Int. J. Electrochem. Sci., 16 **(2021)** Article Number: 211254, doi: 10.20964/2021.12.54

International Journal of
ELECTROCHEMICAL
SCIENCE
www.electrochemsci.org

Electrochemical Detection of Diclofenac and Dibucaine in Synthetic Saliva using Liquid|Liquid Micro-Interface Modified by Silicon Nitride

E. M. Almbrok[1], N. A. Yusof[1,2], J. Abdullah[1,2] and R. M. Zawawi[1,]*

[1] Department of Chemistry, Faculty of Science, University Putra Malaysia, 43400 UPM Serdang, Selangor,
[2] Institute of Advanced Technology, University Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia
[*]E-mail: ruzniza@upm.edu.my

Received: 1 September 2021 / *Accepted:* 7 October 2021 / *Published:* 10 November 2021

In this study, electrochemical characterization and detection of an anti-inflammatory drug diclofenac (DCF) and a local anesthetic drug dibucaine (DIC) at synthetic saliva|1,6- dichlorohexane interface were carried out for the first time using cyclic voltammetry (CV) and differential pulse voltammetry (DPV). Although the CV of synthetic saliva matrix slightly decreased the available potential window at the micro-ITIES, it has no significant effect on the ion-transfer voltammetry of DCF and DIC at liquid|liquid interface. Peak currents response by DPV were linearly increased with both DCF and DIC concentrations in the synthetic saliva matrix over the concentrations ranged 8–40 μmol L^{-1} and 8–24 μmol L^{-1}, and the calculated detection limits were 1.8 ± 0.2 μmol L^{-1} and 1.5 ± 0.14 μmol L^{-1}, respectively. These results demonstrated that DPV at liquid|liquid micro interfaces arrays is a feasible analytical method for ionizable drugs detection in biomimetic matrixes.

Keywords: ion transfer – diclofenac – dibucaine - synthetic saliva - voltammetric analysis

1. INTRODUCTION

Direct detection of drugs in physiological samples, such as blood and its derived samples, is significant in the insight of it offers data concerning diffusing levels. However, this can be obstructed because of drug-protein binding [1,2]. To deal with this limitation, saliva recently has been utilized instead of blood because it contains much fewer proteins and most of them are enzymatic, which consequently reducing the influence of drug-protein binding happens in plasma [3]. The drug's secretion into saliva depends on the dissociation coefficient of drugs, plasma protein binding property, and lipophilicity. The secretion is via passive diffusion, and it can be used for drug detection in saliva as an

alternative to blood [4]. In recent years, diclofenac drug has been detected in saliva using liquid-liquid extraction combined with an optical probe [5] and by high-performance liquid chromatography coupled with ultraviolet detection [6].

The ion transfer process across the interface between two immiscible electrolyte solutions (ITIES) has been of increasing interest in numerous chemical and biological applications, such as the drug behaviour, transport process via a biological membrane, and electrochemically liquid|liquid extraction [7]. The application of electrochemical sensing platforms can be a solution for on-line detection without the need for a sample extraction process. Furthermore, miniaturized sensing platforms offer numerous advantages more than their macro equivalents [8]. Electrochemical sensors based on liquid | liquid micro-interfaces have been developed in recent years [9,10].

Despite a huge number of works published for electrochemical studies of ion transfer of many drug species across the ITIES [11, 12], there are limited reports that presented the design of ITIES as a sensing platform for the detection of disease treatment drugs including ractopamine [13], daunorubicin [14], α1-acid-glycoprotein [15] and propranolol [16]. In a recent study by our group, a commercially available Si_3N_4 membrane was used to modify the voltammetric response of the ion transfer process via the ITIES, the membrane interface was shown to behave like recessed disc microelectrodes [17]. The ITIES is not only applied to analytical studies, but it also can mimic the drug transport across biological membranes, which provides an important insight for understanding the drug transfer mechanism [14]. In addition, only one study reported the effect of synthetic saliva on propranolol detection using ion transfer voltammetry via arrays of micro-interfaces between synthetic saliva and an organogel phase [4].

