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ORIGINAL ARTICLE

# Tetracaine – selective electrodes with polymer membranes and their application in pharmaceutical formulation control

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**KEYWORDS**

Tetracaine hydrochloride;
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**Abstract** The construction and electrochemical response characteristics of poly(vinyl chloride) (PVC) membrane electrodes for tetracaine hydrochloride (TCH) are described. The sensing membranes incorporating ion-association complexes of tetracaine cation with phosphotungstic acid (PTA) or phosphomolybdic acid (PMA) or Sodium tetraphenyl borate (NaTPB) as electroactive materials and di-*n*-butyl phthalate (DBPH) or tri-*n*-butyl phosphate (TBP) as a plasticizer in PVC matrixes were evaluated. The results obtained show the electrodes based on PTA or PMA as electroactive compounds and DBPH as plasticizer with a fast, stable and near-Nernstian response over a wide concentration range ($1 \times 10^{-5}$–$5 \times 10^{-2}$ M), with cationic slopes of 55.02 and 52.05 mV decade$^{-1}$ over a pH range of (2.5–6.5). The electrodes show good discrimination of tetracaine from several inorganic cations and sugars. The electrodes were successfully applied for the determination of tetracaine in pharmaceutical formulations.

## 1. Introduction

Tetracaine hydrochloride (TCH) {amethocaine, 2-(dimethylamino)ethyl 4-(butylamino)benzoate hydrochloride} widely used as a local anesthetic is absorbed by skin, which produces a state of local anesthesia. Because of its high permeability, indolence, long duration and quick onset, it is widely used for surface anesthesia of ophthalmic. Excessive dose and abuse of local anesthetics may restrain the conduction system of the heart and the nerve center system (http://en.wikipedia.org/wiki/Tetracaine).

Some useful methods have been proposed for the analysis of tetracaine hydrochloride, such as liquid chromatography (Ma et al., 2006; Zhang et al., 2006; Wang et al., 2003; Storms and Stewart, 2002; Murtaza et al., 2002), electrochemistry (Wang et al., 2002; Satake et al., 1991), phosphorescence (Kitade et al., 1995), chemical luminescence (Li et al., 2003; Zhang

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et al., 1995), spectrofluorometry (Nevado et al., 2000), sequential injection spectrophotometry (Fan et al., 2005; Pasekovà and Polàšek, 2000), capillary electrophoresis (Lombardo-Agűí et al., 2009; Al-Otaibi et al., 2009) and resonance rayleigh scattering (Qin et al., 2009). However, some of these methods have high sensitivity, but the apparatus used is always complex and the manipulations are time-consuming; others have effective separation, but their costs are higher. There is a need for simple, low-cost, sensitive and rapid alternative methods for the determination of TCH in pharmaceutical formulations.

Potentiometric sensors such as ion-selective electrodes (ISEs) may be used for screening a wide variety of pharmaceutical formulations and biological samples, because these sensors offer the advantages of simple design, construction, and manipulation, reasonable selectivity, fast response time, applicability to colored and turbid solutions and possible interfacing with automated and computerized systems (Gupta et al., 2010; Nassory et al., 2008; Lenik et al., 2004). However, as far as the available literature is concerned, very little is known and insufficient about the use of this technique for tetracaine quantification (Bouklouze et al., 1991).

The aim of the present contribution was to prepare plastic membrane electrodes based on the incorporation of tetracaine-phosphotungstic acid (TC-PTA) or tetracaine-phosphomolybdic acid (TC-PMA) or tetracaine-tetraphenyl borate (TC-TPB) ion-exchangers in polyvinyl chloride (PVC) membranes plasticized by di-*n*-butyl phthalate (DBPH) or tri-*n*-butyl phosphate (TBP).

The results showed that the use of DBPH as a plasticizing solvent mediator in PVC matrix membranes increases, to a large extent, the life span of the electrode. The best electrodes were used successfully as sensors to determine TCH in pure solutions and in pharmaceutical formulations.

