<u>Regular Article</u>



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## Determination of Lithium(I) in Pharmaceutical Products and Biological Samples by a Simple Potentiometric Sensor Based on a Recently Synthesized Chromene Derivative as the Ionophore

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In this research, a coated graphite polyvinyl chloride (PVC) membrane electrode was fabricated for the potentiometric determination of lithium based on 13-(3-nitrophenyl)-12H,14H-benzo[g]chromeno[2,3-b]chromene-7,12,14(13H)-trione (L) as the ionophore. The best Nernstian response was observed from the membrane composition of 31% PVC, 7% L, 2% NaTPB, and 60% dioctyl phthalate (DOP) as the plasticizer. The designed sensor showed a wide linearity over the concentration range of  $1 \times 10^{-8}$ - $1 \times 10^{-3}$  M with a slope of  $60.2 \pm 0.3$  mV decade<sup>-1</sup>, and the limit of detection (LOD) of  $7.5 \times 10^{-9}$  M. The selectivity of the designed sensor was investigated by the matched potential method and no serious interference was observed. The response time and life span of the electrode were 5 s and 16 weeks, respectively. The potential response of the electrode was independent of solution pH in the pH range of 3.0-12.0. The influence of the presence of organic solvents on the potential response of the electrode was also scrutinized, and the results showed that the designed sensor keeps its Nernstian behavior in solutions with 20% non-aqueous content. In the end, the electrode was successfully applied to determine lithium carbonate in tablet, urine, and serum samples with recovery% values of 96.0 to 106.33 and RSD% 1.99-4.45.

Keywords: Ion selective electrode, Potentiometry, Lithium carbonate, PVC membrane, Sensor, Chromene

## INTRODUCTION

Lithium carbonate is a valuable medication for treating bipolar disorder and mania [1]. However, it is crucial to monitor patients' blood lithium levels regularly to prevent potential side effects. Without proper monitoring, patients may experience adverse effects such as kidney failure, digestive issues, weight fluctuations, breathing difficulties, and even seizures [2]. Additionally, the use of this medication can lead to side effects and possible overdose [3]. An overdose of lithium carbonate may result in symptoms like nausea, vomiting, diarrhea, tremors, dry mouth, dizziness, seizures, and in severe cases coma or death due to cardiac or respiratory complications caused by the drug's toxic properties [4].

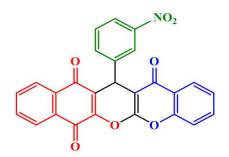
Furthermore, long-term usage of lithium carbonate can give rise to other complications including imbalances in blood electrolyte levels osteoporosis, kidney problems weight loss skin and hair changes increased fatigue decreased sexual potency [5]. Frequent monitoring of lithium levels in patients' blood is vital for treating bipolar disorder and mania due to the extended half-life of lithium carbonate [6]. Physicians typically monitor levels weekly or biweekly, or even more frequently for some patients [7]. This proactive approach allows doctors to adjust dosages if needed and watch out for potential side effects, safeguarding patients from elevated blood lithium levels and associated risks [8]. Recognizing regular measurement of lithium levels as

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fundamental in treating bipolar disorder and mania is essential [9]. Typically, there exists a range of costly and complex techniques for measuring lithium ion levels. For instance, atomic absorption is highly accurate but has a steep price tag and requires sophisticated apparatus. Inductively coupled plasma optical emission spectrometry (ICP-OES) [10] represents another method, yet it is constrained by its high cost and the necessity for intricate equipment. Likewise, ion exchange chromatography [11] delivers precision but is hampered by cost and equipment limitations. Unlike the previously discussed methods, ion-selective electrodes are precious for measuring the levels of different ions in solutions [12]. These electrodes exhibit high selectivity for specific ions and can selectively respond to them, making them widely used and accurate [13]. Ion-selective electrodes offer a simple, compact, and portable approach to measuring solution ion levels [14]. Therefore, for quantifying the concentration of lithium carbonate in biological samples, using an electrochemical sensor for potentiometric measurement can serve as a suitable alternative to the costly and complex methods mentioned earlier [15]. Consequently, ion-selective electrodes with high selectivity and accuracy are widely recognized as beneficial for measuring ion levels in solutions. Additionally, using chromium derivatives as modifiers in the fabrication of ion-selective electrodes enhances their selectivity and improves measurement precision [16].

