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Electrochemical and Thermodynamic Properties of Diclofenac and Dibucaine Ions Across Water|1,6-dichlorohexane Interface

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In this work, the electrochemical behaviour of diclofenac anion and dibucaine cation via a water|1,6-dichlorohexane liquid | liquid interface system was characterised. Both ions have been undergone voltammetry of ion transfer across the liquid-liquid interface. Analytical parameters such as the formal transfer potential, standard Gibbs energy of transfer across the interface, and the partition coefficient for both drugs were determined. The partition coefficient is of great importance for the estimation of the lipophilicity' ions, which plays a role in its distribution in living organisms and its effect on biological media. Furthermore, the different performance characteristics of the cyclic voltammetry (CV) technique were exploited to extract the values of the aqueous diffusion coefficients of both diclofenac and dibucaine, which were in a good agreement with the theoretically predicted values based on their molar mass, $4.18 \pm 0.05 \times 10^{-6}$ cm^2 s^{-1} and $3.43 \pm 0.04 \times 10^{-6}$ cm^2 s^{-1}, respectively.

Keywords: Ion transfer – Diclofenac – Dibucaine – voltammetry – 1,6-dichlorohexane

1. INTRODUCTION

Electrochemistry at the interface between two immiscible electrolyte solutions (ITIES) has aroused the interest of many researchers in the field of analytical chemistry for the past four decades [1]. This field has been developed very rapidly with various applications in recent years, e.g., electrochemically modified liquid-liquid (L|L) extraction, particle precipitation, and charge transfer processes (both electron and ion) across liquid-liquid interfaces [2–7]. The ion transfer process of ionisable drugs across the ITIES has been a great interest in pharmacology for the past 20 years [8–10].

Some of the limitations of the traditional experimental studies with ITIES are the instability of the organic phase and the short width of the potential window. Although there are some exceptions, the water (W)/n-octanol system is not suitable to be used to study the standard assay electrochemically for lipophilicity in the pharmaceutical industry due to the high resistivity of the organic phase [11, 12]. Numerous efforts have been made to overcome these limitations, such as replacing conventional solvents used in ITIES studies, i.e., 1,2-dichloroethane (1,2-DCE) and nitrobenzene (NB), with 2-nitrophenyl octyl ether (NPOE). However, although this solvent it is suitable for the ion transfer at the liquid|liquid interface, it is expensive and difficult to prepare, with a shorter potential window than 1,2-DCE and 1,6-dichlorohexane (1,6-DCH) solvents [13–15]. The 1,6-DCH is a suitable solvent for ion transfer studies across liquid|liquid interfaces, as illustrated by voltammetric studies [16–18], due to its lower permittivity although and a wider potential window than 1,2-DCE, NB and NPOE solvents. Few works have been reported on the W | 1,6-DCH interface with numerous studies on the other solvents such as nitrobenzene,1,2-dichloroethane, and 2-nitrophenyl octyl ether (NPOE) [17].

The study of ion transfer at ITIES by different electrochemical techniques is a simple way for determining the standard Gibbs energy of transferred ions species via a water| oil system. This parameter is directly related to the partition coefficient of the ion, which expresses the relative affinity for the organic phase; i.e. the ion lipophilicity, a critical drug characteristic for the design of new drugs and its transfer in biological systems [13]. Beside lipophilicity parameter, the aqueous diffusion coefficient is readily determined from voltammetry ion transfer across liquid|liquid interfaces, based on the current response as a function of scan rate as expressed by the Randles-Ševčík equation [19]. The diffusion coefficient is an essential parameter in various media to study dynamic drug transfer in a living organism, along with dissociation equilibria, solubility, and lipophilicity [20, 21].

Ion transfer voltammetry via the ITIES is always applied to determine the diffusion coefficients for organic molecules (drugs) compared to the solid | electrolyte interface where a complex redox process often occurs on the solid electrode, which may lead to a mechanical inaccuracy of the number of electrons transferred [22, 23]. A limited number of studies reported the determination of diffusion coefficients for ionised drugs via ion transfer voltammetry at liquid|liquid interfaces compared to several studies for the determination of ionic partition coefficients that expresses the lipophilicity of these ions related to the values of standard transfer potentials [24]. Most of the organic compound molecules such as drugs are present in the form of weak bases, partially ionised weak acids, or in a neutral form (zwitterions). Therefore, the partial ionisation of these drugs may impede the accurate estimation of diffusion coefficients by ion transfer voltammetry at the liquid|liquid interface due to complicated partition/ionisation situation, as previously reported [25].