## 2. Experimental

### 2.1. Materials and solutions

All chemicals were of analytical-reagent grade. Doubly deionized water was used to prepare all solutions. Tetracaine hydrochloride (TCH) was obtained from Aldrich, (Fig. 1). High molecular weight poly(vinyl chloride) (PVC), di-*n*-butyl phthalate (DBPH), tri-*n*-butyl phosphate (TBP), tetrahydrofuran (THF) were obtained from Fluka AG, Switzerland. Sodium tetraphenyl borate (NaTPB) was obtained from BDH, England. Phosphotungstic acid (PTA) and phosphomolybdic acid (PMA) were obtained from Merck, Germany. Injection (10 mg/mL TCH), Akorn Pharm., USA and Tetracaine HCl, eye drops (5 mg/mL TCH), Bausch & Lomb, UK were purchased from local pharmacies. The stock solution of 0.1 M TCH was prepared by dissolving the appropriate amount of TCH in 100 mL of deionized water. Standard TCH solution ($1 \times 10^{-2}$–$1 \times 10^{-6}$ M) was prepared by diluting the appropriate amount in deionized water. Stock solutions of 0.1 M for each of LiCl, NaCl, KCl, $CaCl_2$, $Co(NO_3)_2$, $Ni(NO_3)_2$, $Cu(NO_3)_2$, $Al(NO_3)_3$, $CrCl_3$, $FeCl_3$, glucose and fructose were prepared. Other diluted solutions were prepared by subsequent dilution of the stock solutions.

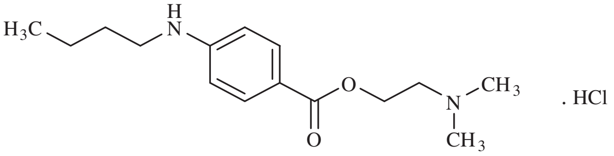

**Figure 1** Chemical structure of tetracaine hydrochloride (TCH).

### 2.2. Apparatus

Electrochemical measurements were made using Orion digital ion analyser (Model-701A) at 25 °C in conjunction with a ceramic junction calomel electrode. A pH-meter (Orion Model 90-02) with a double junction glass electrode was used to check the pH of the solutions.

The electrochemical cell assembly used for this study was as follows: Ag/AgCl|Internal solution (0.01 M) of TCH|PVC membrane|Sample solution|$Hg/Hg_2Cl_2$, KCl (sat'd). A brief schematic diagram of the measuring cell is shown in Fig. 2.

### 2.3. Eye drops and injection samples

An appropriate amount of TCH was diluted to 100 mL with doubly deionized water in volumetric flask to obtain ($1 \times 10^{-3}$–$5 \times 10^{-5}$ M) of TCH.

### 2.4. Preparation of ion-pairs

Upon the addition of 25 mL of $1 \times 10^{-2}$ M of tetracaine hydrochloride (TCH) solutions to 25 mL of $1 \times 10^{-2}$ M sodium tetraphenyl borate (NaTPB) or 75 mL of $1 \times 10^{-2}$ M TCH to 25 mL each of phosphotungstic acid (PTA) or phosphomolybdic acid (PMA), a white or gray or green precipitate of TC-TPB or TC-PTA or TC-PMA was formed, respectively. The precipitate was filtered through Whatman filter paper No. 42, and washed with deionized water until no chloride ion was detected in the washing solution. The precipitate was dried at room temperature and ground to a fine powder in a mortar. Elemental analysis confirmed the formation of 1:1 or 3:1 or 3:1 complexes of TC-TPB or TC-PTA or TC-PMA, respectively as shown in Table 1.

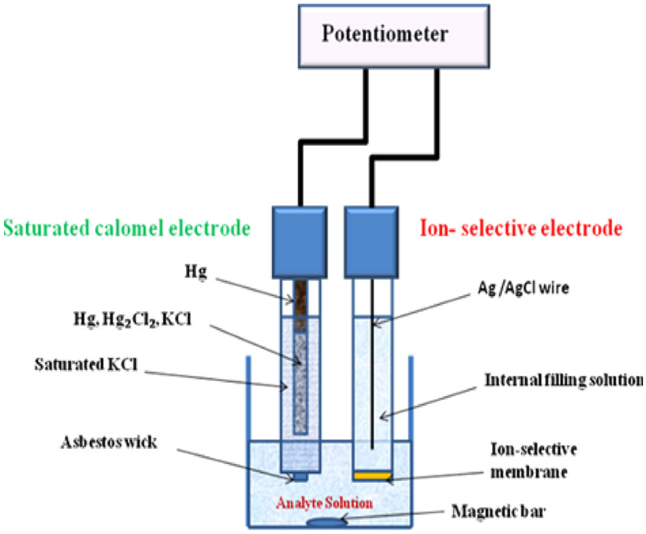

**Figure 2** Schematic diagram of a conventional ion-selective membrane, measuring cell.

**Table 1** Elemental analysis of tetracaine ion-pairs.

| Element (%) | TC-PTA[a] | | TC-PMA[b] | | TC-TPB[c] | |
|---|---|---|---|---|---|---|
| | Found | Calculated | Found | Calculated | Found | Calculated |
| C | 14.80 | 14.72 | 20.73 | 20.66 | 80.10 | 80.26 |
| H | 2.00 | 1.97 | 2.82 | 2.77 | 7.71 | 7.60 |
| N | 2.36 | 2.29 | 3.19 | 3.21 | 4.89 | 4.80 |

