304.92 | 332.49 | 1052.67 | 7.790 | 1.0000 | 0.2591 | 0.8790 | 14,290 | 0.0700 | 0.3967 |
| 20 | 726.45 | 229.68 | 247.74 | 621.66 | 13.190 | 0.5906 | 0.3181 | 0.8684 | 8937 | 0.1119 | 0.3129 |
| 40 | 672.55 | 185.13 | 262.96 | 545.66 | 15.028 | 0.5184 | 0.2771 | 0.8523 | 12,964 | 0.0771 | 0.3772 |
| 60 | 385.17 | 178.20 | 213.69 | 289.67 | 28.308 | 0.2752 | 0.4682 | 0.8253 | 3561 | 0.2808 | 0.1961 |
| 80 | 331.37 | 131.67 | 255.08 | 221.71 | 36.985 | 0.2106 | 0.4035 | 0.7714 | 6157 | 0.1624 | 0.2584 |
| 100 | 293.06 | 110.88 | 402.99 | 159.57 | 51.388 | 0.1516 | 0.3886 | 0.6201 | 10,530 | 0.0950 | 0.3385 |

**Table 3**
Different association parameters for $CuCl_2$ in binary mixtures (EtOH–$H_2O$) in the absence of indomethacin at 298.15 K using the Fuoss-Shedlovsky equation.

| V% of EtOH | $\Lambda_0$ S.cm$^2$. Mol$^{-1}$ | $\Lambda_m$ S.cm$^2$. Mol$^{-1}$ | S | $\Lambda_0\eta$ S.cm$^2$.mPa. s. Mol$^{-1}$ | $10^{-3}R_H$ A$^o$ | $R_x$ | $\alpha$ | $\gamma\pm$ | $K_A$ dm$^3$·mol$^{-1}$ | $10^{-3}K_D$ mol.dm$^{-3}$ | $10^{-3}K_3$ (dm$^3$·mol$^{-1}$)$^2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 1182.37 | 304.92 | 332.49 | 1052.67 | 7.790 | 1.0000 | 0.2591 | 0.8790 | 14,290 | 0.0700 | 0.3967 |
| 20 | 809.23 | 247.50 | 261.91 | 731.98 | 11.202 | 0.6954 | 0.3076 | 0.8701 | 9667 | 0.1034 | 0.3257 |
| 40 | 351.87 | 156.42 | 159.72 | 325.21 | 25.215 | 0.3089 | 0.4488 | 0.8559 | 3735 | 0.2677 | 0.2007 |
| 60 | 196.43 | 130.68 | 129.30 | 187.24 | 43.794 | 0.1779 | 0.6767 | 0.8298 | 1025 | 0.9752 | 0.1031 |
| 80 | 156.26 | 106.92 | 142.41 | 156.28 | 52.470 | 0.1485 | 0.7007 | 0.7671 | 1036 | 0.9657 | 0.1033 |
| 100 | 86.57 | 17.82 | 204.05 | 94.28 | 86.977 | 0.0896 | 0.2129 | 0.4742 | 77,199 | 0.0130 | 0.9097 |

**Table 4**
Different association parameters for $CuCl_2$ in binary mixtures (MeOH–$H_2O$) in the absence of indomethacin at 298.15 K using the Fuoss-Hsia-Fernández-Prini equation.

| V% of MeOH | $\Lambda_0$ S.cm$^2$. Mol$^{-1}$ | $\Lambda_m$ S.cm$^2$. Mol$^{-1}$ | S | $\Lambda_0\eta$ S.cm$^2$.mPa. s. Mol$^{-1}$ | $10^{-3}R_H$ A$^o$ | $R_x$ | $\alpha$ | $\gamma\pm$ | $K_A$ dm$^3$·mol$^{-1}$ | $10^{-3}K_D$ mol.dm$^{-3}$ | $10^{-3}K_3$ (dm$^3$·mol$^{-1}$)$^2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 1186.45 | 304.92 | 332.39 | 1056.30 | 7.763 | 1.0000 | 0.2579 | 0.9629 | 12035.26 | 0.0831 | 0.3064 |
| 20 | 729.86 | 229.68 | 247.67 | 624.58 | 13.129 | 0.5913 | 0.3162 | 0.9552 | 7497.45 | 0.1334 | 0.2373 |
| 40 | 676.07 | 185.13 | 262.89 | 548.51 | 14.950 | 0.5193 | 0.2753 | 0.9528 | 10536.94 | 0.0949 | 0.2800 |
| 60 | 388.86 | 178.20 | 213.64 | 292.45 | 28.039 | 0.2769 | 0.4627 | 0.9274 | 2918.87 | 0.3426 | 0.1268 |
| 80 | 335.68 | 131.67 | 255.02 | 224.59 | 36.510 | 0.2126 | 0.3974 | 0.9099 | 4610.49 | 0.2169 | 0.1616 |
| 100 | 299.88 | 110.88 | 402.89 | 163.28 | 50.219 | 0.1546 | 0.3784 | 0.8439 | 6097.81 | 0.1640 | 0.1580 |