Diclofenac (DCF) as a sodium salt (sodium 2-{2-[(2,6-dichlorophenyl) amino] phenyl} acetate) as shown in Figure 1(a), is a clinical drug commonly utilised as an anti-inflammatory, antipyretic and analgesic agent [26]. However, it affects the endocrine system of biological species even at low environmental concentrations due to toxicity issues in veterinary use in some countries [27, 28]. As such, improved analytical methods for its determination are essential for continuous environmental monitoring. Several methods have been employed for the measurement of DCF, such as gas chromatography-mass spectrometry [29], spectrophotometry [30], and capillary electrophoresis [31]. Electrochemical techniques have also been utilised in the determination of DCF due to its various

advantages: portability, simplicity, minimal cost, and the short response time of analysis compared to other assessment methods [32]. Although several electrochemical approaches have been reported, those reports have been based on electrode|electrolyte interfaces using catalytic materials to modify the electrodes [33–38]. The behaviour of DCF at the ITIES has been reported [10], based on the pH lipophilicity profiles of a series of weak acids, bases, and ampholytes at water|1,2-DCE. The results demonstrated the domains of the predominant species present in both phases in the form of ionic partition diagrams. In our recent work [39], we also studied the electrochemical characterisation of DCF via water|1,6-DCH at the micro-interface, which showed miniaturisation effect of the interface from macroscale to microscale on the electrochemical behaviour of DCF transfer.

Dibucaine (DIC) or cinchocaine is an amide local anaesthetic drug, as shown in Figure 1(b). The present use of DIC is generally restricted to topical and spinal anaesthesia because it is among the most potent and toxic of the long-acting local anaesthetics [40]. The IUPAC name for DIC is 2-butoxy-N-[2-(diethylamino) ethyl] quinoline-4-carboxamide [41]. Many methods were used to determine DIC, including high performance liquid chromatography (HPLC) [42–46], gas chromatography (GC) [47, 48], column liquid chromatography (LC), derivative spectrophotometry techniques [49–51], and voltammetric methods [52,53]. The electrochemical transfer of local anaesthetics, including dibucaine, across a nitrobenzene (NB)|water (W) interface has been studied using polarography [15, 54]. These authors have also discussed the relationship between the pharmacological activity and the half-wave potential of the voltammogram. Similarly, Samec and co-workers [55] also studied the voltammetric and impedance measurements of ion transfer of numerous local anaesthetics, including dibucaine across water|o-nitrophenyl octyl ether interface to characterise the ion transport properties of drugs by the apparent rate constants. Thus, this work here is based on the characterisation of the electrochemical behaviour of dibucaine transfer across water|1,6-DCH to get more information on the thermodynamic parameters and transfer mechanism of DIC ions via the water|1,6-DCH system.

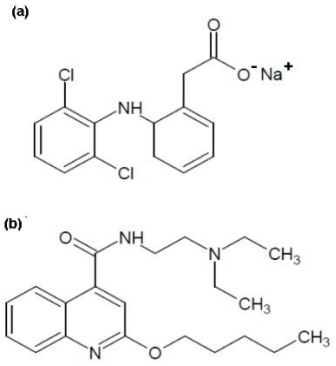

Figure 1. The chemical structure of diclofenac sodium(a) and dibucaine (b).

In this work, ion transfer of ionised drugs (diclofenac and dibucaine), across the water|1,6-DCH interface has been carried out using CV. The thermodynamic parameters such as the formal transfer potential and standard Gibbs energy of transfer across the interface and the partition coefficient of two drugs were determined. In addition to the parameters mentioned above, the different performance

characteristics of the CV method were utilised to determine the aqueous diffusion coefficients of both diclofenac and dibucaine. The results obtained in this study are considered as confirmation and support for previous work [39] to demonstrate the effect of the membrane on drug transfer behaviour.