[a] $[C_{15}H_{24}N_2O_2]_3[PW_{12}O_{40}]$.
[b] $[C_{15}H_{24}N_2O_2]_3[PMo_{12}O_{40}]$.
[c] $[C_{15}H_{24}N_2O_2][B(C_6H_5)_4]$.

### *2.5. Fabrication of TCH membrane electrodes*

Tetracaine-selective membranes were prepared by dissolving 27.5 mg of the ion-pair complexes, 165 mg PVC and 357.5 mg of DBPH or TBP in 5 mL THF. These solutions were poured into glass Petri dishes (5 cm diameter), and were allowed to evaporate overnight at room temperature. The thickness of the obtained membrane was about 0.3 mm. Membranes (10 mm diameter) were cut out and glued to the polished end of PVC tubes by means of a PVC-THF solution. The electrode bodies consisted of a glass tube, to which the PVC tube was attached at one end and filled with an internal solution ($1 \times 10^{-2}$ M of TCH), as shown in Fig. 2. The membrane was conditioned by immersing in $1 \times 10^{-2}$ M TCH solution for 3 h before measurements.

### *2.6. General procedure (calibration graphs)*

The electrodes were calibrated by transferring 20 mL aliquots of $1 \times 10^{-6}$–$1 \times 10^{-1}$ M aqueous solutions of TCH to 50 mL beakers, followed by immersing the ion-selective membrane electrode, together with a calomel reference electrode in the solution. The potential readings were recorded after stabilization to ±0.3 mV, and the e.m.f. was plotted as a function of the logarithm of the TCH concentrations. The calibration graph was used for subsequent determinations of unknown TCH concentrations.

### *2.7. Selectivity of the electrodes*

The selectivity coefficients, $K^{\mathrm{pot}}_{\mathrm{TCH},j^{z+}}$ of the electrode toward different cationic species, $j^{Z+}$, were determined by the separate solution method described previously (Hassan et al., 2009) with a $1 \times 10^{-3}$ M solution of TCH and the interferent.

## 3. Results and discussion

### *3.1. Composition of the membrane*

Five membrane compositions were investigated (Table 2). For each composition, the amount of polymer poly (vinyl chloride) (PVC) was kept constant (30%, w/w) while varying the percentage (w/w) of the ion-pair and plasticizer. The results reveal that the composition having the 5% ion-pair leads to exhibit a better slope (55.0 mV decade$^{-1}$), correlation coefficient (0.9994) and a wide concentration range ($1 \times 10^{-5}$–$5 \times 10^{-2}$ M). In all subsequent studies electrodes made of the membrane composition No. (IV) (PVC, 30%: plasticizer, 65%: ion-pair, 5%) were used.

### *3.2. Sensor characteristics*

The potentiometric response characteristics of the tetracaine sensors based on the use of TC-TPB or TC-PTA or TC-PMA as electroactive materials and DBPH or TBP as a plasticizer in PVC matrixes were evaluated by the IUPAC recommendations (Buck and Lindner, 1994a). Results in Table 3 show the characteristic performance of the PVC membrane sensors. As mentioned above three electroactive materials and two plasticizers were tested to evaluate their effects on the response. Better results (the better slopes) were obtained with DBPH plasticizer as shown in Table 3 and Fig. 3.

### *3.3. Effect of plasticizer*

The influence of plasticizer on the response characteristics of the tetracaine ion – selective electrode was investigated by using two plasticizers of different polarities including di-*n*-butyl phthalate (DBPH) and tri-*n*-butyl phosphate (TBP). The plasticizers

**Table 2** Optimization of membranes by varying the composition of ingredients.

| Membrane | Ion-pair, % (TC-PTA) | PVC, % | Plasticizer, % (DBPH) | Correlation coefficient | Slope/mV decade$^{-1}$ |
|---|---|---|---|---|---|
| I | 1 | 30 | 69 | 0.9970 | 51.20 ± 0.5[a] |
| II | 2 | 30 | 68 | 0.9982 | 52.84 ± 0.5[a] |
| III | 3 | 30 | 67 | 0.9986 | 53.30 ± 0.5[a] |
| IV | 5 | 30 | 65 | 0.9994 | 55.00 ± 0.5[a] |
| V | 10 | 30 | 60 | 0.9790 | 50.48 ± 0.7[a] |

Three hours of soaking in $1 \times 10^{-2}$ M TCH.
[a] Statistical deviation (three preparations).