When constructing ion-selective electrodes, an ionophore ligand that selectively and effectively interacts with the desired analyte is typically employed [17]. This substance acts as a modifier in the electrode and, by modifying the structure of the electrode surface, enhances the sensitivity, linear range, and selectivity of these electrodes [18]. On the other hand, the chromene derivative (13-(3-nitrophenyl)-12H,14H-benzo[g]chromeno[2,3-b]chromene-7,12,14

(13H)-trione abbreviated as (L)) shown in Fig. 1 has several oxygen atoms within its structure that enable selective interaction with hard metal ions like lithium [19]. Furthermore, this ligand offers the benefit of being highly insoluble in water and other polar solvents, resulting in an extended lifespan for electrodes designed using it. This research aimed to develop an ion-selective electrode using L as the ionophore. We carried out the optimization of different parameters that could affect the potential response of the



**Fig. 1.** The chemical structure of (13-(3-nitrophenyl)-12H, -benzo[g]chromeno[2,3-b]chromene-7,12,14(13H)-trione (L).

sensor. Subsequently, we used the developed electrode to analyze lithium(I) in pharmaceutical and biological samples.

## EXPERIMENTAL

#### **Apparatus and Chemicals**

The pH measurements were performed using a Metrohm 827 pH meter equipped with a combined glass electrode. The potential measurements at  $25.0 \pm 0.1$  °C were conducted with a 250 pH/mV meter Corning ion analyzer, utilizing a saturated calomel electrode (SCE) as the reference electrode. The chemicals and reagents utilized were obtained from Sigma-Aldrich or Merck (Darmstadt, Germany) without additional purification. Ionophore L was synthesized following the procedure outlined in [19], and all solutions were prepared using double-distilled water (DDW). Real samples, including three pharmaceutical tablets, were sourced from a local pharmacy in Tehran, Iran. Additionally, urine and serum plasmas were provided by a healthy individual who does not use any medications.

#### **Electrode Fabrication**

The electrode fabrication process involves the precise weighing of various components in a 5-ml beaker, followed by the addition of tetrahydrofuran (THF), ultrasonic treatment to achieve a homogenous solution, immersion of a graphite bar to create a thin-layer polymeric film, drying at room temperature (48 h), and conditioning by soaking in  $1 \times 10^{-3}$  M Li<sub>2</sub>(CO<sub>3</sub>) solution for 24 h. To start the fabrication process, specific amounts of Ionophore (L), polyvinyl chloride (PVC), sodium tetraphenyl borate (NaTPB),

nitrobenzene (NB), dioctyl phthalate (DOP), dibutyl phthalate (DBP), and oleic acid (OA) are weighed in the 5-ml beaker. Subsequently, 3 ml of tetrahydrofuran (THF) is added to the mixture before subjecting it to ultrasonic treatment at low temperature for complete homogenization. The resulting solution settles under a hood over time to form an oily viscous solution.

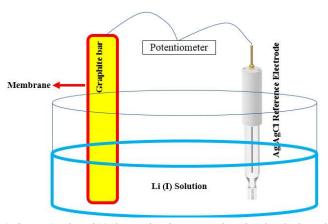
#### **Real Sample Analysis**

For pharmaceutical samples, 30 tablets of lithium carbonate were weighed and an average of tablet weight was calculated. Then, the tablets were crushed into powder and thoroughly mixed until an even blend was achieved. The resulting powder was then dissolved in 500 ml of doubly distilled water (DDW) using sonication and subjected to centrifugation to eliminate any solid particles [20].

In the case of serum samples, firstly varying amounts of lithium carbonate with a 1 ml serum sample, were spiked and followed by adding 0.8 ml acetonitrile to eliminate serum proteins. Subsequently, the remaining serum protein was separated by centrifugation at 4000 rpm for 20 min [21]. The resulting supernatant was carefully transferred to a 25 ml flask and then diluted with DDW. The urine samples were centrifuged and diluted 1:5 after spiking [22].

## **EXPERIMENTAL PROCEDURE**

The membrane was prepared by mixing 7 mg, 2 mg ionic additive, 60 mg DOP, and 31 mg PVC. Then the ingredients were dissolved in THF and it was inserted at room temperature until excess THF was evaporated and an oily viscous solution was obtained. Then, the graphite bar was dipped in the oily solution for about 5 s. Afterward, the electrode was inserted in the room to get dried and subsequently was dipped in a  $1 \times 10^{-3}$  M Li<sub>2</sub>(CO<sub>3</sub>) solution for getting conditioned. In the next step, the electrode was connected to a potentiometer with an Ag/AgCl reference electrode, and the electromotive force between the electrodes was employed as an analytical signal that has a linear relationship with the activity of Li(I) according to the Nernst equation (Scheme 1). The residual Lithium-ion was removed after each measurement by washing with DDW.