**Table 5**

Different association parameters for $CuCl_2$ in binary mixtures (EtOH–$H_2O$) in the absence of indomethacin at 298.15 K using the Fuoss-Hsia-Fernández-Prini equation.

| V% of EtOH | $\Lambda_0$ S.cm$^2$. Mol$^{-1}$ | $\Lambda_m$ S.cm$^2$. Mol$^{-1}$ | S | $\Lambda_o\eta$ S.cm$^2$.mPa. s. Mol$^{-1}$ | $10^{-3}R_H$ A$^o$ | $R_x$ | $\alpha$ | $\gamma\pm$ | $K_A$ dm$^3$·mol$^{-1}$ | $10^{-3}K_D$ mol.dm$^{-3}$ | $10^{-3}K_3$ (dm$^3$·mol$^{-1}$)$^2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 1186.45 | 304.92 | 332.39 | 1056.30 | 7.763 | 1.0000 | 0.2579 | 0.9629 | 12035.26 | 0.0831 | 0.3064 |
| 20 | 812.75 | 247.50 | 261.84 | 735.17 | 11.154 | 0.6960 | 0.3058 | 0.9565 | 8110.35 | 0.1233 | 0.2479 |
| 40 | 354.51 | 156.42 | 159.69 | 327.65 | 25.027 | 0.3102 | 0.4445 | 0.9419 | 3168.48 | 0.3156 | 0.1391 |
| 60 | 199.08 | 130.68 | 129.28 | 189.77 | 43.211 | 0.1797 | 0.6653 | 0.9159 | 901.55 | 1.1092 | 0.0502 |
| 80 | 159.32 | 106.92 | 142.38 | 159.33 | 51.464 | 0.1508 | 0.6842 | 0.8811 | 868.79 | 1.1510 | 0.0446 |
| 100 | 89.13 | 17.82 | 204.01 | 97.06 | 84.480 | 0.0919 | 0.2058 | 0.8225 | 27707.70 | 0.0361 | 0.2952 |

MeOH or EtOH resulted in greater ion pair formation due to a change in the solvent composition caused by hydrogen bonding, which decreased ion mobility, allowing ions to connect.

Consider the association for the following reaction according to Equation (14):

$$M^{n+} + nX^- \Leftrightarrow MXn \tag{14}$$

The association constant is given by Equation (15):

$$K_A = \frac{C_{[MX_n]} \cdot \gamma_{[MX_n]}}{C_{M^{n+}} \cdot \gamma_{M^{n+}} \cdot C_{X^-}^n \cdot \gamma_{X^-}^n} \tag{15}$$

The following Equation (16) was used to calculate the values of the dissociation constant ($K_D$) using the values of the association constant ($K_A$):

$$K_D = 1/K_A \tag{16}$$

Using Equation (17), the values of the triple ion association constant ($K_3$) were computed [30,31].

$$\left[\Lambda_m \, C^{1/2} \, / \, \left(1 - \Lambda_m / \Lambda_o\right)^{1/2}\right] = \left(\Lambda_o \, / \, K_A^{1/2}\right) + \left(\lambda_3^o \, C \, / \, K_3 \, K_A^{1/2}\right) \cdot \left(1 - \Lambda_m / \Lambda_o\right) \tag{17}$$

For $CuCl_2$ in a mixture of (MeOH–$H_2O$) and (EtOH–$H_2O$), the values of the association parameters were computed and are shown in Tables 2–5

### 3.1.4. Determination of the walden product

The Walden product is crucial in explaining the ion-solvent interaction and can be derived using Eq. (18) [32,33].

$$\Lambda_o\eta_o = 0.82\left[1 / r_s^+ + 1 / r_s^-\right] \tag{18}$$

$r$ was used to represent the radius of a hypothetical sphere. Hydrodynamic radii and Walden product values for $CuCl_2 \cdot 2H_2O$ were calculated using the Fuoss Shedlovsky formula (Tables 2, 3, 6 and 7) and Fuoss-Hsia-Fernández-Prini formula (Tables 4 and 5). To explain the inverse values of the hydrodynamic radii, many authors have used the Walden product [34,35].