The ion transfer reactions at ITIES have been used to study electrochemical behaviour for diclofenac and dibucaine drugs in various organic solvents, including 1,2-DCE [20], 1,6-DCH [17,21,22], nitrobenzene (NB) [23, 24], and o-nitrophenyl octyl ether (NPOE) [25], To the best of our knowledge, no studies were conducted on the electrochemical detection of partially ionizable drugs of diclofenac sodium (DCF) ((sodium 2-{2-[(2,6-dichlorophenyl) amino] phenyl} acetate) [18] and dibucaine (DIC) (2-butoxy-N-[2- (diethylamino) ethyl] quinoline-4-carboxamide),[19] in a synthetic saliva matrix based on the ion transfer across the water|1,6-dichlorohexane micro-interface array. This was built on the previous work on electrochemical detection of dibucaine in synthetic serum matrix based on ion-transfer voltammetry across arrays of micro-interfaces between synthetic serum and a 1,6-DCH solvent [21] and the effect of potentially interfering substances on electrochemical detection of diclofenac at water|1,6-DCH micro-interface [17]. The purpose of this present study was to investigate the use of electrochemistry at liquid|liquid micro-interface arrays as an analytical means for the first time of characterization and detection of deprotonated diclofenac and protonated dibucaine in a synthetic saliva matrix, that mimics a biological fluid, using cyclic voltammetry (CV) and differential pulse voltammetry (DPV).

2. EXPERIMENTAL

2.1. Reagents

All the reagents used were purchased from Sigma-Aldrich (Chemolab, Selangor, Malaysia) and used as received, unless stated otherwise: urea (≥ 99%) (BDH Laboratory supplies, Selangor, Malaysia), potassium chloride (KCl) (≥ 98%) (HmbG, Glovix Empire, Selangor, Malaysia), magnesium pyrophosphate (Alfa Aesar, Glovix Empire, Selangor, Malaysia) and sodium chloride (≥ 99.9%) (Fisher Scientific, Selangor, Malaysia). The organic solvent 1,6-dichlorohexane (1,6-DCH) (≥ 98%) (Merck, Global Scientific, Selangor, Malaysia) was purified according to the previously reported procedure [26]. The synthetic saliva as the aqueous phase [4, 27], composed of carboxymethyl cellulose (4 g L^{-1}) (99.5%) (R&M, Glovix Empire, Selangor, Malaysia), magnesium pyrophosphate (0.0016 g L^{-1}), urea (4 g L^{-1}), anhydrous calcium chloride (0.6 g L^{-1}) (≥ 99%) (Friendemann Schmidt, Selangor, Malaysia), disodium hydrogen phosphate (0.6 g L^{-1}) (≥ 99.0%) (Bendosen, Glovix Empire, Selangor, Malaysia), sodium chloride (0.4 g L^{-1}) and potassium chloride (0.4 g L^{-1}). The organic phase contained 10 mmol L^{-1} of organic electrolyte salt, bis(triphenylphosphoranylidine) ammonium tetrakis(4-chlorophenylborate) (BTPPATCB), which was prepared by the metathesis reaction [28,29] of potassium tetrakis(4-chlorophenyl-borate) (KTPBCl) (>98%) (Tokyo Chemical Industry, Tokyo, Japan) and bis(triphenylphos-phoranylidene) ammonium chloride (BTPPACl) (97%) (Sigma-Aldrich, Chemolab, Selangor, Malaysia). All aqueous solutions were prepared in ultrapure water (resistivity of 18 MΩ cm) from Sartorius, Selangor, Malaysia). Diclofenac sodium (DCF) (≥ 98%) (Sigma-Aldrich, chemolab supplies, Selangor, Malaysia) and dibucaine hydrochloride (DIC) (99%) (Fisher Scientific, Selangor, Malaysia) drugs, and tetramethylammonium chloride (TMACl) (≥ 98%) (an internal reference) (Merck, Global Scientific, Selangor, Malaysia) were prepared in 10 mmol L^{-1} LiCl.

2.2. Apparatus

All electrochemical experiments were performed using a potentiostat (PGSTAT101, Metrohm Autolab, Selangor, Malaysia) with Nova 1.1 software. The settings of differential pulse voltammetry (DPV) method were as follows: modulation amplitude (V) = 0.025 V, step potential = 0.005 V, the modulation time of 0.05 s and scan rate = 10 mV s^{-1}. The cell used was polarized in a three-electrode system as previously reported [21]. The micro-interface arrays were modified by microporous silicon nitride membrane as previously described [17,21]. The micropore array consisted of 2500 pores, 1.25 ± 0.04 µm radius (r_a), 100 nm membrane thickness and pore centre-to-centre separation (r_c) 12.65 µm in a cube close-packed (CCP) arrangement. The silicon chip was sealed onto the lower orifice of a cylindrical glass tube using silicone rubber sealant (Selleys, Selangor, Malaysia) and left to dry for 3 days before use. Acetone solvent was used to clean the membrane before and after each electrochemical experiment, and it was left in the air to dry. The cylindrical glass tube with the membrane contained 500 µL of the synthetic as the aqueous phase, and then immersed in a 10 mL glass beaker contained 1.0 mL of 1,6-DCH as the organic phase with 2.0 mL of the organic reference solution as previously reported [21]. The scheme for electrochemical cells used in this study is summarized as follows:

Ag | AgCl | x μmol L^{-1} DCF/DIC in synthetic saliva (W) || 10 mmol L^{-1} BTPPATPBCl (1,6-DCH) | 1.0 mmol L^{-1} BTPPACl in 10 mmol L^{-1} LiCl(W) | AgCl | Ag Cell (1)

3. RESULTS AND DISCUSSION

3.1. Electrochemical behaviour of drugs at synthetic saliva|1,6-DCH Micro-interface

3.1.1. Electrochemical behaviour of diclofenac

Ion transfer of diclofenac anion (DCF^-) via synthetic saliva|1,6-DCH micro-interface was carried out using cyclic voltammetry (CV). The effect of the synthetic saliva matrix demonstrated a slightly decrease in the available potential window relative to that obtained with 10 mmol L^{-1} LiCl [17,21]. Figure 1 represents CV analysis of baseline of synthetic saliva matrix (black line), 60 μmol L^{-1} of DCF^- in synthetic saliva (red line) and 60 μmol L^{-1} of DCF^- with the addition of 40 μmol L^{-1} of tetramethylammonium ion (TMA^+) as a model ion (blue line). The pH of the synthetic saliva (pH~ 7.4) was adjusted by 0.1 mol L^{-1} LiOH above the pKa value of diclofenac (pKa 4.0 ± 0.15 [20] to ensure it was fully deprotonated and to be transferred across the micro-ITIES array. The scanning was begun at 0.5 V towards the positive potential window edge first, where TMA^+ ion started to transfer from the aqueous phase into the organic phase at the peak transfer potential of 0.74 V, resulted in a combination of peak and state steady behaviour. In contrast, the TMA^+ cation turns back from the organic phase to the aqueous phase at the transfer potential of 0.67 V in a negative direction, showing the peak behaviour. The behaviour of the membrane used here was consistent with the different diffusion fields on either side of the membrane, as previously reported [17]. However, under these conditions, the DCF^- anion stayed in the aqueous phase, as the potential was swept in the negative direction. The DCF^- anions started to transfer from the aqueous phase to the organic phase at applied potential (0.17 V), which was closed to the lower limit of the potential window. These anions were transferred back from the organic phase into the aqueous phase, during the scan towards the positive potential direction at a peak transfer potential of 0.24 V. The addition of TMA^+ was evidence of the suitable operation of the system cell. It can be observed that the transfer of TMA^+ and diclofenac was not overlapped, and the TMA^+ transfer in both forward and reverse scans was separated by ~70 mV, which was consistent with the reversible transfer of a singly charged species [30].

The microporous silicon nitride membrane used here showed recessed micro-interfaces behaviour so that the pores were filled with the aqueous phase and the interface was within the pore length and at the organic phase side [17]. Generally, for recessed micro-ITIES array, linear diffusion dominates within the confines of the channel, while radial diffusion is observed at the pore opening. The recessed interface shows a lower limiting current (I_{lim}) than the inlaid interface by a factor equal to ($4l + \pi r_a$) + 1, as reported by Bond and co-workers [31]. This is due to the shielding effect of the surrounding pore wall. Thus, the limiting current can be calculated by recessed microdisk electrodes:

$$I_{ss} = n\frac{4\pi z_i FDCr^2}{4L + \pi r} \qquad (1)$$

where I_{ss} is the steady-state current, z_i is the charge of the transferring ion species, n is the number of pores, F is the Faraday constant, C is the bulk concentration of the transferring species, D is the diffusion coefficient, L is the recess depth of the membrane used, in this case, is 100 nm, and r is the radius of the pore (1.25 µm).