2. EXPERIMENTAL PART

2.1. Materials

All chemical reagents used in this work were purchased from Sigma Malaysia and used as received unless otherwise specified. The supporting electrolyte for the aqueous phase, 10 mM lithium chloride (LiCl), was prepared in ultrapure water (18.2 MΩ cm) from Water Systems (Sartorius). Meanwhile, the supporting electrolyte for the organic phase was prepared by metathesis of bis(triphenylphosphoranylidene) ammonium chloride (BTPPACl; Sigma) and potassium tetrakis(4-chlorophenyl) borate (KTPBCl; Sigma). Then, 10 mM of the product (BTPPATPBCl) was dissolved in 98% 1,6-dichlorohexane (1,6-DCH) solvent from Sigma to prepare the organic phase. The purification of the 1,6-DCH solvent was carried out according to the procedure previously reported [16]. Both solvents water and 1,6-DCH were pre-saturated mutually before use. The organic reference solution was prepared by dissolving 1.0 mM of BTPPACl in the aqueous solution of 10 mM LiCl. Diclofenac sodium (Sigma), dibucaine hydrochloride (Fisher) as the selected drug, and tetramethylammonium chloride (TMACl) as an internal reference were prepared in aqueous 10 mM LiCl according to the desired concentrations.

2.2. Measurements

CV measurements were carried out by an Autolab potentiostat (PGSTAT101, Metrohm, Malaysia) together with Nova 1.1 software supplied with the apparatus. The cell of the water | 1,6-DCH interface was polarised by four-electrodes, comprising of two Ag/AgCl (saturated NaCl) electrodes as reference electrodes and two platinum mesh as counter electrodes as shown in Figure (2). The cell was custom-made from a glass tube with 15 mm inner diameters. All measurements were performed at room temperature 25 °C. The electrochemical cell used is as shown in this scheme:

Scheme 1

Ag	AgCl	1.0 mM BTPPACl in 10 mM LiCl (W)	10 mM BTPPATPBCl (1,6-DCH)	x µM drug at 10 mM LiCl pH/ HCl or LiOH (W)	AgCl	Ag	Cell 1

where x refers to the drug concentration in the aqueous phase, the transfer of the tetramethylammonium cation (TMA^+) as an internal reference was used to calibrate the cell potential scale to the absolute scale with its literature value on the absolute scale ($\Delta_o^w \emptyset'^{\circ}_{TMA^+}$) = 173 mV [13].

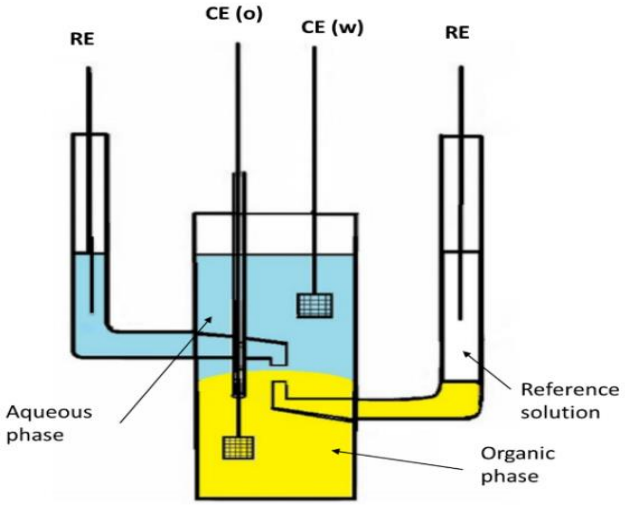

Figure 2. Diagram of the four-electrode cell employed for the ITIES experiments.

3. RESULTS AND DISCUSSION

3.1. Transfer of model ion across a water | 1,6-DCH interface

Ion transfer of tetramethylammonium cation (TMA^+) via water|1,6-DCH at the liquid|liquid interface using cyclic voltammetry was carried out to calibrate the experimental system. Before the addition of the model analyte ion, a sequence of CVs of the background electrolyte solutions was recorded to limit the potential window. Figure 3(a) represents the voltammograms of 16 µM of TMA^+ corresponding to the transfer from the aqueous to the organic phase, then back to the aqueous phase at a scan rate of 5 mV/s. The voltammogram on the forward and reverse scans exhibited symmetric behaviour, with sharp peaks on both forward and reversed sweeps and transfer peak potentials at approximately +0.73 V and +0.67 V, respectively. The peak-to-peak separation at the lowest sweep rate is approximately 60 mV, proportionate to the reversible transfer reaction of a single charge, as previously reported [16].