The value of the Walden product decreased as the methanol or ethanol concentration rose. Alcohol causes the mobility of ions to drastically decrease with increasing temperature, which increases the limiting molar conductance. It is possible to explain the decline in Walden product values with rising methanol or ethanol concentrations by assuming that the cation has larger solvation shells surrounding it, which reduces its mobility and Walden product. Equation (19) was also used to calculate the fluidity ratios ($R_x$) [36].

$$\overset{x}{R} = \frac{\overset{o}{\Lambda}\overset{o}{\eta} (\text{organic solvent})}{\overset{o}{\Lambda}\overset{w}{\eta} (\text{in water})} \tag{19}$$

**Table 6**

Different association parameters for $CuCl_2$ in binary mixtures (MeOH–$H_2O$) in the presence of indomethacin at 298.15 K using the Fuoss-Shedlovsky equation.

| V% of MeOH | $\Lambda_0$ S.cm$^2$. Mol$^{-1}$ | $\Lambda_m$ S.cm$^2$. Mol$^{-1}$ | S | $\Lambda_o\eta$ S.cm$^2$.mPa. s. Mol$^{-1}$ | $10^{-3}R_H$ A$^o$ | $R_x$ | $\alpha$ | $\gamma\pm$ | $K_A$ dm$^3$·mol$^{-1}$ | $10^{-3}K_D$ mol.dm$^{-3}$ | $10^{-3}K_3$ (dm$^3$·mol$^{-1}$)$^2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 579.00 | 405.41 | 193.73 | 515.48 | 15.907 | 1.0000 | 0.7018 | 0.9672 | 9708 | 0.1030 | 2.1630 |
| 20 | 375.00 | 271.76 | 159.30 | 320.91 | 20.235 | 0.6225 | 0.7268 | 0.9642 | 8343 | 0.1199 | 1.9979 |
| 40 | 319.00 | 231.66 | 162.25 | 258.81 | 41.075 | 0.5021 | 0.7288 | 0.9596 | 8319 | 0.1202 | 1.9922 |
| 60 | 248.00 | 196.02 | 166.75 | 186.51 | 62.792 | 0.3618 | 0.7943 | 0.9516 | 5401 | 0.1851 | 1.5966 |
| 80 | 221.00 | 174.49 | 204.01 | 147.87 | 65.072 | 0.2868 | 0.7948 | 0.9352 | 5570 | 0.1795 | 1.6194 |
| 100 | 180.00 | 142.56 | 306.64 | 98.01 | 209.162 | 0.1901 | 0.8019 | 0.8839 | 5916 | 0.1690 | 1.6655 |

**Table 7**
Different association parameters for CuCl$_2$ in binary mixtures (EtOH–H$_2$O) in the presence of indomethacin at 298.15 K using the Fuoss-Shedlovsky equation.

| V% of EtOH | $\Lambda_0$ S.cm$^2$. Mol$^{-1}$ | $\Lambda_m$ S.cm$^2$. Mol$^{-1}$ | S | $\Lambda_0\eta$ S.cm$^2$.mPa. s. Mol$^{-1}$ | $10^{-3}R_H$ A$^o$ | $R_x$ | $\alpha$ | $\gamma\pm$ | $K_A$ dm$^3$.mol$^{-1}$ | $10^{-3}K_D$ mol.dm$^{-3}$ | $10^{-3}K_3$ (dm$^3$.mol$^{-1}$)$^2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 579.00 | 405.41 | 193.73 | 515.48 | 15.907 | 1.0000 | 0.7018 | 0.9672 | 9708 | 0.1030 | 2.1630 |
| 20 | 448.00 | 320.76 | 172.29 | 405.24 | 25.553 | 0.7861 | 0.7179 | 0.9647 | 8823 | 0.1133 | 2.0579 |
| 40 | 216.00 | 181.17 | 122.03 | 199.63 | 31.683 | 0.3873 | 0.8423 | 0.9606 | 3613 | 0.2768 | 1.2990 |
| 60 | 137.00 | 130.00 | 109.54 | 130.59 | 43.965 | 0.2533 | 0.9550 | 0.9530 | 816 | 1.2258 | 0.5994 |
| 80 | 126.00 | 115.83 | 128.11 | 126.01 | 55.456 | 0.2445 | 0.9266 | 0.9338 | 1470 | 0.6804 | 0.8115 |
| 100 | 36.00 | 22.28 | 136.78 | 39.20 | 83.665 | 0.0761 | 0.6340 | 0.8248 | 20,073 | 0.0498 | 2.9084 |

It was observed that the molar and limiting molar conductance of the CuCl$_2$·2H$_2$O solutions using binary MeOH–H$_2$O mixed solvents decrease with increasing MeOH content, and the same trend occurs when using EtOH as the solvent because the MeOH and EtOH solvents have dipole moments less than that of water (32.7, 24.5, and 78.35, respectively, at 298.15 K) [37], and the dielectric constant decreases with increasing organic solvent content (MeOH or EtOH). This decrease is caused by the destruction of water hydrogen bonds by organic solvent molecules [38–40]. Except when employing pure EtOH solvent at the same temperature, the association constant (KA) decreases as the amount of organic solvent increases in the binary (MeOH–H$_2$O) and (EtOH–H$_2$O) mixed solvents. Because the relative permittivity of organic solvents is low in pure solvents, there is a decrease in the mobility of the ions, which creates the opportunity for ions to associate. This causes the association constant (KA) values to decrease.

