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Electrochemical Impedance Study of Li-µISE Based on PPy[$LiClO_4$] as a Solid Contact

[1, 2] Safae MERZOUK, [3] Mourad TAHA JANAN, [2] Mohamed AGOUZOUL, [4] Joan BAUSELLS, [1] Nicole JAFFREZIC-RENAULT, [1] Abdelhamid ERRACHID, [1] Nadia ZINE

[1] Institut des Sciences Analytiques (ISA), Université de Lyon, Université de Claude Bernard Lyon 1, UMR 5280, 5 rue de la Doua, 69100 Villeurbanne, France
[2] Université Mohamed V Agdal, Ecole Mohammadia d'ingénieurs, Equipes de Recherche Modélisation et Multimédia Mécanique (ERD3M), BP 765, Agdal Rabat Maroc
[3] Université Mohamed V Souissi, Ecole Normale Supérieure de l'Enseignement Technique, 10100, Rabat Maroc
[4] Centre Nacional de Microelectrònica (IMB-CSIC), Campus U.A.B., 08193 Bellaterra, Spain
Tel.: +33 437 42 35 69
E-mail: safae_merzouk@yahoo.fr, nadia.zine@univ-lyon1.fr

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Abstract: The development of ion-selective microelectrodes for monitoring lithium ions in blood or serum is very important in the field of clinical chemistry. For this interest, all-solid-state microsensors based on impedance measurement for the detection of Li^+ has been developed. The selective PVC membrane composition used was obtained by dissolving 1.2 % (w/w) Lithium ionophore III, 66 % (w/w) o-nitrophenyloctyl ether, 0.4 % of (potassium tetrakis(4-chlorophenyl)borate and 32.4% (w/w) polyvinylchloride (PVC) in tetrahydrofuran (THF). Then, the selective membrane was deposited onto gold microelectrodes containing a conducting polymer (polypyrrole doped with Lithium perchlorate) as solid contact layer. The developed Li^+-ISE provides excellent performance towards the determination of lithium with a low detection limit of 6×10^{-8} M and a wide linear range from $1x10^{-7}$ M to $1x10^{-1}$ M covering the clinically interesting of Lithium range (0.5×10^{-3} to 1.5×10^{-3} M); The selectivity properties have been examined obtaining good results. *Copyright © 2014 IFSA Publishing, S. L.*

Keywords: Ion-selective microelectrode (µISE), Conducting polymer, Electrochemical Impedance Spectroscopy, Lithium ion, Electropolymerization.

1. Introduction

Ion-selective microelectrodes (ISEs) are very attractive for ion activity measurements in biological and environmental systems. The therapy of manic depressive psychosis with lithium salts requires periodic measurements of the Li concentration in whole blood, plasma, urine or serum [1-3]. The analysis is difficult because of the low lithium concentration compared to the high content of the natural cations (especially Na^+) [4]. Lithium has a narrow therapeutic range (0.5-1.5 mM), and too low

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of a dosage leads to ineffectiveness and too high leads to severe toxicity [5]. Accurate and rapid monitoring of the Li activity in blood for the patients in lithium therapy is critically important as the gap between its therapeutic and toxic levels are very close. Lithium-selective electrode has been developed for such purpose, and several commercial analyzers are now routinely used in many clinical laboratories [6-8]. For this interest, in this work we report all-solid-state sensing microdevice based on impedance measurement for the detection of Lithium. Lithium Ionophore III was used as ionophore for membrane preparation. The selective membrane was deposited onto gold microelectrodes containing a conducting polymer (polypyrrole doped with lithium perchlorate) as solid contact layer.

2. Experimentation

2.1. Reagents

Pyrrole (Aldrich Chemicals) was distilled under vacuum prior to its use. All the membrane components (analytical reagent grade), namely, Lithium ionophore III (ETH 1810) (62558), Potassium tetrakis(4-chlorophenyl)borate (60591),2-Nitrophenyl octyl ether (73732), Poly(vinyl chloride) high molecular weight (81392) were purchased from Fluka. Standard solutions and buffers were prepared with di-ionised water.