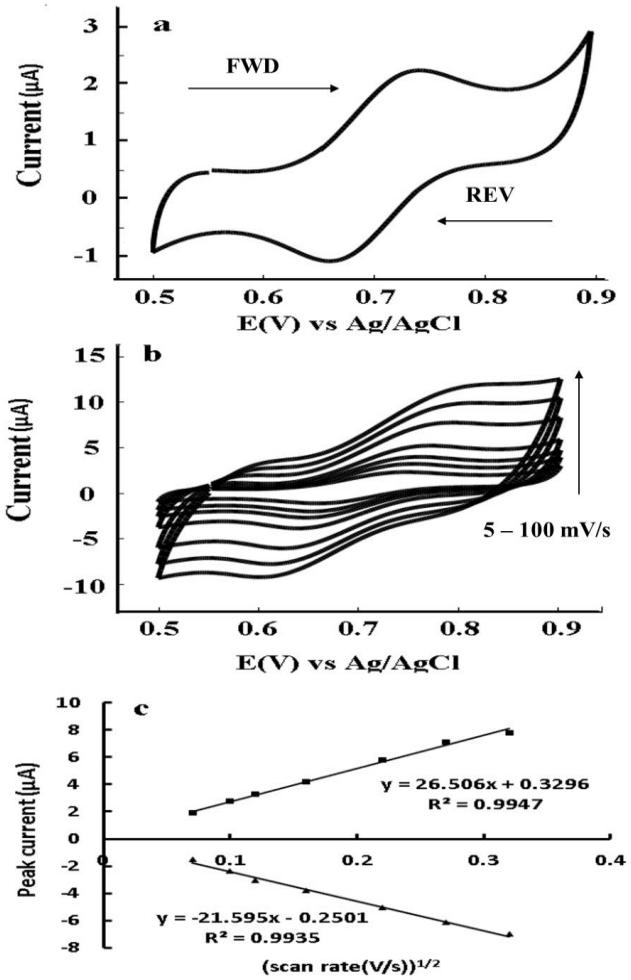

Figure 3. CV of ion transfer TMA^+ (16µM) ion at the range of scan rate 5 mV/s (a) across the ITIES (water|1,6-DCH). Effect of scan rate (5 – 100 mV/s) on TMA^+ transfer(b). The plot of the linear relationship between the peak currents for both forward (positive) and reverse(negative) sweep and the square root of scan rate $(mV/s)^{1/2}$ (c).

In this study, the sweep rate was varied between 5 and 100 mV/s in the presence of 16 µM of TMA^+. The resulting CVs are shown in Figure 3(b), demonstrating both forward and reverse peaks shift to a more positive and negative potential with increasing sweep rate. As a result, the current peaks become broader and less pronounced, due to the increase in capacitive charging current and assuming that uncompensated resistance is present in the cell. A plot of the peak current of the background-subtracted forward scan versus the square root of the scan rate is shown in Figure 3(c). The linearity between the peak currents for both forward and reverse, and the square root of the scan rates (5 - 100 mV/s) indicated a diffusion-controlled transfer process, as defined by the Randles-Ševčík in Equation 4[56].

$$I_p = 0.4463 \left(\frac{z_i^3 F}{RT}\right)^{1/2} FAD_{aq}^{1/2} C_{aq} \nu^{1/2} \quad (4)$$

where z_i is the charge number of the transferred ion i, F = 96485 C mol^{-1} is the Faraday constant, A is the interfacial area between the two liquids, D_{aq} is the aqueous diffusion coefficient of the ion, v is the scan rate, C_{aq} is the bulk concentration of the ion, T is the thermodynamic temperature, and R = 8.314 Jmol^{-1}K^{-1} is the gases constant. By plotting the peak currents as a function of the square root of scan rates (I_p vs. $v^{1/2}$) and obtaining the slope of the linear fit, the aqueous diffusion coefficient can be determined accurately.

The linear regression equation is y = 26.506x + 0.0704 and a correction coefficient (R^2) of 0.999 for the forward scans (positive direction) and y = -18.083x + 0.724, (R^2) of 0.9724 for the reverse scans. From Equation 4 and the slope of the plot obtained in Figure 3(c), the aqueous diffusion coefficient of TMA^+ was calculated to be 1.17×10^{-5} cm^2s^{-1}, in a good agreement with the previous value reported ($1.18 \pm 0.02 \times 10^{-5}$ cm^2s^{-1}) [25].