**Table 3** Performance characteristics of tetracaine membrane sensors.

| Parameter | Sensor No. 1 | Sensor No. 2 | Sensor No. 3 | Sensor No. 4 | Sensor No. 5 | Sensor No. 6 |
|---|---|---|---|---|---|---|
| Membrane ingredients | TC-PTA-DBPH | TC-PMA-DBPH | TC-TPB-DBPH | TC-PTA-TBP | TC-PMA-TBP | TC-TPB-TBP |
| Slope (mV decade$^{-1}$) | 55.02 | 52.50 | 54.64 | 51.66 | 51.02 | 52.92 |
| Linear concentration range (M) | $1\times10^{-5}$–$5\times10^{-2}$ | $1\times10^{-5}$–$5\times10^{-2}$ | $5\times10^{-5}$–$5\times10^{-2}$ | $1\times10^{-5}$–$1\times10^{-2}$ | $1\times10^{-5}$–$1\times10^{-2}$ | $1\times10^{-4}$–$5\times10^{-2}$ |
| Intercept (mV) | 219.05 | 204.76 | 225.47 | 207.77 | 173.38 | 217.72 |
| Correlation coefficient, *r* | 0.9995 | 0.9993 | 0.9994 | 0.9990 | 0.9985 | 0.9975 |
| Lower detection limit (M) | $7.5\times10^{-6}$ | $7.8\times10^{-6}$ | $5.0\times10^{-5}$ | $8.1\times10^{-6}$ | $8.0\times10^{-6}$ | $8.5\times10^{-5}$ |
| Response time for $1\times10^{-3}$ (M) solution (s) | 9 ± 0.5 | 9 ± 0.5 | 10 ± 0.5 | 10 ± 0.5 | 10 ± 0.5 | 11 ± 0.5 |
| Working pH range | 2.5–6.5 | 2.5–6.5 | 2.5–6.5 | 2.5–6.5 | 2.5–6.5 | 2.5–6.5 |
| Life time (day) | 45 | 37 | 21 | 24 | 21 | 14 |

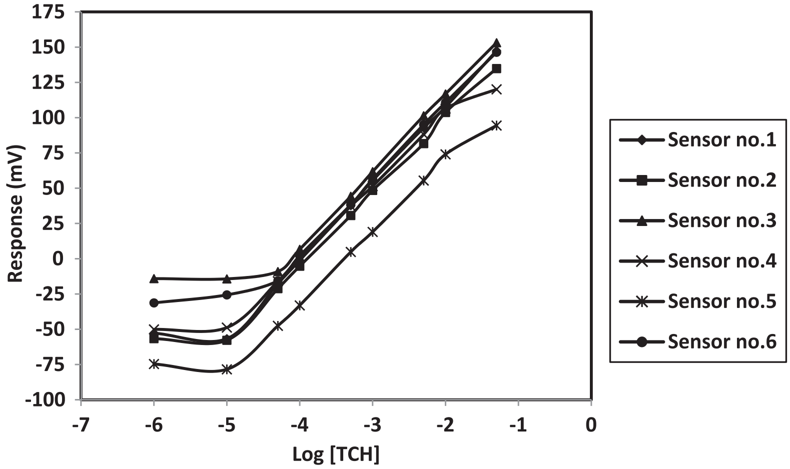

**Figure 3** The calibration curves and effect of ion-pairs and plasticizers on potentiometric response for the characteristic performance mentioned in Table 3 at 25 °C.