### 3.1.5. Association thermodynamic parameters

By applying Equation (20), the association Gibbs free energy change ($\Delta G_A$) of CuCl$_2$·2H$_2$O in (MeOH–H$_2$O) and (EtOH–H$_2$O) mixtures was computed [36].

$$\Delta G_A = - 2.303 \; RT\log K_A \tag{20}$$

Equation (21) were used to calculate the change in transfer free energies ($\Delta G_t$) from water (w) as the reference solvent to MeOH or EtOH solvents (s) or mixed solvents.

$$\Delta G_t = \Delta G_{A\;(s)} - \Delta G_{A\;(w)} \tag{21}$$

Association thermodynamic parameters for CuCl$_2$ in the binary mixtures (MeOH–H$_2$O) and (EtOH–H$_2$O) were listed in Tables 8 and 9.

When the results of two applicable equations were compared, the values were found to be quite close, specifically the values of Gibbs free energy association and Gibbs free energy of transfer. We discovered that the differences between the thermodynamic parameters obtained from two distinct equations are quite minimal, suggesting that the equations are valid and that salt behavior is unaffected by changes made to the equation.

## 3.2. Electrochemical voltammetry of copper chloride

### 3.2.1. Effect of CuCl$_2$ concentration

In 30 ml (0.1) M KBr as a supporting electrolyte, the redox behavior of Cu$^{2+}$ ions was investigated in a 1 to −1 V potential window at a scan rate of 0.1 V s$^{-1}$ and 298.15 K. Stepwise addition of the CuCl$_2$ solution was performed from 0.6 ml (1.961 × 10$^{-6}$) mol·cm$^{-3}$ to 1.2 ml (3.846 × 10$^{-3}$) mol·cm$^{-3}$. These data are shown in Fig. 4, which illustrates the correlation between the concentration of copper chloride solution introduced and the measured redox behavior of Cu$^{2+}$ ions.

The electrochemical behavior of a system can be greatly influenced by the concentration of metal ions present in the solution. The peak current, peak potential, and voltammogram's form in voltammetric tests can all be impacted by the metal ion concentration. Low concentrations may result in a weak or non-existent voltammetric response. This occurs because the solution contains insufficient

**Table 8**
CuCl$_2$ association thermodynamic parameters in the binary mixtures (MeOH–H$_2$O) at 298.15 K.

| V% of MeOH | Fuoss-Shedlovsky eq. | | Fuoss-Hsia-Fernández-Prini eq. | | Fuoss-Shedlovsky eq. | |
|---|---|---|---|---|---|---|
| | $\Delta G_A$ kJ mol$^{-1}$ | $\Delta G_t$ kJ mol$^{-1}$ | $\Delta G_A$ kJ mol$^{-1}$ | $\Delta G_t$ kJ mol$^{-1}$ | $\Delta G_A$ kJ mol$^{-1}$ | $\Delta G_t$ kJ mol$^{-1}$ |
| | in absence of indomethacin | | in absence of indomethacin | | in presence of indomethacin | |
| 0 | −23.72 | 0.000 | −23.29 | 0.000 | −22.76 | 0.000 |
| 20 | −22.56 | 1.164 | −22.12 | 1.173 | −22.39 | 0.376 |
| 40 | −23.48 | 0.241 | −22.96 | 0.330 | −22.38 | 0.383 |
| 60 | −20.28 | 3.445 | −19.78 | 3.512 | −21.31 | 1.454 |
| 80 | −21.63 | 2.088 | −20.92 | 2.379 | −21.38 | 1.378 |
| 100 | −22.96 | 0.757 | −21.61 | 1.686 | −21.53 | 1.228 |

**Table 9**

CuCl$_2$ association thermodynamic parameters in the binary mixtures (EtOH–H$_2$O) at 298.15 K.

| V% of EtOH | Fuoss-Shedlovsky eq. | | Fuoss-Hsia-Fernández-Prini eq. | | Fuoss-Shedlovsky eq. | |
|---|---|---|---|---|---|---|
| | $\Delta G_A$ kJ mol$^{-1}$ | $\Delta G_t$ kJ mol$^{-1}$ | $\Delta G_A$ kJ mol$^{-1}$ | $\Delta G_t$ kJ mol$^{-1}$ | $\Delta G_A$ kJ mol$^{-1}$ | $\Delta G_t$ kJ mol$^{-1}$ |
| | in absence of indomethacin | | in absence of indomethacin | | in presence of indomethacin | |
| 0 | −23.72 | 0.000 | −23.29 | 0.000 | −22.76 | 0.000 |
| 20 | −22.75 | 0.969 | −22.32 | 0.979 | −22.52 | 0.237 |
| 40 | −20.39 | 3.327 | −19.99 | 3.309 | −20.31 | 2.451 |
| 60 | −17.19 | 6.531 | −16.87 | 6.425 | −16.62 | 6.140 |
| 80 | −17.21 | 6.507 | −16.78 | 6.517 | −18.08 | 4.681 |
| 100 | −27.90 | −4.182 | −25.36 | −2.067 | −24.56 | −1.801 |
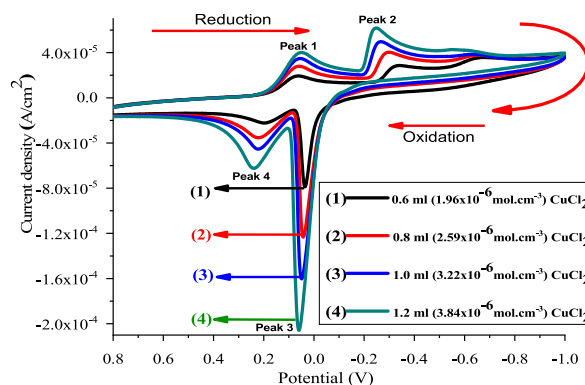