3.2. The electrochemical behaviour of diclofenac

The electrochemical behaviour of ion transfer process of diclofenac anion (DCF^-) across a water|1,6-DCH at the ITIES was examined. Figure 4(a) shows background-subtracted voltammogram of 80 µM of DCF^- (black line) and 25 µM of TMA^+ (grey line) at scan rate 5 mV/s. Diclofenac sodium is a salt of a weak acid in which the pKa of the phenylacetate ion is 3.99 ± 0.02 [10]; hence it is negatively charged at pH up to ~ 7.4 pKa maintained using 0.1 M LiOH solution to ensure it is at fully deprotonated state. The scan was started at 0.5 V towards the positive potential window edge first, where TMA^+ cation transfers from the aqueous phase into the organic phase at the peak transfer potential of 0.74 V. While DCF^- anion stays in the water phase under these conditions. As the potential difference between water and 1,6-DCH phase is swept to negative values i.e., the water phase is made negatively charged, the TMA^+ cation starts to transfer back into the aqueous phase at the transfer potential of 0.65. The DCF^- anion starts to transfer to the 1,6-DCH at a very negative applied potential difference (0.17 V), close to the lower limit of the potential window. This anion was transferred back into the aqueous phase, during the reverse scan (positive potential direction) at a peak transfer potential of 0.24 V. Although, the forward peak current of DCF^- anion was close to the applied transfer potential of background electrolyte ions in the limit of the potential window, the peak shape can still be obtained. TMA^+ was added to the aqueous phase as a potential axis reference ion.

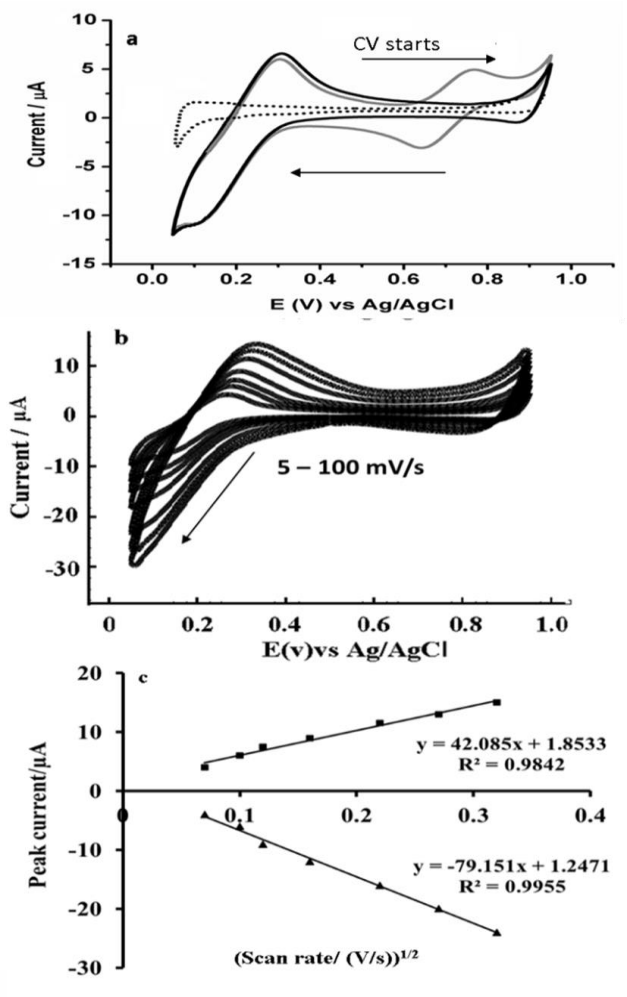

Figure 4. CV of ion transfer DCF^-(80µM) ion at scan rate 5 mV/s (black line) and 80 µM of $DCF^-$with internal reference molecule 25 µM of TMA^+(grey line) across the ITIES (water|1,6-DCH) (a). Effect of scan rate (5 – 100 mV/s on 80 µM of DCF^- transfer (b). The plot of the linear relationship between the peak currents for both forward (positive) and reverse(negative) sweep and the square root of scan rate (c).

he type of the processes occurring at the interface was investigated, CV at a fixed concentration (80 µM) of DCF was achieved at scan rates in the range of 5–100 mV s^{-1} (Figure 4(b)). The increase in the scan rate (5 – 100 mV/s) induced an increase in both forward and reverse peak currents, which resulted in the shifting to more positive potential and negative potential directions, respectively. As a result, the linear relationship, between the peak currents for the forward and reverse scans against the square root of scan rates, exhibited a significant intercept on the current axis, of ca. 1.8 µA (Figure 4(c)). This behaviour is due to an increase in heterogeneous kinetics and IR drops associated with increasing scan rate.