2.2. Preparation of all-solid-sate Lithium Microelectrode

2.2.1. Electrochemical Polymerization of PPy[$LiClO_4$]

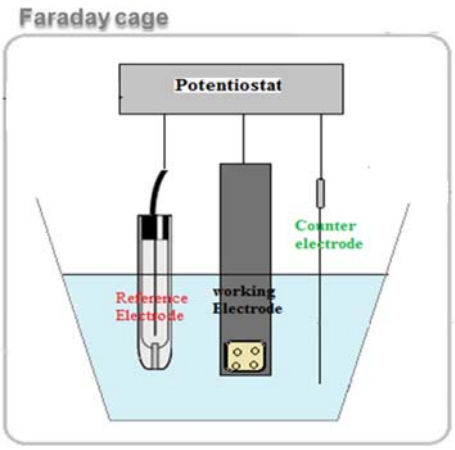
The fabrication process for the microelectrodes has been performed at the Centro Nacional de Microelectronica (CNM) of Barcelona. The microelectrodes are circular with a diameter of 400 μm, and are deposited over silicon dioxide on a silicon chip. The metal interconnects to the chip bonding pads are passivated with silicon nitride. The conductive solid internal contact layer of the microelectrode was prepared by electropolymerization of the pyrrole (0.1 M) in presence of $LiClO_4$ (10 mM) in acetonitrile with 1 wt.% in water. The PPy-[$LiClO_4$] films were grown over the surface of the gold microelectrodes, using cyclic voltammetry applying a potential range of 100 to 800 mV with a scan rate of 100 mV/s for 10 cycles in a single compartment cell with a standard three electrode system at a using a VoltaLab (PGZ401) potentiostat–galvanostat.

2.2.2. Lithium Membrane Preparation

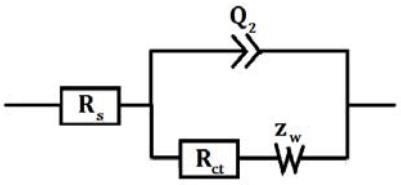
The composition of the ion-selective membrane sensitive to Lithium was , 1.20 wt% ionophore (ETH 1810), 0.40 wt% potassium tetrakis(4-chlorophenyl)borate as additive, 65.60 wt% 2-Nitrophenyl octyl ether as plasticizer and 32.80 wt% Poly(vinyl chloride) as matrix . The membrane components were dissolved in 3 ml of tetrahydrofuran (THF). The mixture was thoroughly stirred using agitateur vortex until homogeneous, then the membrane cocktail (~2 μl) was applied on the active area PPy[$LiClO_4$] using a transfer pipette. After complete evaporation of the tetrahydrofuran (THF) (24h), the microelectrodes doped PPy[$LiClO_4$] containing the selective membrane were conditioned in LiCl solution at c=10^{-3}M over 30 min prior to use.

2.3. EIS Measurements

All impedance spectroscopy measurements (EIS) were performed at room temperature using a one compartment three-electrodes cell where a microelectrode of gold-doped PPy-[$LiClO_4$] and modified by a selective membrane sensitive to Lithium was used as the working microelectrode (Fig. 1a).



(a)



(b)

Fig. 1. (a) Cell of EIS measurements, (b) Equivalent circuit.

The reference electrode was a saturated calomel electrode with a double junction and a platinum wire of 1 mm in diameter as the auxiliary electrode and the working electrode is. The impedance analysis was performed using an EC-Lab software impedance analyzer and biological vmp3 as a potentiostat. The

impedance spectra were recorded in the frequency range 100 kHz-100 Hz by using a sinusoidal excitation signal with amplitude of 100 mV. The measurements of the Li^+-ISE were determined in a Tris-HCl buffer solution (c=0.05 M; pH= 7.2) by adding low volumes of LiCl solutions and varying the lithium concentrations from $c=10^{-8}$ M to $c=10^{-1}$ M. All experiments were performed at open-circuit potential in darkness and in a Faraday box to eliminate electrical interference.

3. Results and Discussion

3.1. Growing of PPy[LiClO4]

Fig. 2b shows the cyclic voltammetry response of doped Pyrrole for LiClO4 mixture solution at scan rate 100 mV/s. Microelectrode image has been taken using Leica microscope EZ4D after polymerization to check the surface. We can appreciate that the PPy-LiClO4 was growth only on the active areas of the microelectrodes.