Scheme 1. The Li(I) determination procedure by the designed electrode

## **RESULTS AND DISCUSSION**

#### **Optimization of Membrane Composition**

The performance of a potentiometric sensor depends heavily on the composition of the membrane. Factors such as the type and quantity of ionophore, the dielectric constant of the plasticizer, and the content of ionic additives affect the membrane response [23]. When creating a new PVCmembrane ion-selective electrode, it is crucial to start by optimizing the membrane composition. In this study, we prepared 13 different electrodes with varying compositions and evaluated their potential responses, as shown in Table 1. One important factor we investigated was the amount of ionophore used. We constructed six different electrodes with varying amounts of L (membranes 2-7) and studied their performance. The results demonstrate that the choice of ionophore significantly impacts the potential response of the sensor. The ionophore-free electrode (membrane 2) had a narrow linear range and a low slope. However, increasing the amount of ionophore to 7% (membrane 6) led to an excellent Nernstian response (57.1 mV Decade<sup>-1</sup>) over a wide dynamic range  $(1.0 \times 10^{-8} \text{ to } 1.0 \times 10^{-3})$ . This suggests that L has a strong interaction with Li<sup>+</sup> [24].

The findings suggest that the saturation of the membrane due to the further addition of an ionophore can decrease the slope of the calibration curve. Furthermore, the amount of ionic additive is crucial in improving sensitivity and widening the linear range, with 2% NaTPB identified as the

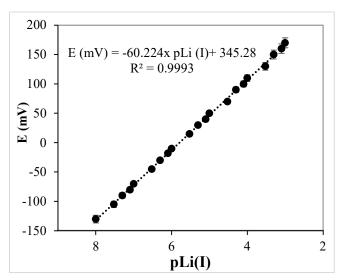
No	PVC	Ionophore	NaTPB	Plasticizer	Linear range	Slope	LOD
	(%wt)	(%wt)	(%wt)	(%60)		(mV Decade <sup>-1</sup> )	
1	40	0	0	DBP	$1.0{\times}10^{\text{-4}}$ to $1.0\times10^{\text{-3}}$	9.2±0.2	9.5×10 <sup>-5</sup>
2	38	0	2	DBP	$1.0 \times 10^{-4}$ to $1.0 \times 10^{-3}$	12.8±0.3	9.0×10 <sup>-5</sup>
3	37	1	2	DBP	1.0×10 <sup>-5</sup> to 1.0×10 <sup>-3</sup>	$28.6 \pm 0.2$	9.5×10 <sup>-6</sup>
4	36	2	2	DBP	1.0×10 <sup>-5</sup> to 1.0×10 <sup>-3</sup>	30.4±0.1	9.0×10 <sup>-6</sup>
5	34	4	2	DBP	1.0×10 <sup>-5</sup> to 1.0×10 <sup>-3</sup>	42.9±0.3	8.0×10 <sup>-6</sup>
6	31	7	2	DBP	1.0×10 <sup>-8</sup> to 1.0×10 <sup>-3</sup>	57.1±0.2	8.5×10 <sup>-8</sup>
7	30	8	2	DBP	1.0×10 <sup>-9</sup> to 1.0×10 <sup>-3</sup>	56.2±0.2	9.0×10 <sup>-8</sup>
8	33	7	0	DBP	5.0×10 <sup>-7</sup> to 1.0×10 <sup>-3</sup>	$50.8 \pm 0.1$	6.0×10 <sup>-7</sup>
9	32	7	1	DBP	1.0×10 <sup>-7</sup> to 1.0×10 <sup>-3</sup>	52.5±0.3	3.5×10 <sup>-7</sup>
10	30	7	3	DBP	1.0×10 <sup>-8</sup> to 1.0×10 <sup>-3</sup>	56.8±0.2	9.0×10 <sup>-9</sup>
11	31	7	2	OA	3.0×10 <sup>-8</sup> to 1.0×10 <sup>-3</sup>	55.1±0.1	1.0×10 <sup>-8</sup>
12	31	7	2	DOP	1.0×10 <sup>-8</sup> to 1.0×10 <sup>-3</sup>	60.2±0.3	7.5×10 <sup>-9</sup>
13	31	7	2	NB	5.0×10 <sup>-8</sup> to 1.0×10 <sup>-3</sup>	56.2±0.2	1.0×10 <sup>-8</sup>

