

THE DESIGN AND APPLICATION OF LITHIUM ION-SELECTIVE  
ELECTRODES FOR CLINICAL PURPOSES<sup>a)</sup>

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Ideally a lithium ion-selective electrode should detect 0.1mM lithium in the presence of about 150mM sodium as well as the usual blood components. About 40 cyclic and acyclic ionophores have been examined potentiometrically. PVC electrodes with three such ionophores have been evaluated for the analysis of real sera using a micro conduit flow injection technique. Each of the sensors suffered serious interferences from unidentified serum components.

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## 1. INTRODUCTION

Lithium is an effective therapeutic agent for the treatment of manic depression [1,2] wherein the level of blood lithium is maintained between about 0.5 and 1.0 mM. Adverse side effects appear around 2mM and higher levels are fatal [3]. Thus its facile assay in blood samples from patients prescribed with lithium salts is clinically desirable. For this purpose a viable lithium ion-selective electrode is considered to be an attractive, alternative approach to measurements by flame photometry.

Sodium is the main ionic interferent in such blood assays where its concentration is typically over 1400 times higher than the lowest lithium level and in the first instance the ion-selective device should be capable of measuring 0.1 mM lithium in about 150 mM sodium. Other parameters, particularly interference from organic serum components, constitute further problems. This review is largely concerned with the development of sensors based on such ionophores and the problems associated with their clinical application.

## 2. TYPES OF LITHIUM ION-SELECTIVE ELECTRODES

To date, lithium ion-selective electrodes have been designed with sensor membranes comprising diverse materials such as glass [4], lithium stearate [5] and lithium vanadium bronzes [6], but their performances have been generally poor, eg,  $k_{Li,Na}^{pot} \sim 0.3$  for the LAS 15-25B glass electrode.

More encouraging results have been reported for lithium ion-selective electrodes with sensor membranes consisting of neutral carrier molecules, admixed with compatible solvent mediators in poly(vinyl chloride) matrices (Tables 1-3). Two broad classes of neutral carrier ionophores are recognised, namely, cyclic [7-16] and acyclic [7,8,17-27].

### 2.1 Crown ethers (cyclic polyethers)

Crown ethers were first reported by Pedersen [28] to form complexes with lithium and other alkali metal ions. The factors influencing their formation and stability as outlined by Pedersen are:

- (a) the relative sizes of the metal ion and the cavity of the polyether ring
- (b) the number of oxygen atoms in the polyether ring
- (c) the coplanarity of the oxygen atoms
- (d) the symmetrical placement of the oxygen atoms
- (e) the basicity of the oxygen atoms
- (f) steric hindrance in the polyether ring
- (g) the tendency of the metal ion to associate with the solvent and
- (h) the electrical charge on the ion and the types of binding sites in the ring.

Table 1. Selected properties of lithium ises based on crown compounds



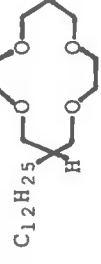
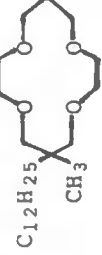


Sensor/ Membrane Number	Composition of PVC Electrode Membrane/mass %.		Selectivity Coefficient / $k_{Li,B}^{pot}$	
	Solvent mediator	PVC		Sensor
 Membrane I (Ref. 9)	TINTM (69)	30.5	0.5	Na 0.12 K 0.66 NH <sub>4</sub> 0.09 Ca 3.1x10 <sup>-4</sup> Mg 1.6x10 <sup>-4</sup>
 C <sub>12</sub> H <sub>25</sub> CH <sub>3</sub> Membrane II (Ref. 10)	o-NPOE (70.2)	28.1	1.0 +0.7% KTPClPB	9.8
 C <sub>12</sub> H <sub>25</sub> H Membrane III (Refs. 10, 12)	o-NPOE (70.2)	28.1	1.0 +0.7% KTPClPB	0.016

Table 1 (cont.)

 C <sub>12</sub> H <sub>25</sub> CH <sub>3</sub> Membrane IV (Refs. 10-12)	o-NPOE (70.2)	28.1	1.0 +0.7% KTPClPB	6.6x10 <sup>-3</sup> 7.0x10 <sup>-3</sup> (2x10 <sup>-3</sup> ) <sup>a</sup>
 C <sub>12</sub> H <sub>25</sub> H CH <sub>3</sub> CH <sub>3</sub> Membrane V (Ref. 10)	o-NPOE (70.2)	28.1	1.0 +0.7% KTPClPB	6.2x10 <sup>-3</sup>
 C <sub>12</sub> H <sub>25</sub> CH <sub>3</sub> CH <sub>3</sub> Membrane VI (Ref. 10)	o-NPOE (70.2)	28.1	1.0 +0.7% KTPClPB +1%TOPO	7.2x10 <sup>-3</sup>

<sup>a</sup> PVC membranes also contain trioctylphosphine oxide (18m/m)  
TINTM: triisonyltrimelitate  
KTPClB: potassium tetrakis(p-chlorophenyl)borate  
o-NPOE: o-nitrophenyl octyl ether