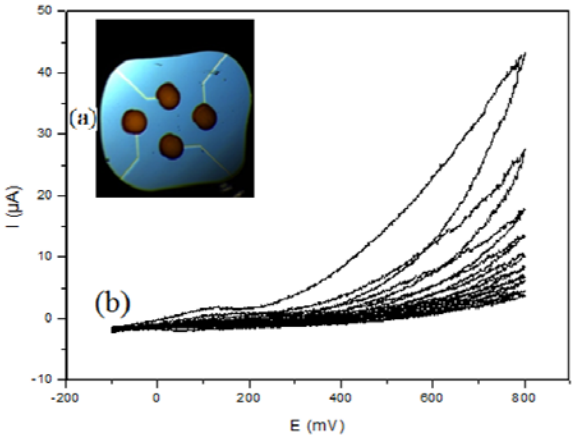


Fig. 2. (a) Image of the Microelectrode after Polymerization, (b) voltammetric response of doped PPy-LiClO4 at scan rate of 100 mV/s.

3.2. Sensitivity to Li^+

For the EIS measurements response, The calibration was performed by adding different concentrations of LiCl to 25 ml of supporting electrolyte Tris-HCl buffer solution (c=0.05; pH= 7.2). Impedance spectra for the Li^+-µISE studied are shown in Fig. 3. It is noticed that the size of the semicircles decreases with increasing concentration of lithium.

Among the equivalent circuits proposed for an ion-selective membrane in contact with aqueous solutions [9] the most common is circuit presented in Fig. 1b. It combines four elements of the electrolyte resistance (R_s), the constant phase element Q_2, the charge transfer resistance (R_{ct}) and the Warburg impedance Z_w. Using this equivalent circuit was used for the fitting of experimental data (Fig. 1-b)), the normalized Rct(i) varies linearly with the concentration of Lithium as seen in Fig. 4. The developed Li^+µISE provides excellent sensitivity with a low detection limit of 6×10^{-8} M and a wide linear range from 1×10^{-7} M to 1×10^{-1} M covering the clinically interesting of Lithium range (0.5×10^{-3} to 1.5×10^{-3} M) (Fig. 4). The developed Li^+-µISE exhibited better performance to those measured for PVC based on the same and other types of ionophores using a potentiometric measurement [10, 11].

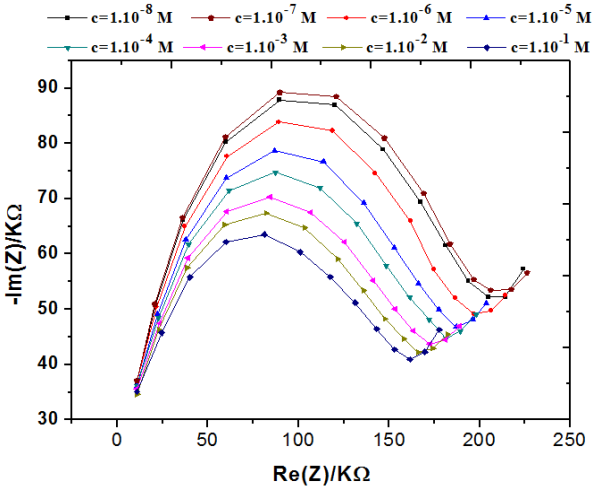


Fig. 3. Impedance response of the µISE for different concentrations of Lithium (c = 1.10^{-8} M to C = 1.10^{-1}M).

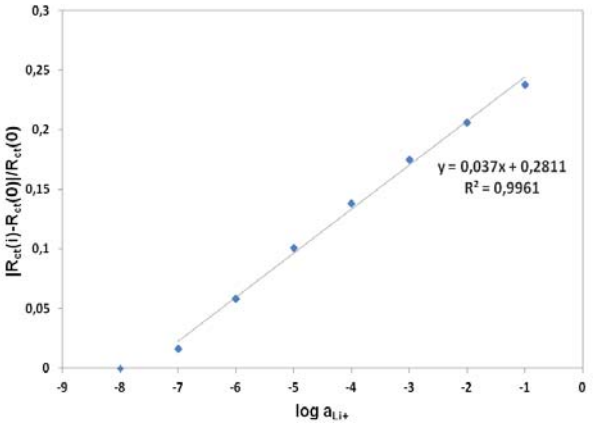


Fig. 4. Linear relationship of the $|R_{ct}(i) - R_{ct}(0)|/R_{ct}(0)$ vs. log a_{Li+}.

3.3. Selectivity

There are always several types of ions present in real samples and they can interfere on the response of the Li+-µISE toward the primary ion. Selectivity is one of the most important characteristics of microsensor, as it helps to determine whether a reliable measurement in the target sample is possible.