3.3 Electrochemical behaviour of dibucaine

Figure 5(a) shows the cyclic voltammogram for ion transfer of 40 µM dibucaine cation (DIC^+) and 16 µM TMA^+ across the water|1,6-DCH interface. The pKa of the amine group in DIC is 8.30 [15];

thus, pH of the aqueous phase 10 mM LiCl was adjusted to pH 4 below pKa of dibucaine to ensure that the DIC drug is strongly protonated. The voltammogram obtained demonstrated two sharp peaks on the potential forward sweep to transfer DIC^+ and TMA^+ ions from the aqueous phase to the organic phase at transfer potentials of +0.47 V and +0.74, respectively. The same sharp peaks are observed on the reverse scan at +0.40V and +0.67, respectively. The addition of 16 µM TMA^+ to the aqueous phase acts as a reference ion to verify adequate experimental setup. It can be seen that the transfers of TMA^+ and dibucaine are not overlapped, while the DIC^+ forward and reverse transfers are separated by ~70 mV, due to uncompensated resistance in the cell as observed in section 3.1.

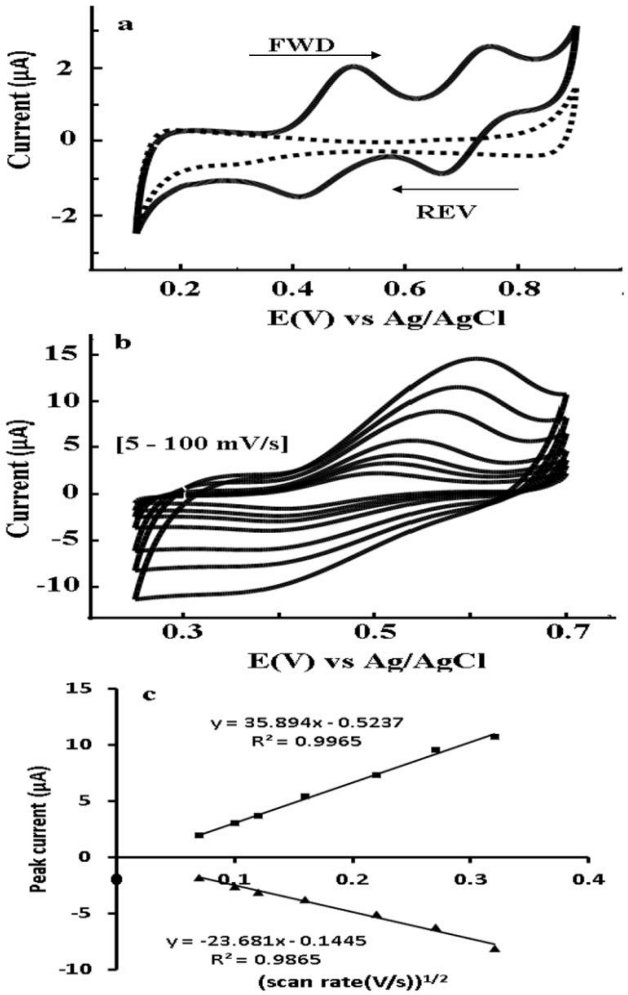

Figure 5. CV of the blank experiment (no analytes, dotted line) and 40 µM of DIC^+ transfer with internal reference molecule 16 µM of TMA^+ across the ITIES (water|1,6-DCH) at scan rate 5 mV/s. (a). Effect of scan rate (5–100 mV/s) on 40 µM of DIC^+transfer (b). The plot of the linear relationship between the peak currents for both forward (positive) and reverse(negative) sweep and the square root of scan rate (c).