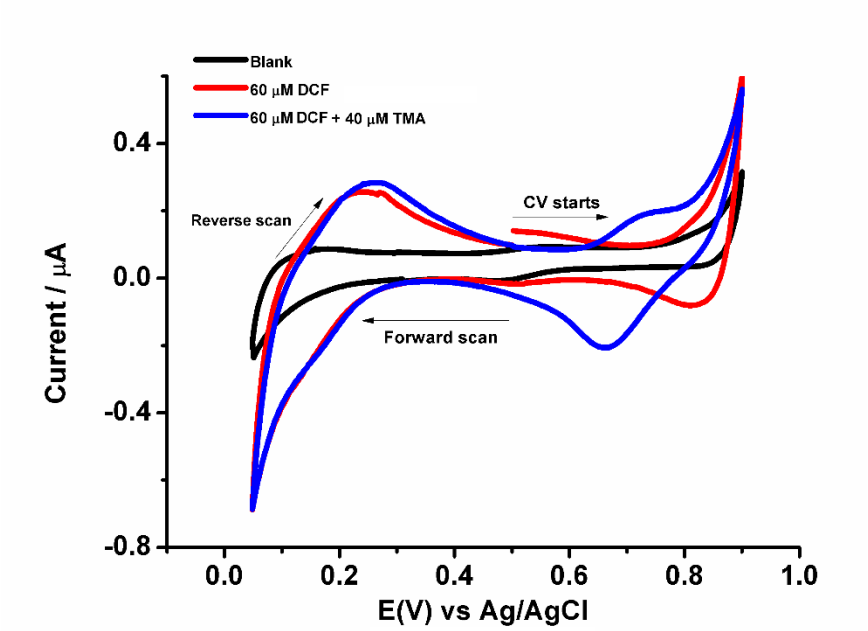

Figure 1. CV of background electrolyte transfer (black line), 60 µmol L^{-1} of DCF^- transfer (red line) and 60 µ mol L^{-1} of DCF^- with 40 µ mol L^{-1} of TMA^+transfers (blue line) via synthetic saliva|1,6-DCH at the micro-ITIES array at pH 7.4 and scan rate 10 mV s^{-1}.

The aqueous diffusion coefficient of diclofenac in synthetic saliva was determined by Equation 1 and the limiting current from the CV was shown in Figure (1). The measured aqueous diffusion coefficient was found to be 1.42 ± 0.2 × 10^{-8} cm^2 s^{-1}, which was two orders lower than the published value of 4.18 × 10^{-6} cm^2 s^{-1}, in aqueous LiCl [22], and the previously reported value of 2.67 × 10^{-6} cm^2 s^{-1} via the chronoamperometric response at solid-liquid [32]. This difference is due to the case of a recessed interface and the diffusion zone overlap, resulting in lower currents, as previously reported [21].

3.1.2. Electrochemical behaviour of dibucaine

The electrochemical behaviour of protonated dibucaine (DIC^+) was studied using synthetic saliva as the aqueous phase, at pH 5.45 of the synthetic saliva matrix. The pKa of the amine group in dibucaine is 8.3 [22] and under this condition the drug is cationic. Figure 2 shows the voltammogram of ion transfer of 60 µmol L^{-1} dibucaine (red line) from the synthetic saliva aqueous phase to the organic phase on the forward CV sweep. In the reverse scan, these ions are transported back into the aqueous phase from the organic phase under controlled potential. The potential peaks were observed at approximately 0.52 and 0.47 V for the forward and the reverse scans, respectively. Following this experiment, 40 µmol L^{-1} of TMA^+ was spiked into the solution of 30 µmol L^{-1} of DIC^+ in the synthetic saliva (blue line) to behave

as a model ion and a potential axis reference ion, respectively [10]. The aim of TMA^+ addition was evidence of the suitable setup of the experimental cell. As observed in Figure 2. DIC^+ ions transfer on the forward and reverse scans are at transfer potentials 0.72 V and 0.67 V, respectively. CV shape resulting demonstrated a combination of peak and steady-state behaviour on the potential forward sweep, while the peak-sharped were observed on the reverse scan as discussed in Section 3.1.1. The diffusion coefficient for dibucaine in synthetic saliva was determined using Equation (1) and data from the CV in Figure 2, to be 2.4×10^{-8} cm^2 s^{-1}, which was two orders lower than the previous value obtained in aqueous LiCl, 3.43×10^{-6} cm^2 s^{-1}, via w|1,6-DCH macro-interface [21], as discussed in the case of DCF above.