Table 1. The Effect of Membrane Composition on the Potentiometric Response of the Electrode

optimum amount. The nature of the plasticizer also influences the electrode's performance, with DOP demonstrating the best response among the studied plasticizers. The use of DOP as a plasticizer is attributed to its non-polar nature and low dielectric constant, which potentially facilitates a stronger interaction between the analyte and the plasticizer. This finding is particularly relevant for applications involving Li(I) as a monovalent cation [25]. The calibration curve of membrane 12 that showed the best potential response is represented in Fig. 2.

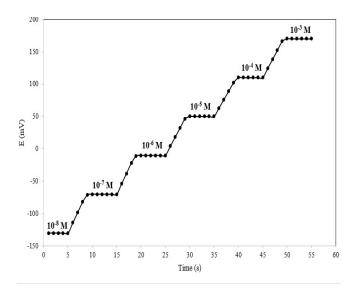
# Response Time, Lifespan, Repeatability, and Reproducibility

The response time of a potentiometric sensing system is a crucial parameter that determines its efficiency in detecting and measuring ion concentrations. The time required for the system to reach 90% of its final constant potential after immersion in the test solution is known as the response time. It is influenced significantly by the speed of exchange kinetics of complexation-decomplexation of the analyte ions in the presence of the ionophore at the membrane surface [26]. To evaluate this parameter, the reference and indicator electrodes were immersed in a series of Li(I) solutions with a 10-fold difference in activity. The electromotive force of the system was recorded at every second to analyze the response

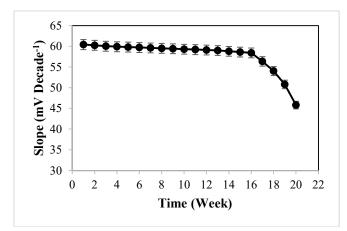


**Fig. 2.** The calibration curve of the designed sensor at ambient temperature and neutral pH.

time. The results indicated that the fabricated sensor exhibited a response time of 5 seconds (Fig. 3). The investigation of the electrode's longevity included observing the linear range and slope of the calibration curve over 20 weeks. As depicted in Fig. 4, the sensor demonstrated a relatively consistent slope over a long period of 16 weeks, exhibiting no deviation from Nernstian behavior. This favorable outcome can be attributed to the limited solubility of L in inorganic solvents, as well as its exceptional chemical stability. Besides, the increase in LOD of the target sensor to  $5.0 \times 10^{-8}$  in the 17th week has resulted in a narrower linear range. To evaluate the repeatability of the designed potentiometric sensor, five different solutions of Li<sup>+</sup> with two different activities of  $1.0 \times 10^{-7}$  and  $1.0 \times 10^{-5}$  were prepared.



**Fig. 3.** The response time of the designed sensor at ambient temperature and neutral pH.



**Fig. 4.** The lifetime of the developed electrode at ambient temperature and neutral pH.

The potential response of these solutions was measured using the constructed coated graphite electrodes, and the RSD% values were calculated. The RSD% values obtained were 3.71% and 2.21% for the  $1.0 \times 10^{-7}$  and  $1.0 \times 10^{-5}$  solutions, respectively. Furthermore, to investigate the reproducibility of the developed analytical method, five different electrodeswere constructed. The potential response of two Li<sup>+</sup> solutions at activities of  $1.0 \times 10^{-7}$  and  $1.0 \times 10^{-5}$  was measured using these electrodes, and the RSD% values were calculated. The resulting RSD% values were 5.09% and 4.11% for the respective solutions. These findings demonstrate the precision and consistency of the designed potentiometric sensor in measuring the potential response of Li<sup>+</sup> solutions at varying activities [27].