The electrochemistry of dibucaine (40 µM) at increasing scan rates was also examined (Figure 5(b)). The increase in the scan rate (5 - 100 mV/s) induced an increase in the peak current with the shifting of the forward peak current to a more positive potential direction, while the reverse peak behaviour became less discernible due to uncompensated resistance is present in the cell as observed in sections 3.1 and 3.2. The linear relationship between the peak current and the square root of the scan rate

indicates a 1-dimensional diffusion-controlled process (Figure 5(c)). For the forward scan, the linear response is expressed by the slope equation I_p (µA) = 33.166 $\nu^{1/2}$ (V s^{-1})$^{1/2}$ + 0.073 (µA), R^2 = 0.9941, while for the reverse scan the linear response is given by I_p (µA) = -20.985 $\nu^{1/2}$ (V s^{-1})$^{1/2}$ – 0.5795 (µA), R^2 = 0.9987 as shown in Figure 5(c)).

3.4 Thermodynamic parameters of ionic species transfer at the water|1,**6**-*dichlorohexane interface*

The thermodynamic parameters for the diclofenac and dibucaine transfer across the water|1,6-DCH system were determined from the experimental CV data and summarised in Table (1). The $\Delta_o^w\emptyset_i^\circ$ can be determined by measuring the half-wave potentials for the internal ion reference $\Delta_o^w\emptyset_{ref}^{1/2}$ and ion analyst $\Delta_o^w\emptyset_i^{1/2}$ in the CV by a given value of the formal transfer potential of the reference $\Delta_o^w\emptyset_{ref}^\circ$ [55]:

$$\Delta_o^w\emptyset_i^{1/2} - \Delta_o^w\emptyset_i^\circ = \Delta_o^w\emptyset_{ref}^{1/2} - \Delta_o^w\emptyset_{ref}^\circ \quad (1)$$

The value of standard transfer potential of TMA^+ (173 mV) [14] was used to convert the obtained difference potential values to the Galvani potential scale. TMA^+ion was chosen as a potential axis ion because it has no mutual intervention with the selected drugs. Therefore, the value calculated of $\Delta_o^w\emptyset_{DCF^-}^\circ$ was – 0.32 V in a good agreement with the previous value (–0.32V) [39] and almost two-fold higher than the reported value via the water|1,2-DCE system (–0.124 V)[10]. This difference may be due to the ion-pair formation of the transferring anion with the supporting electrolyte cation present in the organic phase, as previously reported [18]. The value for $\Delta_o^w\emptyset_{DIC^+}^\circ$ was –0.092 V, i.e., in a good agreement with the literature value (–0,097 V) from the previous study [55] via the W|o-NPOE interface and lower than –0.169 V, as reported via NB/W interface [15].

The Gibbs energy of transfer ($\Delta G_{tr,Drug}^{0,w\to o}$) is directly associated with the standard transfer potential of the ion transfer by Equation 2 [57, 58].

$$\Delta G_i^{\circ,w\to o} = z_i F \Delta_o^w\emptyset_i^\circ \quad (2)$$

As a result, the ($\Delta G_{tr,DCF^-}^{0,w\to o}$) of DCF^- from the aqueous to 1,6-DCH phase was determined to be 30.6 kJ, while the value calculated of ($\Delta G_{tr,DIC}^{0,w\to o}$) was determined to be – 8.9 kJ mol^{-1}. Although diclofenac anion has a smaller standard transfer potential than dibucaine cation, it requires a considerable Gibbs transfer energy compared to the automatic transfer of dibucaine ion from the aqueous to the organic phase.

4.1. Determination of partition coefficient

The partition behaviour of the drug represents its relative affinity for the aqueous (hydrophilic) or the organic (lipophilic) phase and can be described by the partition coefficient $logP_i$. The calculated values of $\Delta_o^w\emptyset_i^{\circ\prime}$and $\Delta G_i^{\circ\prime,w\to o}$ are determined using Equation 3 to obtain the $logP_i$ for both drugs, as listed in Table 1.

$$logP_i = -\frac{\Delta G_i^{\circ\prime,w\to o}}{2.303RT} \quad (3)$$

hus, the partition coefficient of diclofenac ($logP_{DCF}^{\circ}$) was determined to be – 5.36. In the case of the comparison between the partition coefficient of the neutral form of DCF in n-octanol|water systems ($logP_{n-oct}^{\circ}$) (4.51) [59] and the obtained $logP_{DCF}^{\circ}$ of its ionised form in W|1,6-DCH system, the diclofenac exists under physiological conditions as a highly hydrophilic anion and thus favour the solvation in the aqueous phase. This behaviour is supported by the chemical structure of DCF containing two phenyl groups and two chlorine atoms which have positive fragmental constants and thus favour the solvation in the organic phase [10]. The charge on the phenylacetate ion group does not produce considerable stability of the ion in the organic phase.