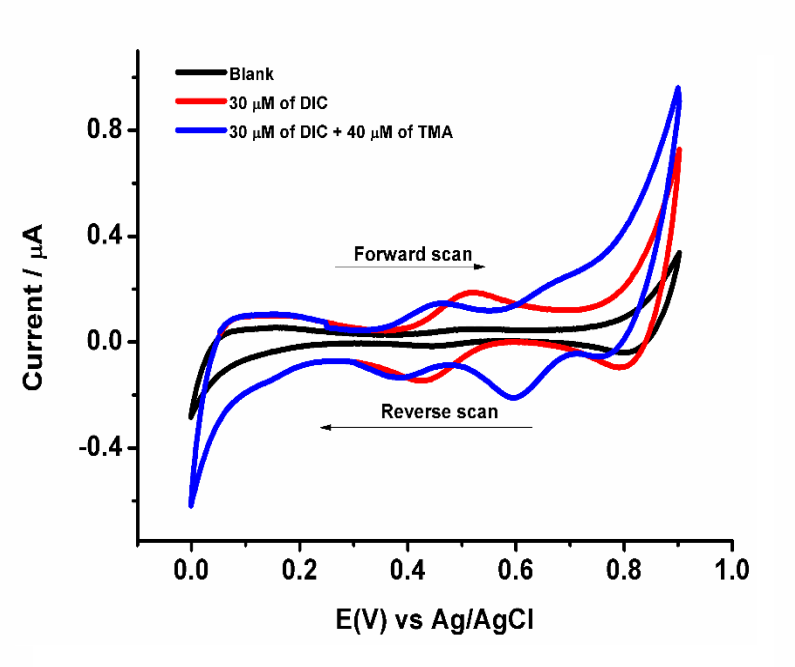

Figure 2. CV of baseline (black line), ion transfer of 30 µmol L^{-1} DIC^+ (red line) and 30 µmol L^{-1} DIC^+ with the addition of 40 µmol L^{-1} of TMA^+ (blue line) in a synthetic saliva matrix at the micro-ITIES array and scan rate of 10 mV s^{-1}.

3.2. Electrochemical detection at the Micro-ITIES Array

As observed in electrochemical behaviour sections, diclofenac and dibucaine could be detected by CV. In contrast, voltammetric techniques with greater sensitivity are necessary for the detection of lower concentrations of transferring species. DPV under optimized conditions specified in Cell 1 was utilized as the analytical method for better sensitivity of drug detection. The analyte samples were added from a stock solution of both diclofenac and dibucaine to the synthetic saliva as an aqueous phase.

3.2.1. Diclofenac detection in synthetic saliva

The experimental conditions specified in scheme 1 for the electrochemical cell in the experimental section were set up using synthetic saliva as the aqueous phase at pH 7.4. DPV of background-subtracted voltammogram of the increased concentrations of the DCF in synthetic saliva as

the aqueous phase was introduced in Figure 3(a). The scan was in the negative direction from 0.4 to 0.11 V to drive the transfer of DCF^- ions from the aqueous phase to the organic phase, in which these ions were under the initial potential in the aqueous phase. The peak potential of DCF^- transfer was found to be 0.25 ± 0.08 V. A calibration curve was plotted for increasing concentrations in the range of 8 – 40 μmol L^{-1} of DCF (Figure 3(b)). The peak currents increased linearly with an increase in the concentration of diclofenac, according to the linear regression equation of i_p = –0.0038 (μA μmol^{-1} L) (concentration) – 0.002 (μA), R^2 0.9930, (n = 3). The limit of detection (LOD) based on 3 times the standard deviation of the blank (3sb) was calculated to be 1.8 ± 0.2 μmol L^{-1}, which was slightly higher than the obtained value for detecting DCF^- in aqueous LiCl solution (1.5 μmol L^{-1}) [17]. This difference can be attributed to the interference of ions present in the synthetic saliva matrix. This LOD compares well with limits of detection previously reported for detecting DCF including 2.45 μmol L^{-1} (A bare graphite electrode using DPV) [33], 2.0 μmol L^{-1} (multiwall carbon nanotubes electrode using square wave voltammetry (SWV) [34], 1.6 μmol L^{-1} (platinum electrode using SWV) [35], 3.28 μmol L^{-1} (tyrosine-modified carbon paste electrode using DPV) [36] and 9.1 μmol L^{-1} (ion-selective electrode using potentiometric method) [37]. The analytical parameters including the added and found concentrations, the recoveries, and the relative standard deviation (RSD) are summarized in Table 1.