#### **Applicable pH Range**

Cation-selective sensors that operate based on potentiometric measurements are essential for accurately determining the pH range in which they can provide reliable and precise performance. These sensors must display electromotive force independent of pH within a specific range, ensuring accurate measurements. Furthermore, Nernstian behavior, vital for ion-selective electrodes, can only be observed within this particular pH range. Therefore, investigating the applicable pH scope is a fundamental step in developing such electrodes. To scrutinize the effect of pH, a  $1.0 \times 10^{-5}$  Li(I) solution was prepared and its pH was evaluated at varying values from 1.0 to 14.0 by using small volumes of concentrated sodium hydroxide and hydrochloric acid solutions (Fig. 5). The resulting potential values were then recorded and plotted against pH. The outcomes revealed that the constructed sensor demonstrated an independent response within the pH range of 3.0 to 12.0. It was noticed that under acidic conditions with pH values below 3.0, the ionophore became protonated, causing competition between hydronium ions and the analyte for complex formation with the ionophore [28]. On the contrary, in alkaline environments where the pH exceeded 12., hydroxyl ions formed complexes with the cation [28]. Therefore, it was concluded that the accurate and precise functionality of this fabricated ionselective electrode could be maintained only within a limited phase of pH ranging from 3.0 to 12.0.

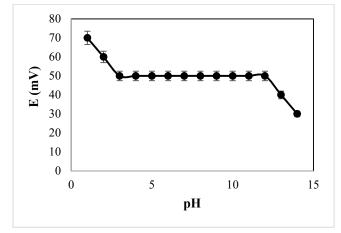


Fig. 5. The effect of pH on the potential response of the developed electrode in a  $1 \times 10^{-5}$  M solution of lithium(I) at ambient temperature.

 Table 2. The Calculated Selectivity Coefficients Based on MPM

Ion	K <sub>MPM</sub>	Ion	K <sub>MPM</sub>
$Ca^{2+}$	5.1×10 <sup>-3</sup>	$Al^{3+}$	1.5×10 <sup>-3</sup>
$Mn^{2+}$	2.2×10 <sup>-4</sup>	$\mathrm{Co}^{2^+}$	1.2×10 <sup>-3</sup>
$Mg^{2+}$	1.9×10 <sup>-3</sup>	$\mathrm{Se}^{4+}$	2.1×10 <sup>-4</sup>
Fe <sup>2+</sup>	3.2×10 <sup>-3</sup>	$\mathrm{Cu}^{2^+}$	9.8×10 <sup>-4</sup>
Fe <sup>3+</sup>	9.6×10 <sup>-3</sup>	$\mathbf{K}^+$	2.3×10 <sup>-3</sup>
$Ag^+$	1.1×10 <sup>-3</sup>	$Na^+$	8.9×10 <sup>-3</sup>
$Pb^{2+}$	2.1×10 <sup>-2</sup>	Ni <sup>2+</sup>	5.3×10 <sup>-3</sup>
$Cd^{2+}$	4.5×10 <sup>-3</sup>	$Zn^{2+}$	4.6×10 <sup>-3</sup>

#### Selectivity

The selectivity of the designed sensor was evaluated using the matched potential method (MPM) [16] across 16 different ionic species, and the selectivity coefficients ( $K_{MPM}$ ) were subsequently calculated. The calculated  $K_{MPM}$  values (Table 2) provide insight into the sensor's response to the analyte and interfering ions [29]. A  $K_{MPM}$  value close to 1 indicates an equal potential response towards the analyte and interfering ion, while a value close to 0 suggests a poor affinity towards the interfering ion. Analysis of Table 2 reveals that all selectivity coefficients are 100-10000 folds smaller than 1, indicating excellent selectivity of the developed sensor towards Li(I).

## Performance of the Designed Sensor at Partially Non-aqueous Mediums

Investigating the proposed sensor's performance in partially non-aqueous mediums is crucial for assessing its applicability in analyzing real samples, particularly those containing organic solvents [48]. To address this, three series of Li<sup>+</sup> solutions with varying amounts of ethanol, acetone, and a combination of ethanol and acetone (50:50) were prepared. The objective was to evaluate the sensor's behavior in the presence of organic solvents. Subsequently, the linear range and calibration curve slope were determined. The findings, as depicted in Table 3, revealed that the fabricated electrode maintains its sensitivity and linear range in solutions with 20% organic content. However, with the further addition of organic ingredients, there was a decrease in the slope and an increase in the limit of detection (LOD). This observation may be attributed to the potential leakage of the ionophore and other membrane components into the test solution in high organic solvent-containing mediums [30]. These results underscore the importance of understanding the sensor's performance in non-aqueous environments, particularly when analyzing samples with organic solvent components. Further exploration and refinement of the sensor's design and composition may be necessary to enhance its robustness and accuracy in challenging sample matrices.