**Fig. 4.** Cyclic voltammogram of CuCl$_2$ at different concentrations.

metal ions to induce a noticeable electrochemical reaction. The voltammetric reaction will get stronger and more pronounced as the metal ion concentration rises, enabling more exact and accurate measurements. However, at high concentrations, the electrochemical behavior may become more complicated and difficult to interpret. For this reason, it's critical to precisely adjust the CuCl$_2$ concentration in order to obtain precise and trustworthy data in electrochemical studies. It is generally advised to stay away from concentrations that are too high or too low and to utilise concentrations that fall within the linear range of the calibration curve as shown in Fig. S1.

The following equations were used to discuss and explain cathodic/anodic peaks in the electrochemical redox behavior of copper ions using a gold electrode at steady-state current (22–27) [41,42]:

$$i_p = 0.4463\ n^{3/2}\ F^{3/2}\ A\ C\ D^{1/2}\nu^{1/2} \Big/ (R\ T)^{1/2} \tag{22}$$

$$\Delta E_P = E_{Pa}\ -\ E_{Pc} \tag{23}$$

$$k_h = 2.18 * [F\ \alpha\ n_a\ D_C\ \nu/RT]^{1/2}\ *\exp[F\ \alpha^2\ n\ \Delta E_P \big/ RT] \tag{24}$$

$$\alpha\ n_a = 1.857\ RT \Big/ (E_{pc} - E_{pc/2})\ F \tag{25}$$

$$\Gamma = i_p\ 4RT \big/ n^2\ F^2\ A\ \nu \tag{26}$$

$$Q = n\ FA\ \Gamma \tag{27}$$

where the peak current density, i$_p$, is measured in amperes, the working electrode surface area (A) in cm$^2$, the diffusion coefficient (D) in cm$^2$/sec, the scan rate ($\nu$) in Vs$^{-1}$, and the Cu$^{2+}$ ion concentration [M]. The term "$\Delta E_P$" stands for the "peak potential difference,' (n) refers to the quantity of electrons involved in redox reactions, (k$_s$) stands for the "standard heterogeneous electron transfer rate constant in cm/sec, ($\alpha$) stands for the "charge transfer coefficient,' (n$_a$) refers to the quantity of electrons transferred in the rate-determining step,' and (E$_{pc/2}$) refers to the half-wave potential for the cathodic peak. $\Gamma$ is the surface coverage in mol.cm$^{-2}$, and Q is the amount of charge used up during the reduction or adsorption of the adsorbed layer [43–45].

The various cyclic voltammetric data [Ep$_a$, Ep$_c$, Ip$_a$, Ip$_c$, $\Delta E_P$, E$_{pc/2}$, D$_a$, D$_c$, k$_s$, $\Gamma_a$, $\Gamma_c$, Q$_a$ and Q$_c$] were calculated and are listed in Tables S1 and S2 for the reduction or oxidation peak of peaks.

The relationship between the cathodic and anodic peak currents density (Ip$_c$ & Ip$_a$) against various copper ion concentrations was studied using the Randless Sevicek equation, which yields straight lines to represent diffusion-controlled processes [46,47], as shown

in Fig. S1; it enables the calculation of crucial parameters, including the redox reaction's number of involved electrons and diffusion coefficient.

The ease with which particles flow across a medium is gauged by its diffusion coefficient. Because solvent molecules envelop the ions in liquid electrolytes, thereby impeding their mobility, the diffusion coefficient may be extremely low. Accordingly, the diffusion coefficient by itself might not provide a realistic picture of the ion diffusion in a liquid electrolyte. To completely comprehend the diffusion behavior of ions in liquid electrolytes, additional aspects including ion pairing, solvation, and electrostatic interactions must also be taken into account. Temperature, pressure, viscosity, and concentration are just a few of the variables that might affect the diffusion coefficient. A larger diffusion coefficient is produced at low concentrations because there is less chance of interaction and more room for the ions to roam around. It can slow down the ions' diffusion and produce a lower diffusion coefficient at larger concentrations because the ions get more crowded and likely to interact with one another. Diffusion behavior of the ions may also be impacted by the solvent molecules becoming more structured or organised at greater concentrations. Since these components interact intricately, it is possible for the diffusion coefficient values to fluctuate inconsistently with concentration.