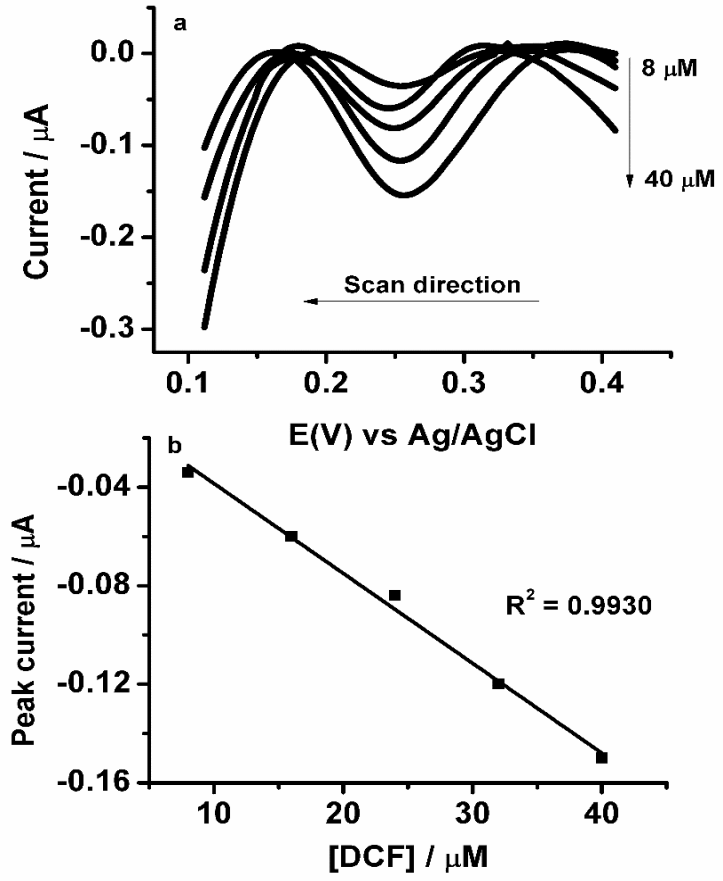

Figure 3. a) DPV of increasing concentrations of diclofenac (8, 16, 24, 32 and 40 μmol L^{-1}) in the synthetic saliva. b) Calibration curve of peak currents vs. concentrations.

Table 1. Determination of DCF in synthetic saliva samples using DPV

Parameters			
Added concentration (μmol L^{-1})	Found concentration (μmol L^{-1}) ±SD [a]	Recovery%	RSD [b] % (n=3)
8.0	8.4 ± 0.32	105.0	3.8
16.0	16.3 ± 0.25	101.9	1.5
24.0	22.8 ± 0.43	95.0	1.9
32.0	32.1 ± 0.4	100.3	1.2
40.0	40.5 ± 0.29	101.3	0.72

[a] SD: standard deviation

[b] RSD: relative standard deviation

3.2.2. Dibucaine detection in synthetic saliva

Figure 4 (a) shows DPV background subtraction voltammograms for DIC^+ transfer from the aqueous phase to the organic phase, scanning in a positive direction. Voltammograms exhibited that the peak current increased as the DIC concentration increased. The peak potential for the ion transfer of DIC^+ from the aqueous phase to the organic phase was found to be 0.47 ± 0.06 V. A plot of peak currents versus concentrations ranged from 8 to 24 μmol L^{-1} of DIC in the aqueous phase is shown in Figure 4(b), with a linear regression equation of i_p = 0.0068 (μA μmol^{-1} L) (concentration) – 0.0275 (μA), R^2 0.9752, (n = 3). The LOD was determined to be 1.5 ± 0.14 μmol L^{-1}, which was slightly lower than obtained value for detecting DIC^+ in artificial serum matrix (1.9 ± 0.12 μmol L^{-1}) and slightly higher than the obtained value in aqueous LiCl solution (0.9 ± 0.06 μmol L^{-1}) [21], as discussed in the case of DCF^- detection above. There are very few electrochemical methods for detection dibucaine in pharmaceutical formulations and biological samples, such as detection of DIC by by activated glassy carbon using SWV with LOD was 0.9 μmol L^{-1}[38] and a carbon paste electrode using DPV with LOD was 10 μmol L^{-1} [39].

The obtained results showed that the DPV was successfully utilized for the quantification of diclofenac and dibucaine in synthetic saliva (Table 1 and 2). The method's accuracy was evaluated by calculating recoveries during spiked experiments. The recoveries of drugs in the synthetic saliva matrix were determined from the linear slope equations. According to these results, the components present in this aqueous mixture do not affect drugs detection. The proposed electrochemical methods in this study were used for the first time to characterise and detect diclofenac and dibucaine drugs directly in synthetic saliva. Thus, the results obtained were not compared with other methods for electrochemical detection of diclofenac and dibucaine drugs in a synthetic saliva. DPV demonstrated good reproducibility, good performance, and sensitivity for the determination of DCF and DIC drugs in synthetic saliva matrix.