In the same way, the calculated value of $logP_{DIC}^{\circ}$ was obtained as 1.56. It was compared to the partition coefficient of the neutral form of DIC^+ $logP_{n-oct}^{\circ}$ (4.4) [60], which indicates that the ionisable form of DIC exists under these conditions were less lipophilic cation. The results indicate that the partition coefficients of the neutral form of both drugs in n-octanol–water systems were equally lipophilic. However, in ionic forms, diclofenac is more hydrophilic than dibucaine.

4.2. Determination of diffusion coefficient across the interface

From the negative (cathodic) peak current, one could determine the diffusion coefficient of the transferred anion in water (or equivalently for this sign of current, for a cation in the 1,6- DCH phase). Similarly, the positive (anodic) peak current would yield the diffusion coefficient of the transferred cation in water, or anion in 1,6-DCH, respectively. Measuring the peak current at different scan rates allows the determination of the diffusion coefficient in the respective phase. Equation 4 was used to calculate the aqueous diffusion coefficient from the slopes obtained in Figures (4c) and (5c).

The aqueous diffusion coefficient of DCF^- was determined to be 4.18×10^{-6} cm^2 s^{-1}, which is in good agreement with the predicted value from its molar mass, 4.25×10^{-6} cm^2 s^{-1} by previously reported expression, $\log D_{aq} = -4.15 - 0.488 \log M_r$ [61] and slightly lower than a recent study report (5.75×10^{-6} cm^2 s^{-1} [39]. Different values of the aqueous diffusion coefficient of DCF^-were observed in the range of 2.67×10^{-6} to 3.7×10^{-4} depending on the pH used, hence, essential and accurate diffusion coefficient value is still needed [39]. Similarly, the measured D_{aq} of the dibucaine cation was 3.43×10^{-6} cm^2 s^{-1}, in a good agreement with a theoretically expected value according to its molar mass of 3.99×10^{-6} cm^2 s^{-1} [61] and two-fold lower than the previous value reported (7.9×10^{-6} cm^2 s^{-1}) across water|o-nitrophenyl octyl ether interface (NPOE) [55]. The results indicated that diffusion coefficient values for both drugs (diclofenac and dibucaine) are consistent in terms of the molecular mass, as the smaller diclofenac ion would be expected to diffuse more rapidly.

Table 1. The formal transfer potential, the standard Gibbs energy of transfer, the partition coefficient, and the aqueous diffusion coefficient of ionised diclofenac and dibucaine drugs in the water | 1,6-DCH system

Parameter	**DCF** ± SD	**DIC** ± SD
pK_a	3.99 ± 0.02 [a]	8.30 ± 0.12 [c]
$\Delta^{w}_{DCE}\emptyset^{\circ}$ (mV)	– 0.32 ± 0.02	– 0.092 ± 0.12
$\left(\Delta G^{0,w\rightarrow o}_{tr,DFC}\right)$(kJ mol^{-1})	30.6 ± 0.04	– 8.9 ± 0.01
$logP^{\circ}_{DCF}$	– 5.36 ± 0.18	1.56 ± 0.03
$logP^{\circ}_{n-oct}$(neutral)	4.51 [b]	4.4 [d]
D_{aq}(cm^2 s^{-1})	4.18 ± 0.05 × 10^{-6}	3.43 ± 0.04 × 10^{-6}

a) Ref. [10]
b) Ref. [59]
c) Ref. [15]
d) Ref. [60]

5. CONCLUSIONS

The electrochemical behaviour of diclofenac and dibucaine across water|1,6-DCH was characterised using cyclic voltammetry (CV). Both ions were found to undergo ion-transfer voltammetry at the liquid-liquid interface. The analytical parameters such as the standard potential, standard Gibbs energy of ion transfer across the interface and lipophilicity and aqueous diffusion coefficients for both drugs were determined. The results show that conventional voltammetry gives reliable data for determination of the diffusion coefficients of both DCF and DIC drugs accurately, based on ion transfer process across the ITIES.

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CONFLICTS OF INTEREST
The authors declare no conflict of interest.

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