#### **Analytical Applications**

The designed electrode was used to analyze Li(I) levels in serum, urine, and tablet samples, demonstrating its effectiveness in real sample assessment. Tables 4 and 5, present the results, illustrating consistent average outcomes with labeled values for Li(I) pharmaceutical preparations. Furthermore, a recovery test was conducted to validate the accuracy and applicability of the technique for determining SUM in human serum and urine samples within pharmaceutical compositions. Results from Tables 4 and 5 demonstrate reliable quantification of Li(I) in all human serum, urine samples, and prescription formulations using the designed electrode. This highlights its potential practical application in real samples.

Nonaqueous content	Slope	Dynamic range	
(%v/v)	(mV Decade <sup>-1</sup> )	(M)	
0	60.2±0.3	1.0×10 <sup>-8</sup> to 1.0×10 <sup>-3</sup>	
Ethanol			
5	$60.2 \pm 0.3$	1.0×10 <sup>-8</sup> to 1.0×10 <sup>-3</sup>	
10	58.7±0.4	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
15	55.6±0.3	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
20	53.4±0.2	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
25	42.5±0.2	$1.0 \times 10^{-7}$ to $1.0 \times 10^{-3}$	
Acetone			
5	$60.2 \pm 0.3$	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
10	59.1±0.4	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
15	56.1±0.2	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
20	54.2±0.3	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
25	43.3±0.5	$1.0 \times 10^{-7}$ to $1.0 \times 10^{-3}$	
Mixed 1:1 (Ethanol:Acetone)			
5	60.0±0.3	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
10	57.7±0.2	1.0×10 <sup>-8</sup> to 1.0×10 <sup>-3</sup>	
15	54.5±0.3	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
20	52.6±0.4	$1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$	
25	$40.8{\pm}0.2$	$1.0 \times 10^{-7}$ to $1.0 \times 10^{-3}$	

Table 3. The Developed Electrode Potential Response in Non-aqueous Mediums

**Table 4.** Analysis of Li(I) in Pharmaceutical Preparations (n = 3)

Sample	Found	Labeled	%Recovery	
	(mg)	(mg)		
Tablet brand1	295.1±1.2ª	300	98.37	
Tablet brand2	301.8±2.3	300	100.60	
Tablet brand3	298.5±1.8	300	99.50	

<sup>a</sup>Standard deviation based on three replicates.

**Table 5.** Analysis of Li(I) in Human Serum and Urine Samples (n = 3)

Sample	Added	Found	%Recovery	%RSD
	(M)	(M)		
Serum	0	N. D	-	-
	3×10 <sup>-7</sup>	2.88×10 <sup>-7</sup>	96.00	3.44
	5×10 <sup>-5</sup>	5.31×10 <sup>-5</sup>	106.20	2.91
	1×10 <sup>-3</sup>	9.93×10 <sup>-4</sup>	99.30	1.99
Urine	0	N. D	-	-
	3×10 <sup>-7</sup>	3.28×10 <sup>-7</sup>	109.33	4.45
	5×10-5	4.81×10 <sup>-5</sup>	9620	3.98
	1×10 <sup>-3</sup>	9.91×10 <sup>-4</sup>	99.10	3.01

## CONCLUSION

The research presents the fabrication and performance of a coated graphite PVC membrane electrode for the potentiometric determination of lithium. The electrode utilized 13-(3-nitrophenyl)-12H,14H-benzo[g] chromeno[2, 3-b]chromene-7,12,14(13H)-trione (L) as the ionophore. The membrane composition of 31% PVC, 7% L, 2% NaTPB, and 60% DOP as the plasticizer exhibited the best Nernstian response. The sensor demonstrated a wide linearity over a concentration range of  $1 \times 10^{-8}$ -1  $\times 10^{-3}$  M with a slope of  $60.2 \pm 0.3$  mV decade<sup>-1</sup> and LOD of 7.5  $\times$  10<sup>-9</sup> M. The selectivity of the designed sensor was assessed using the matched potential method, revealing no significant interference. Additionally, the response time of the electrode was determined to be 5 s, with a life span of 16 weeks. The potential response of the electrode remained consistent across a pH range of 3.0-12.0, and the sensor maintained its Nernstian behavior in solutions containing up to 20% nonaqueous content. Furthermore, the electrode was successfully applied to determine lithium carbonate in tablet, urine, and serum samples, yielding %recovery values ranging from 96.0 to 106.33 and %RSD of 1.99-4.45. These findings demonstrate the potential applicability of the fabricated electrode for accurate and reliable lithium determination in various sample matrices.

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