Table 2. Selected properties of lithium ises based on acyclic compounds

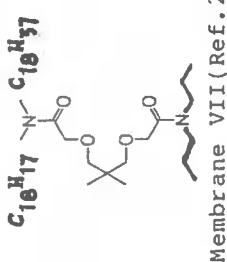
Sensor/ Membrane Number	Composition of PVC Electrode Membrane/mass %		Selectivity Coefficient /k <sub>Li,B</sub> <sup>pot</sup>	
	Solvent mediator	PVC		Sensor
$C_{16}H_{17}$  $C_{16}H_{17}^+$ Membrane VII (Ref. 21)	o-NPOE (65-66)	33	1-2	Na 0.07
	TEHP (62.8)	31.4	5.8	Na 0.05 K $7.9 \times 10^{-3}$ $NH_4$ 0.05 Ca $5 \times 10^{-4}$ Mg $1.99 \times 10^{-4}$
Membrane VIII (Refs. 19, 21, 26)	o-NPOE (65-66)	33	1-2	Na 0.08

Table 2 (cont.)

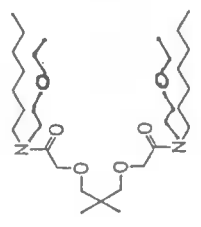
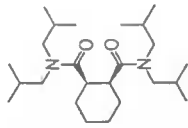
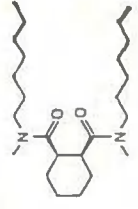
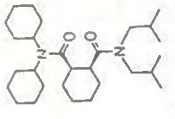
 Membrane IX (Refs. 24, 27)	TEHP (66.7)	29.4	3.9	Na 0.051 K $5.3 \times 10^{-3}$ Ca $3.6 \times 10^{-3}$ Mg $4.0 \times 10^{-4}$	0.063 0.104 $7.1 \times 10^{-3}$ $2.5 \times 10^{-4}$	0.047 ± 0.005 (n=3)
	DOA (63.8)	28.2	8.0	Na 0.065 K 0.07 Ca $9.2 \times 10^{-3}$ Mg $2.1 \times 10^{-3}$	Na 0.085	
 Membrane X (Refs. 21, 26)	TINTM (55.9)	24.7	19.4	Na $7.9 \times 10^{-3}$ K $6.3 \times 10^{-3}$ $NH_4$ $7.9 \times 10^{-3}$ Ca $10^{-3}$ Mg $6.3 \times 10^{-3}$	Na 0.085	
	oNPOE (65-66)	33	1-2			
TEHP (64.6)	28.5	6.9			0.15	0.082

Table 2 (cont.)

Sensor/ Membrane Number	Composition of PVC Electrode Membrane/mass %		Selectivity Coefficient /k <sup>pot</sup> <sub>Li,B</sub>
	Solvent mediator	PVC	
 Membrane XI (Refs. 21,22)	o-NPOE (65-66)	33	0.4
	o-NPOE (65.6)	32.8	5x10 <sup>-3</sup> 3.16x10 <sup>-3</sup> 3.55x10 <sup>-3</sup>
 Membrane XII (Refs. 22,25)	BBPA (65.6)	32.8	3.4x10 <sup>-2</sup>
	BBPA (65.6)	32.8	

TEHP: tris(2-ethylhexyl)phosphate; o-NPOE: o-nitrophenyloctylether; DOA: dioctylazelaate  
 BBPA: bis(1-butylpentyl)adipate; TINTM: triisononyltrimellitate

Table 3. Selectivity coefficients of three different PVC ion-selective electrodes (Ref.7)

Sensor material /Ise Type	Composition of PVC electrode/ % mass		Selectivity coefficient /k <sup>pot</sup> <sub>Li,Na</sub>
	Solvent mediator	PVC	
Ba(PPG1025) <sub>0.69</sub> •(TPB) <sub>2</sub> (Type 1)	DOPP (63)	30	4.4x10 <sup>-2</sup>
	7		1.7x10 <sup>-2</sup>
Dodecylmethyl-14-crown-4 (6-dodecyl-6-methyl-1,4,8,11-tetraoxacyclotetradecane) IV (Type 2)	o-NPOE (69.5)	28	9.4x10 <sup>-3</sup>
	+0.5%KTPClPB +1%TOPO <sub>2</sub>		6.6x10 <sup>-3</sup> 3.2x10 <sup>-2</sup>
N,N,N',N'-tetraiso-butyl- cyclohexane-cis-1,2- dicarboxylic diamine X (Type 3)	o-NPOE (65-66)	33	2.0x10 <sup>-3</sup> (Ref.11)
	+30mol% KTPClPB		1.0x10 <sup>-2</sup> (Ref.21)

<sup>a</sup> Trioctylphosphine oxide

Research on their development for lithium ISEs has centred on 12-crown-4 through 16-crown-4 type molecules [7-16, Table 1]. Crown ethers suitable for lithium should have a cavity size comparable with the lithium ion diameter (0.68Å). Crown ethers with such specifications range from 12-crown-4 to 14-crown-4, whereas the 15-crown-4 and 16-crown-4 ethers with larger cavity diameters are more selective for larger cations.