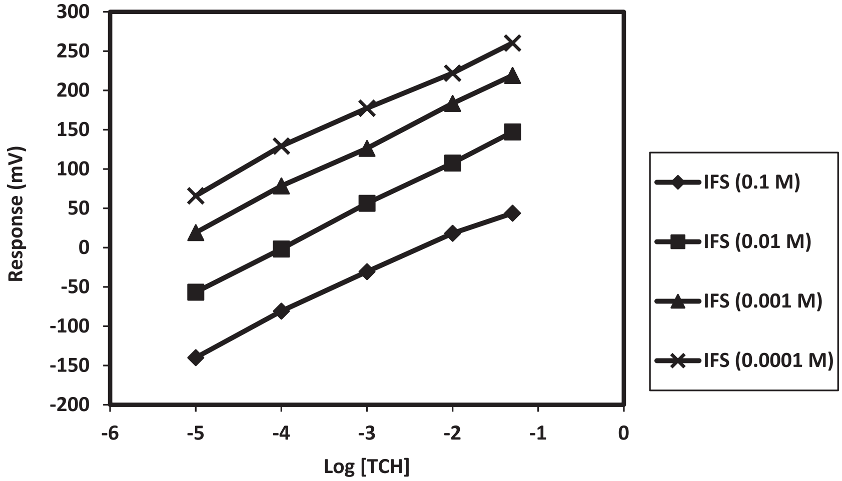

**Figure 4** The effect of the internal filling (IFS) solution on the response of the tetracaine – selective electrode using sensor No. 1 based on (TC-PTA) ion-pair complex with DBPH as a plasticizer.

dissolve the ion-pair complex and adjust both of the membrane permittivity and ion-exchanger site mobility to give the highest possible selectivity and sensitivity (Faridbod et al., 2007). The membranes incorporating DBPH showed better potential responses, i.e., better slopes and wider linearity of the calibration plots. Sensor Nos. 1–3 are preferred as it offered better life times compared to Sensor Nos. 4–6 based on the use of TPB as plasticizing solvent, Table 3. It seems that DBPH, as a lower polarity, a less viscosity (Klingender, 2008) and a relatively high mobility, with respect to TBP, provides appropriate conditions for incorporation of highly lipophilic tetracaine ion. Thus, all further studies were conducted using DBPH as plasticizer.

### 3.4. *Effect of soaking*

The performance characteristic of the tetracaine-selective electrode was investigated as a function of soaking time. The sensor No. 1 based on TC-PTA as ion-pair and DBPH as a plasticizer was soaked continuously in $1 \times 10^{-2}$ M solution of tetracaine hydrochloride (TCH) at room temperature for 1, 3, 5, 8, 24, and 48 h. The results indicate that, in the case of a conventional membrane electrode, the slope remains constant near 55 mV decade$^{-1}$ for up to 8 h soaking, then it slightly decreased, reaching 49.53 mV decade$^{-1}$ after 48 h soaking due to the leaching of the active ingredients to the bathing solution. The optimum conditioning time for the membrane sensor in $1 \times 10^{-2}$ M TCH solution was 3 h. The electrode should be kept dry in an opaque closed vessel and stored in a refrigerator while not in use.

### 3.5. *Effect of the internal filling solution*

The influence of the concentration of internal solution on the potential response of the polymeric membrane electrode for tetracaine ion was studied. The concentration was varied (from $1 \times 10^{-4}$ to $1 \times 10^{-1}$ M) and the potential response of the electrodes has been observed as shown in Fig. 4. It was found that the best results in terms of slope (55.017 mV decade$^{-1}$) and working concentration range (from $1 \times 10^{-5}$ to $5 \times 10^{-2}$ M) have been obtained with internal filling solution (IFS) ($1 \times 10^{-2}$ M) as shown in Table 4. Thus, $1 \times 10^{-2}$ M concentration of IFS was quite appropriate for all electrodes.

**Table 4** The effect of the internal filling (IFS) solution on the response of the tetracaine – selective electrode using sensor No. 1 (TC-PTA-DBPH).

| Conc. of IFS (M) | $10^{-1}$ | $10^{-2}$ | $10^{-3}$ | $10^{-4}$ |
|---|---|---|---|---|
| Slope (mV decade$^{-1}$) | 49.830 | 55.017 | 53.749 | 51.262 |
| Correlation coefficient | 0.9950 | 0.9997 | 0.9990 | 0.9959 |

### 3.6. *The effect of pH*

The influence of pH on the potential of the electrodes was investigated by measuring the e.m.f. of the cell at $1 \times 10^{-4}$, $1 \times 10^{-3}$ and $1 \times 10^{-2}$ M of TCH solutions. The pH values of the cell were adjusted by the addition of very small volumes of (0.01–0.1 M) hydrochloric acid or sodium hydroxide. The results are shown in Fig. 5; it is evident that the electrodes do not respond to pH changes in the range 2.5–6.5 for all the electrodes. At pH values higher than this range, the decrease in the potential readings is most probably attributed to the formation of the free TC base in solution, leading to a decrease in the concentration of TC cation (Hassan et al., 2011; Vaze and Srivastava, 2008). The decrease in potential readings at pH values lower than 2.5 may be due to penetration of $H^+$ ion into the membrane surface or the formation of TC diprotonated species.