### 3.2.2. Effect of indomethacin

Equations 22–27 were used to study the electrochemical redox behavior of $Cu^{2+}$ ions at the steady-state current at the gold electrode in the presence of various indomethacin concentrations (Fig. 5). Since there was no wave observed for indomethacin alone, negative shift in potentials for the cathodic peak and positive shift in the anodic peak were observed by increasing addition of different indomethacin concentrations to $(3.85 \times 10^{-6})$ mol·cm$^{-3}$ CuCl$_2$ which confirmed the formation of complex between them. The solvation and kinetic characteristics of interactions between $(3.84 \times 10^{-6})$ mol·cm$^{-3}$ $Cu^{2+}$ ions and various indomethacin concentrations at scan rates of 0.1 V s$^{-1}$ and 298.15 K are presented in Table S3 for the reduction and oxidation peaks (1 & 3) and Table S4 for the reduction and oxidation peaks (2 & 4). The electrochemical behavior of $Cu^{2+}$ ions in solution is influenced by the presence of indomethacin as a ligand, which attaches themselves to metal ions to produce complexes that differ from the free metal ion in terms of their chemical and physical characteristics. The effect of the concentration of indomethacin on surface coverage Γ was investigated. It was observed from Tables S1 and S2 that as the concentration of indomethacin increased, the surface coverage also increased accordingly due to increasing in the geometric area. This study provides valuable insights into the effect of different indomethacin concentrations on the electrochemical behavior of $Cu^{2+}$ ions; the findings help to elucidate how the concentration of indomethacin affects the redox behavior and provides a basis for further research in this area. For instance, indomethacin as ligands can cause peak potential to shift to more negative values and peak current to decrease when they form stable complexes with $Cu^{2+}$ ions. The negative shift in potential was not only attributed to the complexation of Cu ions with indomethacin but also to the adsorption of indomethacin on the electrode surface. This is because fewer free metal ions are available for electrochemical reactions at the electrode surface as a result of the metal-ligand complex formation. We provide a CV of pure indomethacin for reference in Supplementary Materials as shown in Fig. S2; Compared with Fig. 4, a new reduction peak appears near peak 3 in Fig. 5. It is appear to be due to a new reaction of indomethacin interacting with $Cu^{2+}$ ions forming Cu-indomethacin complex which is in equilibrium with a free $Cu^{2+}$ ions in solution [Eq. (28)].

$$Cu^{2+} + \text{indomethacin} \leftrightarrow \text{Cu-indomethacin} \tag{28}$$
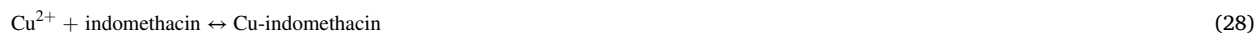
Randless Sevicek's equation was used to analyze the relationship between the cathodic and anodic peak currents density with respect to various copper ion concentrations when indomethacin was present, as shown in Fig. S3.

### 3.2.3. Effect of scan rates

The electrochemical behavior of metal ions in solution can be influenced by the voltammetric experiment's scan rate in addition to the presence of ligands. The pace at which the potential changes throughout the experiment is referred to as the scan rate. Low scan rates may give the electrochemical reaction enough time to reach equilibrium, giving the voltammogram distinct peaks. On the other hand, enlarged or distorted peaks in the voltammogram could result from the electrochemical reaction not having enough time to reach equilibrium at high scan speeds. The kinetics of the electrochemical reaction, the concentration of the species in solution, and the composition of the electrode material can all have an impact on how scan rate affects the electrochemical behavior of metal ions. Fig. 6 shows the results of the study on the influence of the varied scan rates (0.10, 0.05, 0.02, and 0.01) Vs$^{-1}$ on the interaction between $(3.636 \times 10^{-6}$ mol cm$^{-3}$ CuCl$_2$ and $(3.955 \times 10^{-7}$ mol cm$^{-3}$ indomethacin). Table S5 details the solvation and kinetic properties of various $Cu^{2+}$ ion scan rates in the presence of indomethacin.