This is measured in terms of the selectivity coefficients ($K^{pot}_{Li,j}$). The behaviour of the microelectrodes was tested in the presence of other cations (K^+, Na^+, NH_4^+ and Mg^{2+}). The $K^{pot}_{Li,j}$ was determined by using the fixed interference method (FIM) (Table 1) [12]. The interference measurements were performed in 25 ml solution of interfering ion at a concentration of 10^{-3} M; we follow successively the variation of the Lithium concentrations ranging from 1.10^{-8} to 1.10^{-1} M.

Table 1. Selectivity coefficients log $K_{Li^+,j}$.

Interfering ions « j»	Selectivity coefficients log $K_{Li+,j}$
Mg^{2+}	-3,4
NH_4^+	-2,9
K^+	-2,4
Na^+	-2,1
Li^+	___

As expected from Fig. 5, the Li^+-µISE exhibits a higher preference for lithium ion compared with the other metal ions examined. Only Na^+ and K^+ produce interferences. However, these ions do not cause any disturbance to the performance of the developed Li^+-µISE.

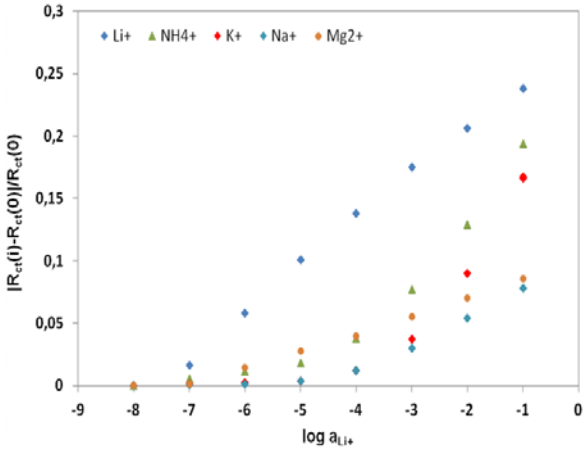


Fig. 5. Linear relationship of the $|R_{ct}(i) - R_{ct}(0)|/R_{ct}(0)$ versus log a_{Li+} for interference response.

The selectivity coefficients of the proposed Li^+µISE based on ionophore ETH 1810 are superior to the corresponding values previously reported for PVC-membrane lithium-selective electrodes based on different ionophores [10, 11].

3.4. Effect of pH

The pH influence response for the microelectrode was tested over the pH range 1.5–11.0 using 1.0×10^{-3} M Li^+ ions. The principle of measurement is in 25 ml of the LiCl solution ($c=10^{-3}$ M; pH = 11) was gradually added small volumes of HCl to decease the pH; in each addition, we expect the pH stability for a given value and we start on our impedance measurement under the same conditions used before. Fig. 6 shows that the constant range is between pH 6.5 and 9.0, the same may be taken as the working pH range that including physiological pH.

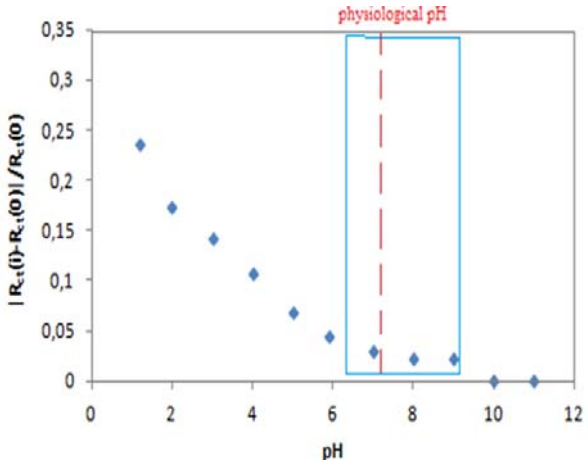


Fig. 6. Effect of the pH of test solution on the impedance response of the proposed Li^+-µISE at a 10^{-3} M Li^+ concentration.

4. Conclusions

The experiment results founds in this work using electrochemical impedance spectroscopy (EIS) as an electrochemical method for the detection of Lithium, have shown a best performance with respect to linear response, good sensitivity covering the clinically interesting Li^+ range (0.5–1.5 mM) . The response were compared to different interference cations for Lithium detection which confirm that , the analysis is difficult due to the low concentration of lithium compared to the high content of cations (especially Na^+). Selectivity coefficients confirmed that sodium is the largest interfering element compared to other species studied containing in blood. Furthermore, the developed µISE will be a promising biosensing device for the measurement of Lithium in pharmaceutical preparations of Lithium treatments.

Acknowledgements

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