### 3.7. *Response time and lifetime*

The time required for the proposed tetracaine-selective membrane electrodes to reach values within ±0.3 mV of the final equilibrium potentials was measured after immersion in different TCH solutions ranging from $1 \times 10^{-5}$ to $1 \times 10^{-2}$ M in concentration, the measurements were from low to high concentrations. The average response time at $t_{95}$ varied from 10 s for TCH solutions with concentrations $\geqslant 10^{-3}$ M to 22 s for solutions with concentrations $\leqslant 10^{-4}$ M.

The average lifetime for most of reported ion-selective electrodes is in the range of 3–8 weeks. After this time the slope of the electrode will decrease, and the detection limit will increase. The tetracaine-selective electrodes were tested for 7 weeks and the calibration curve was plotted periodically with a standard solution ($1 \times 10^{-6}$–$1 \times 10^{-1}$ M) of TCH. The experimental results showed that the lifetime of the sensor Nos. 1 and 2 was over 5 weeks, Table 3. During this time, the detection limit and the slope of the electrode remained almost constant,

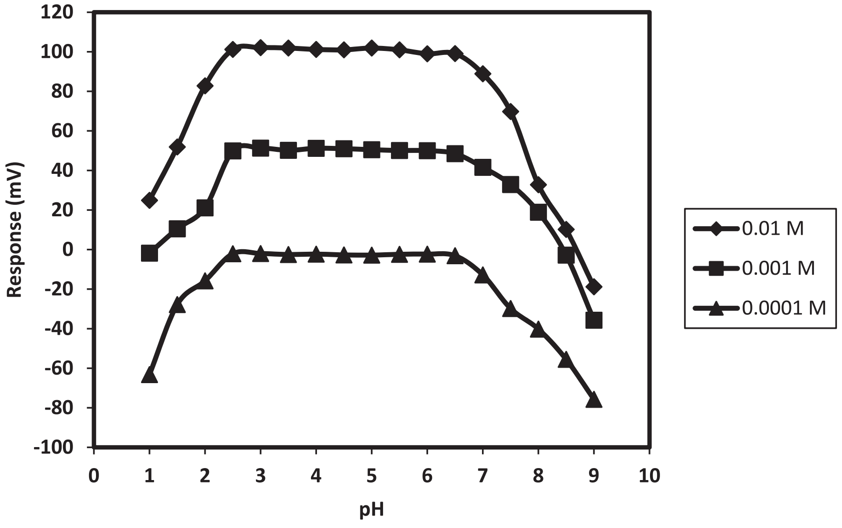

**Figure 5** Effect of pH on the response of proposed sensor No. 1 (pH range 2.5–6.5).

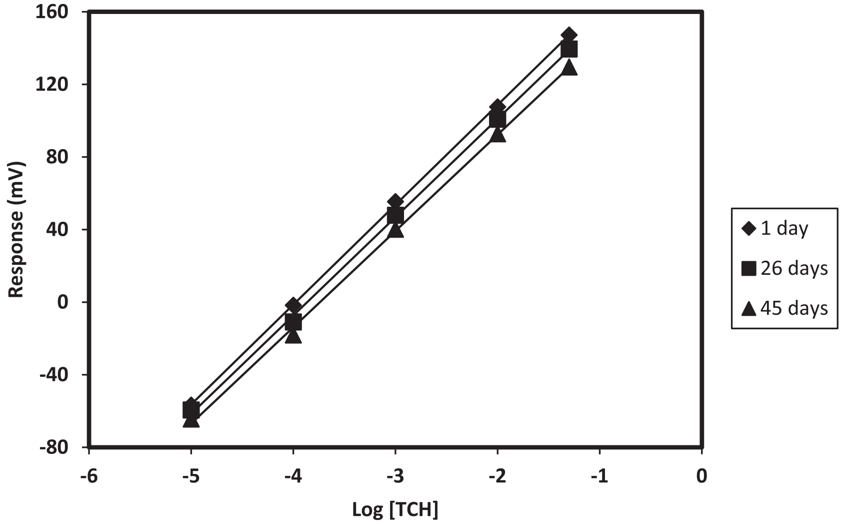

**Figure 6** Calibration curve of sensor No. 1 as a function of time.

Fig. 6. While sensor No. 3 showed operative lifetime of about 3 weeks with a slight gradual decrease in slope from 54.59 to 49.56 mV decade$^{-1}$ and an increase in the detection limit from $5 \times 10^{-5}$ to $8 \times 10^{-5}$ M. It is well established that the loss of plasticizer, ionic sites from the polymeric membrane due to leaching into the sample is a primary reason for the limited lifetimes of the sensor No. 3 (El-Saharty et al., 2006).