### 3.2.4. Electrochemical behavior of CuCl$_2$ and indomethacin complexation

Complex formation is favored over complex dissociation, as indicated by the stability constant ($\beta_j$). A more stable complex is one that is less likely to dissociate into its component ions, which is indicated by a larger value of ($\beta_j$). The complex's behavior under various conditions can be predicted using the stability constants, and experiments can be created to better understand the complex's properties [48–52]. The following Equations 29–31 are used to compute the stability constants ($\beta_j$) of the copper complex for each addition:

$$\Delta E° = E°_C + E°_M = 2.303 \, (RT / nF)\left(\log \beta_j + j \log C_x\right) \tag{29}$$

$$\Delta E° = \left(E_{pa} + E_{pc}\right) / 2 \tag{30}$$

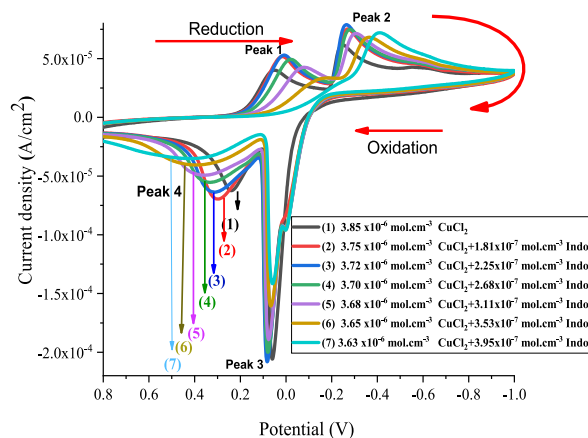**Fig. 5.** Cyclic voltammograms for the interaction of $(3.84 \times 10^{-6})$ mol·cm$^{-3}$ CuCl$_2$ with various indomethacin concentrations at scan rates of 0.1 V s$^{-1}$ and 298.15 K.
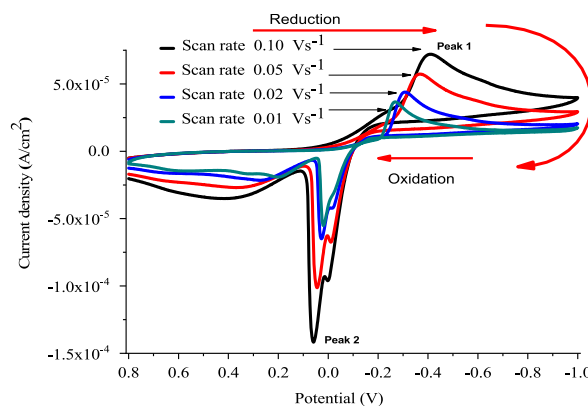


**Fig. 6.** Cyclic voltammogram of $(3.636 \times 10^{-6})$ mol·cm$^{-3}$ CuCl$_2$ with $(3.955 \times 10^{-7})$ mol·cm$^{-3}$ indomethacin at different scan rates and 298.15 K.

$$\Delta G = -\ 2.303\ RT\log \beta_j \tag{31}$$



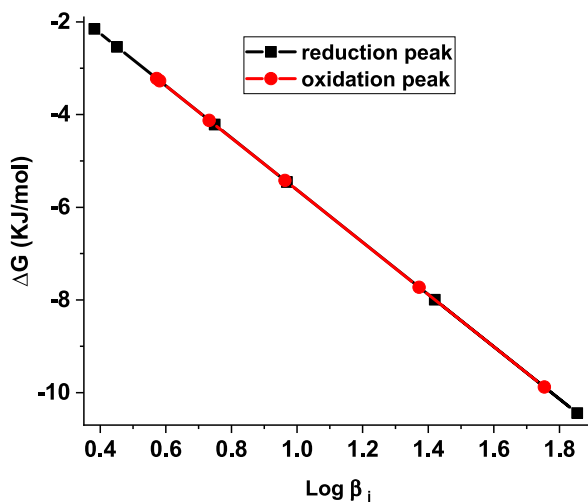**Fig. 7.** Relationship between ($\Delta G$) Gibbs free energy and (Log $\beta_j$) stability constant for (■) reduction peak and (●) oxidation peak at 298.15 K & a scan rate of 0.1 V s$^{-1}$.

where $E°_M$ is the formal peak potential of copper ions at final addition in the absence of indomethacin, $E°_C$ is the formal peak potential of the copper complex after each addition of indomethacin, the coordination number of the stoichiometric complex is j, the concentration of indomethacin in the solution is $C_x$, the formal potential is $E°$, the anodic peak potential is $Ep_a$, the cathodic peak potential is $Ep_c$, the stability constant is $β_j$, and the Gibbs free energy of the interaction between copper ions and indomethacin is $ΔG$.

By drawing the relation between the Gibbs free energy ($ΔG$) of the interaction of copper ions with indomethacin against the Log of stability constant (Log $β_{MX}$), a straight line is obtained, as shown in Fig. 7.

The estimated and compiled values of $E°$, $β_j$ and $ΔG$ for the copper complex are shown in Table 10 for the first couple of peaks and Table 11 for the second couple of peaks. A higher stability constant indicates a stronger interaction between the $Cu^{2+}$ ions and indomethacin [53–55].