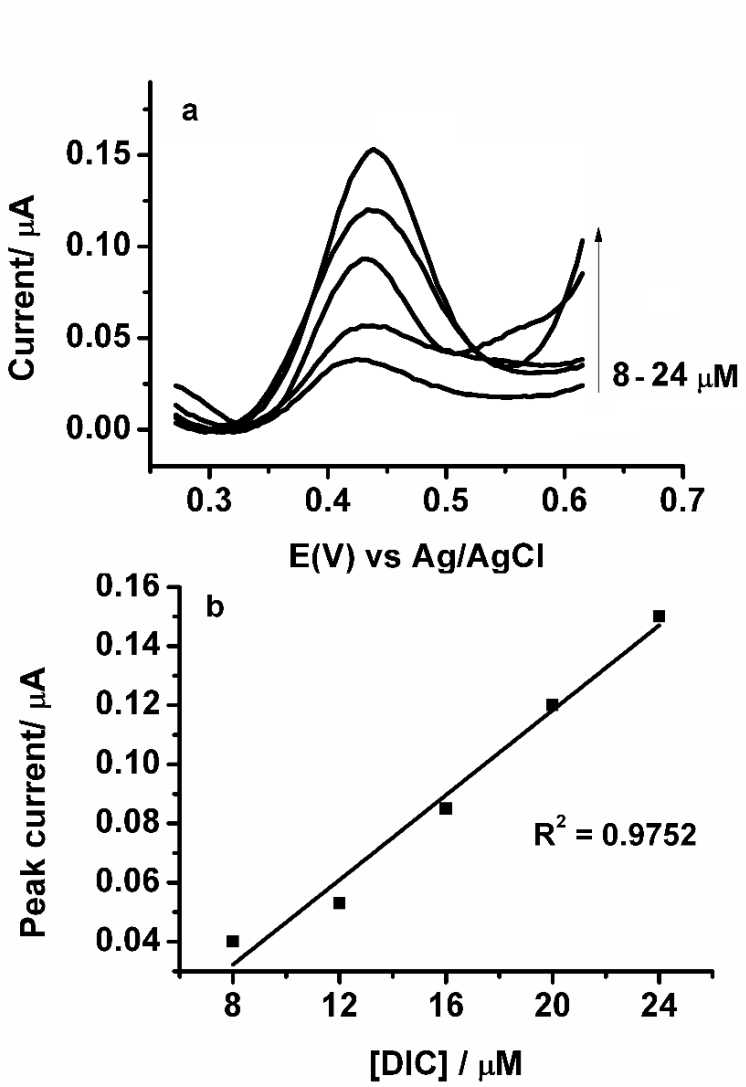

Figure 4: a) DPV of increasing concentrations of dibucaine (8, 12, 16, 20 and 24 µmol L^{-1}) in the synthetic saliva. b) Calibration curve of peak current vs. concentration.

Table 2. Determination of DIC in synthetic saliva samples using DPV.

Parameters			
Added concentration (µmol L^{-1})	Found concentration (µmol L^{-1}) ±SD	Recovery%	RSD % (n=3)
8.0	8.5 ± 0.09	106.3	1.1
12.0	11.5 ± 0.08	95.8	0.71
16.0	15.9 ± 0.14	99.4	0.85
20.0	20.3 ± 0.32	99.0	1.6
24.0	24.7 ± 0.3	101.3	1.3

4. CONCLUSION

The study presented proved that electrochemistry at liquid|liquid could be applied for the electrochemical detection of ions from complex matrices. Electrochemical behaviour of ion transfer of the anti-inflammatory drug DCF and local anaesthetic drug DIC via synthetic saliva |1,6- DCH micro-interface was achieved. The results showed that DCF^- and DIC^+ could be detected in synthetic saliva by CV and DPV, in which the components of synthetic saliva showed no significant effect on the transfers of DCF^- and DIC^+. DPV was utilized to detect low concentrations for both drugs, where peak currents responses were linear with DCF and DIC concentrations in the synthetic saliva matrix over the concentrations ranged between 8 – 40 μmol L^{-1} and 8 – 24 μmol L^{-1} and the calculated detection limits were 1.8 ± 0.2 μmol L^{-1} and 1.5 ± 0.14 μmol L^{-1} for diclofenac and dibucaine, respectively.

ACKNOWLEDGMENTS
Authors are grateful to the Deputy Dean of Universiti Putra Malaysia and Putra Grant, Universiti Putra Malaysia (GP-IPS/9618600) for the support. Eissa as one of authors would like to thank Libyan Ministry of Education for scholarship (MOE-LY).

CONFLICTS OF INTEREST
The authors declare no conflict of interest.