### 3.8. Selectivity of the electrodes

The influence of some inorganic cations, such as $Li^+$, $Na^+$, $K^+$, $Mg^{2+}$, $Ca^{2+}$, $Zn^{2+}$, $Ni^{2+}$, $Co^{2+}$, $Cu^{2+}$, $Al^{3+}$, $Cr^{3+}$, $Fe^{3+}$ and sugars (glucose, fructose) on the electrode response was investigated. The selectivity coefficients ($K^{\mathrm{pot}}_{\mathrm{TCH},j^{z+}}$) were used to evaluate the degree of interference. Selectivity coefficients were determined by the separate solution method (Lindner and Umezawa, 2008; Umezawa et al., 2000; Buck and Lindner, 1994b) in which the following equation was applied:

$$\log K^{\mathrm{pot}}_{\mathrm{TCH},j^{z+}} = (\mathrm{E}_2 - \mathrm{E}_1)/S + \log[\mathrm{TCH}] - \log[j^{z+}]^{1/z} \tag{1}$$

where $E_1$ is the electrode potential in a $1.0 \times 10^{-3}$ M TCH solution; $E_2$ the potential of the electrode in a $1.0 \times 10^{-3}$ M solution of the interferent ion ($j^{z+}$) and $S$ the slope of the calibration plot.

**Table 5** Potentiometric selectivity coefficients of some foreign ions on the tetracaine electrodes[a].

| Foreign ion | $\log K^{\mathrm{pot}}_{\mathrm{TCH,jz+}}$ | | |
|---|---|---|---|
| | Sensor No. 1 | Sensor No. 2 | Sensor No. 3 |
| $Li^+$ | −2.38 | −2.16 | −1.84 |
| $Na^+$ | −2.42 | −2.28 | −1.95 |
| $K^+$ | −2.42 | −2.47 | −2.02 |
| $Mg^{2+}$ | −3.70 | −3.41 | −2.85 |
| $Ca^{2+}$ | −3.62 | −3.37 | −2.88 |
| $Zn^{2+}$ | −3.64 | −3.64 | −2.81 |
| $Co^{2+}$ | −3.85 | −3.56 | −3.60 |
| $Ni^{2+}$ | −3.72 | −3.43 | −3.49 |
| $Cu^{2+}$ | −3.38 | −3.31 | −3.18 |
| $Al^{3+}$ | −3.86 | −3.92 | −3.43 |
| $Cr^{3+}$ | −3.90 | −4.00 | −3.56 |
| $Fe^{3+}$ | −3.73 | −3.76 | −3.66 |
| Glucose | −2.76 | −2.19 | −2.17 |
| Fructose | −2.97 | −2.33 | −2.19 |

[a] Three determinations.

The results in Table 5 showed that tetracaine-PVC membrane electrodes are selective for tetracaine ion over many inorganic cations and sugars. It is evident from the data in Table 5 that the sensor Nos. 1 and 2 based on TC-PTA and TC-PMA complexes, respectively, have a relatively high selectivity toward tetracaine relative to interference cations and sugars, this attributed probably to the large difference in the mobilities and permeabilities of the ions in TC-PTA and TC-PMA electrodes as compared to TC-TPB electrode (sensor No. 3). The mechanism of selectivity is mainly based on the stereospecificity and electrostatic environment, and is dependent on how much similarity is present between the locations of the lipophilic sites in the two competing species in the bathing solution side and those present in the receptor of the ion-exchanger (Bakker et al., 2000). The inorganic cations do not interfere owing to the differences in ionic size, and consequently their mobilities and permeability, as compared with those of tetracaine cation. Also, the smaller the energy of hydration of the cation, the greater the response of the membrane. In the case of sugars, the high selectivity is due to the difference in polarity and lipophilic character (Kormosh et al., 2009; Ensafi and Allafchian, 2008).