## 4. Conclusions

We examined the experimental conductance data using the Fuoss-Shedlovsky and Fuoss-Hsia-Fernández-Prini models. The variation between the association parameters obtained from the two different equations is remarkably small. The association constant values increased with the alcohol content, suggesting that it was more likely that ion pairs would form. The value of the Walden product decreased as the methanol or ethanol concentration rose. When indomethacin was added, the electrical conductance of copper chloride solutions decreased; this effect was more noticeable in methanol than in ethanol and in their binary mixture with water; this could be a result of indomethacin's interaction with copper chloride, which lowers the amount of free ions in the solution. The Randless Sevicek equation was used to analyze the cyclic voltammetry investigation of the electrochemical redox behavior of copper chloride using a gold electrode and its interaction with indomethacin. The copper chloride cyclic voltammogram differs when indomethacin is present from when it is not. A change in the redox behavior or kinetics is indicated by a shift in the peak potentials. Indicating changes in reaction rates or electron transfer mechanisms, the peak currents may also change. In general, this knowledge can be helpful in comprehending the electrochemical characteristics and prospective uses of indomethacin and copper chloride, as well as in creating novel drugs or therapeutic agents. According to these results, copper chloride might be useful in pharmaceutical formulations and drug delivery. It has been demonstrated that copper chloride possesses potential anti-inflammatory, antibacterial, and antioxidant qualities, which may make it helpful in medicinal compositions. For instance, it might be added to dietary supplements to lower oxidative stress or utilized as an active component in topical gels or creams to cure skin inflammation. Furthermore, the anti-inflammatory properties of copper ions have been demonstrated, and they are being investigated as a possible treatment for inflammatory conditions including rheumatoid arthritis [56,57].

## Data availability

Data will be made available on request.

## CRediT authorship contribution statement

**AbdulAziz A. Alayyafi:** Resources, Project administration, Funding acquisition. **Hany A. Nasef:** Writing – review & editing, Formal analysis, Conceptualization. **Shereen E. Salem:** Investigation, Formal analysis, Data curation. **Esam A. Gomaa:** Writing – original draft, Supervision, Software, Resources. **Elsayed M. AbouElleef:** Writing – review & editing, Writing – original draft, Supervision, Resources, Methodology, Investigation.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e24071.

**Table 10**
Formal potential $E°$, stability constant $β_j$ and Gibbs free energy $ΔG$ of copper complexes for the reduction and oxidation peaks (1 & 3) at scan rates of 0.1 V s$^{-1}$ and 298.15 K.

| [M] ($10^{-6}$ mol cm$^{-3}$) | [L] ($10^{-7}$ mol cm$^{-3}$) | $Ep_a$ (V) | $Ep_c$ (V) | j | Log [L] | Log $β_j$ | $β_j$ | $ΔG$ (KJ/mol) |
|---|---|---|---|---|---|---|---|---|
| 3.750 | 1.813 | 0.149 | 0.160 | 0.048 | −3.742 | 0.382 | 2.409 | −2.151 |
| 3.727 | 2.252 | 0.149 | 0.162 | 0.060 | −3.648 | 0.451 | 2.825 | −2.540 |
| 3.704 | 2.685 | 0.149 | 0.177 | 0.073 | −3.571 | 0.749 | 5.604 | −4.216 |
| 3.681 | 3.113 | 0.149 | 0.188 | 0.085 | −3.507 | 0.969 | 9.309 | −5.457 |
| 3.659 | 3.537 | 0.149 | 0.237 | 0.097 | −3.451 | 1.854 | 71.422 | −10.441 |
| 3.636 | 3.955 | 0.149 | 0.210 | 0.109 | −3.403 | 1.420 | 26.296 | −7.997 |

**Table 11**

Formal potential E°, stability constant β$_j$ and Gibbs free energy ΔG of copper complexes for the reduction and oxidation peaks (2 & 4) at scan rates of 0.1 V s$^{-1}$ and 298.15 K.

| [M] ($10^{-6}$ mol cm$^{-3}$) | [L] ($10^{-7}$ mol cm$^{-3}$) | E$_{pa}$ (V) | E$_{pc}$ (V) | j | Log [L] | Log β$_j$ | β$_j$ | ΔG (KJ/mol) |
|---|---|---|---|---|---|---|---|---|
| 3.750 | 1.813 | 0.151 | 0.173 | 0.048 | −3.742 | 0.572 | 3.734 | −3.223 |
| 3.727 | 2.252 | 0.151 | 0.172 | 0.060 | −3.648 | 0.581 | 3.809 | −3.271 |
| 3.704 | 2.685 | 0.151 | 0.178 | 0.073 | −3.571 | 0.732 | 5.400 | −4.125 |
| 3.681 | 3.113 | 0.151 | 0.190 | 0.085 | −3.507 | 0.963 | 9.179 | −5.422 |
| 3.659 | 3.537 | 0.151 | 0.211 | 0.097 | −3.451 | 1.372 | 23.543 | −7.727 |
| 3.636 | 3.955 | 0.151 | 0.231 | 0.109 | −3.403 | 1.754 | 56.760 | −9.879 |

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