References

1. C. J. Collins, C. Lyons, J. Strutwolf, D. W. Arrigan, *Talanta*, 80(2010)1993-8
2. Y. J. Hu, Y. Liu, T. Q. Sun, A. M. Bai, J. Q. Lü, Z. B. Pi, *Int. J. Biol. Macromol*., 39(2006)280
3. S. Townsend, L. Fanning, R. O'Kennedy, *Anal. Lett*., 41(2008)925-948
4. C. J. Collins, D. W. Arrigan, *Anal. Chem.,* 81*(*2009)2344-2349
5. A. Pochivalov, C. Vakh, V. Andruch, L. Moskvin, A. Bulatov, *Talanta*, 169(2017)156-162
6. M. Ramos-Payan, S. Maspoch, A. Llobera, *Anal. Chim. Acta*, 946(2016)56-63
7. D. W. Arrigan, *Anal. Lett*., 41(2008)3233-3252
8. S. Liu, Q. Li, Y. Shao, *Chem. Soc. Rev*., 5(2011)2236-2253
9. B. Liu, M. V. Mirkin, *Electroynalysis*, 12(2000)1433-1446
10. R. Zazpe, C. Hibert, J. O'Brien, Y. H. Lanyon, D. W. Arrigan, *Lab. Chip.,* 7(2007)1732-1737
11. H. Alemu, *Pure Appl. Chem.,* 76(2004)697-705
12. R. Gulaboski, M. N. D. Cordeiro, N. Milhazes, J. Garrido, F. Borges, M. Jorge, C. M. Pereira, I. Bogeski, A. H. Morales, B. Naumoski, A. F. Silva, *Anal. Biochem.,* 361(2007)236-243
13. M. Sairi, D. W. Arrigan, *Talanta*, 132(2015)205-214
14. J. A. Ribeiro, F. Silva, C. M. Pereira, *Anal. Chem.,* 85(2013)1582-1590
15. P. Lopes, R. Kataky, *Anal.Chem.,* 84(2012)2299-2304
16. P. Vazquez,G. Herzog, C. O'Mahony, J. O'Brien, J. Scully, A. Blake, C. O'Mathuna, P. Galvin, *Sens. Actuators. B,* 201(2014)572-578
17. E. M. Almbrok, N. A. Yusof, J. Abdullah, R. M. Zawawi, *Chemosensors*, 8(2020)11
18. B. Yilmaz, *Chromatographia*, 71(2010)549-551
19. H. Chiniforoshan, L. Tabrizi, N. Pourrahim, *J. Appl. Electrochem.,* 45(2015)197-207
20. F. Reymond, V. Chopineaux-Courtois, G. Steyaert, G. Bouchard, P. A. Carrupt, B. Testa, H. H. Girault, *J. Electroanal. Chem.,* 462(1999)235-250
21. E. M. Almbrok, N. A. Yusof, J. Abdullah, R. M. Zawawi, *Chemosensors*, 9(2021)15

22. E. M. Almbrok, N. A. Yusof, J. Abdullah, R. M. Zawawi, *Int. J. Electrochem. Sci*., 16(2021) 210246
23. K. Arai, M. Ohsawa, F. Kusu, K. Takamura, *Bioelectrochem. Bioenerg.,* 31(1993)65-76
24. Y. Kubota, H. Katano, M. Senda, *Anal. Sci.,* 17(2001)65-70
25. Z. Samec, J. Langmaier, A. Trojanek, E. Samcová, J. Málek, *Anal. Sci.,* 14(1998)35-41
26. H. Katano, H. Tatsumi, M. Senda, *Talanta*, 63(2004)185-193
27. A. Vahed, N. Lachman, R. D. Knutsen, *Dent. Mater.,* 23(2007)855-861
28. H. J. Lee, P. D. Beattie, B. J. Seddon, M. D. Osborne, H. H. Girault, *J. Electroanal. Chem.,* 440(1997)73-82
29. H. J. Lee, H. H. Girault, *Anal. Chem.,* 70(1998)4280-4285
30. C. J. Collins, A. Berduque, D. W. Arrigan, *Anal. Chem.,* 80(2008)8102-8108
31. A. M. Bond, D. Luscombe, K.B. Oldham, C. G. Zoski, *J. Electroanal. Chem. Interfacial Electrochem.,* 249(1988)1-14
32. G. Parvizi-Fard, E. Alipour, P. Y. Sefidi, R. E. Sabzi, *J. Chin. Chem. Soc*., 65(2018)472-484.
33. G.Y Aguilar-Lira, G.A. Álvarez-Romero, A. Zamora-Suárez, M. Palomar-Pardavé, A. Rojas-Hernández, J. A. Rodríguez-Ávila, M. E. Páez-Hernández, *J. Electroanal. Chem*., 794(2017)182–188.
34. A. Mokhtari, H. Karimi-Maleh, A. A. Ensafi, H. Beitollahi, *Sens. Actuators B Chem.* 169(2012) 96–105.
35. U. Ciltas, B. Yilmaz, S. Kaban, B. K. Akcay, G. Nazik*, Iran. J. Pharm. Res*., 14(2015)715.
36. E. Brennan, P. Futvoie, J. Cassidy, B. Schazmann, *Int. J. Environ. Anal. Chem*., 97(2017)588–596.
37. B. K. Chethana, S. Basavanna, Y. A. Naik, *Ind. Eng. Chem. Res*., 51(2012)10287–10295.
38. H.M. Elqudaby, H.A. Hendawy, E.R. Souaya, G.G. Mohamed, G. M. Eldin, *Int. J. Pharm. Anal.,* 40(2015)1269–1284.
39. E.A.S. Elashery, E.Y. Frag, A.A.E. Sleim, *Measurement,* 2020, 108549.