### 3.9. Analytical applications

The prepared electrodes have been successfully used for the determination of tetracaine in aqueous solutions and in pharmaceutical preparations (eye drops and injection) by using the direct and standard addition methods and the results are summarized in Table 6. The direct method is the simplest of obtaining quantitative results using ion-selective membrane electrode (Gründler, 2007; Wang, 2006). The calibration graph

**Table 6** Tetracaine hydrochloride injection and eye drop analyses by using Direct and standard addition methods for the proposed electrodes.

| Sample | Taken (M) | Direct method , recovery (%), (RSD[a], %) | | | Standard addition method, recovery (%), (RSD[a], %) | | |
|---|---|---|---|---|---|---|---|
| | | Sensor No. 1 | Sensor No. 2 | Sensor No. 3 | Sensor No. 1 | Sensor No. 2 | Sensor No. 3 |
| Pure solution | $1 \times 10^{-4}$ | 101.5 (0.30) | 101.3 (0.40) | 102.5 (0.7) | 102.0 (0.40) | 102.3 (0.45) | 104.5 (0.70) |
| Tetracaine HCl, injection (10 mg) | $1 \times 10^{-3}$ | 102.0 (0.45) | 103.1 (0.47) | 105.3 (0.90) | 101.4 (0.33) | 103.0 (0.50) | 105.2 (0.70) |
| Tetracaine HCl, eye drops (5 mg) | $5 \times 10^{-5}$ | 101.4 (0.40) | 102.4 (0.40) | 106.0 (1.10) | 100.7 (0.44) | 99.4 (0.50) | 103.8 (0.75) |

[a] RSD, Relative standard deviation (four determinations).

**Table 7** The comparison of proposed ion-selective electrode with the standard BP method using *t*- and *F*-statistical tests.

| Parameter | Proposed method | BP method |
|---|---|---|
| Mean | 101.2 | 100.5 |
| RSD | 0.858 | 0.913 |
| *N* | 4 | 4 |
| Variance | 0.736 | 0.833 |
| Pooled standard deviation (*S*) | 0.885 | – |
| Student's *t* | 1.073 (2.447)[a] | – |
| *F* test | 1.312 (9.277)[a] | – |

[a] The values between parenthesis are the corresponding theoretical values of *t* and *F* at the 95% confidence level.

was constructed and the concentration of the unknown was calculated by linear equation of the calibration curve. This method has been applied for the determination of TCH in eye drops and injection, the results are summarized in Table 6 including the repeatability data ($N = 4$). The content of TCH in its formulation using the proposed electrodes is with a good agreement with declared amount while the standard addition method was applied by adding a small portion (0.1 mL) of $1.0 \times 10^{-2}$ M standard TCH solution to 20 ml aliquot samples of various pure and formulation TCH concentrations ($1.0 \times 10^{-3}$–$5.0 \times 10^{-5}$ M). The change in potential readings (at a constant temperature of 25 °C) was recorded after each addition and used to calculate the concentration of TCH sample solutions (Buck and Lindner, 1994a) by the following equation:

$$C_x = C_s V_s / [(V_x + V_s) \times 10^{\Delta E/S} - V_x] \tag{2}$$

]where, $C_x$ and $V_x$ are the concentration and the volume of an unknown sample, respectively. $C_s$ and $V_s$ are the concentration and the volume of the standard, respectively. $S$ is the slope of the calibration graph (mV decade$^{-1}$). $\Delta E$ is the change in the potential (mV).

In order to compare two methods for the determination of tetracaine hydrochloride (TCH) in some pharmaceutical preparations, the results obtained from ion-selective electrode using sensor No. 1 (TC-PTA-DBPH) were compared with those obtained by the standard British Pharmacopoeia (BP) method (British Pharmacopoeia on CD-ROM, 2001). The results obtained by the two different methods, (Table 7) were statistically compared, using student's *t*-test and variance ratio *F*-test at 95% confidence level (Miller and Miller, 2005; Farrant, 1997). In all cases, the calculated *t*- and *F*-values, Table 7 did not exceed the theoretical values, which indicate that there is no significant difference between either methods in accuracy and precision in the determination of tetracaine hydrochloride (TCH) in pharmaceutical formulations.

## 4. Conclusion

Potentiometric sensors for TCH are prepared, characterized and used for continuous drug determination. Sensors based on the use of plasticized PVC matrix membranes incorporating TC-PTA or TC-PMA or TC-TPB ion exchangers are prepared and used for quantitative determination of TCH at concentration level down to $1 \times 10^{-5}$ M with an accuracy of 101.2 ± 0.8%. The drug is determined in pure powders and in dosage forms. The proposed method has some important advantages: the electrode proved to be successful, providing a rapid, simple, low cost, precise, accurate and inexpensive solution regarding reagent consumption and equipment involved. They can therefore be used for routine analysis of the drug in quality control laboratories.

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