Complexation between lithium and crown ethers, L, may be simply represented by:



The reversibility and extent of this exchange process is important in the design of crown ether sensors for lithium. The 12-crown-4 ether(I) with its "ideal" cavity size for lithium has been investigated as such a sensor. The electrode exhibited Nernstian response at low lithium levels ( $10^{-5}$ - $10^{-4}$ M) and its pH range was 4.0 to 5.5 but the selectivity was poor, particularly with respect to sodium [9]. This response to sodium is possibly due to sandwich compound formation between two 12-crown-4 ether ligands and one sodium ion.

In an attempt to further establish the relation between cavity size of crown-4 derivatives and lithium selectivity, Kitazawa et al have examined the potentiometric behaviour

of a series of fourteen highly lipophilic crown-4 compounds with 12-, 13-, 14-, 15- and 16-member rings respectively [10] and the fixed compositions of each of the PVC sensor membranes (II-VI) make for a facile comparison of their respective potentiometric behaviour (Table 1).

In general, the 13-membered ring compounds, eg II, are much less selective for lithium than the 14-, and 15- membered compounds studied. Benzo-13-crown-4 derivatives also showed poor lithium selectivities and it was concluded that all of the 12-crown-4, 13-crown-4 and benzo-13-crown-4 compounds preferred the other alkali metal ions to lithium.

However, the lithium selectivity was dramatically enhanced in the case of the larger 14- and 15- crown-4 derivatives but this desirable feature again reversed in the largest ring compounds examined, namely, 16-crown-4 derivatives. This characteristic was also reported independently by Aalmo and Krane for 16-crown-4 and its hexamethyl derivative when used in conjunction with tris-(2-ethylhexyl)phosphate mediator [15].

The effect of the methyl substituent attached to the quaternary carbon of the crown-4 derivatives on the lithium selectivity is particularly interesting [9-13]. Thus the dodecyl methyl derivatives of both 14- and 15-membered ring molecules are superior to the corresponding dodecyl derivatives in terms of lithium selectivity relative to sodium and also potassium. This was attributed to some steric influence of

the methyl group on the crown ring regarding complexation of cations and the possible formation of sandwich-type 2:1 complexes of the crown ethers and the cations. This is supported by the dependence of the selectivity coefficients on the concentration of the crown ethers III and IV in the PVC membrane. Thus in the dodecyl methyl-14-crown-4 membrane system IV, the selectivity coefficients for sodium and potassium were essentially unchanged on increasing the sensor levels. On the other hand, the selectivity coefficients for these cations increased with increasing amounts of the sensor in the dodecyl-14-crown-4 system(III). It was concluded that dodecyl-14-crown-4 can complex  $\text{Na}^+$  and  $\text{K}^+$  on a 2:1 and 1:1 stoichiometric basis whereas the methyl derivative has difficulty in forming sandwich complexes even at high crown ether levels. Thus it is concluded that the methyl group in sensor IV functions as a steric barrier and so offsets the access of two crown ether molecules to sandwich formation and so enhances lithium selectivity, i.e., the prevention of 2:1 crown ether-metal complexes with alkali metal cations, other than lithium, enhances the lithium selectivity of the original crown ether. In similar fashion, incorporation of two methyl groups into the opposite side of the crown ether rings of V and VI also improved the lithium selectivity (Table 1). Thus sensors based on the three 14-crown-4 derivatives IV to VI portray sodium selectivities on a par with acyclic neutral carriers (Table 2). PVC membrane electrodes comprising dibenzo-14-crown-4 sensor with either o-nitrophenyl phenyl ether or

dioctylsebacate mediators showed quite poor lithium response in the presence of sodium [14]. This feature was only marginally improved by incorporating potassium tetrakis (p-chlorophenyl) borate in the PVC membranes.

To date, the best lithium ion-selective electrode is realised with the 14-crown-4-derivative IV on the basis of its low sodium response,  $k_{\text{Li,Na}}^{\text{pot}} = 2 \times 10^{-3}$  [11]. The quest for even better cyclic lithium sensors continues and one interesting study has been conducted with a PVC membrane incorporating octaphenylcyclotrasiloxan as sensor coupled with tris-(2-ethylhexyl)phosphate solvent mediator. Unfortunately, the sodium selectivity was rather poor,  $k_{\text{Li,Na}}^{\text{pot}} \sim 0.1$  [29]. An immense variety of sensor-mediator systems remains to be evaluated, some typical examples of prospective sensors being aza-12-crown-4 [30] and various cryptands [31].

## 2.2 Lipophilic diamides

Acyclic quadridentate amido-ethers preferentially complex lithium [17] when their molecular structures are such that four oxygen atoms tend to form a cavity comparable in size with the rings of some crown ethers. A range of such acyclic compounds VII-XII (Table 2) has been synthesised and

evaluated as prospective lithium sensors in conjunction with different solvent mediators [7,8,17-27]. Three of them, namely, VIII, X, and XXII are commercially available with appropriate contents of solvent mediator and PVC as ready to use lithium sensor cocktails.

The lipophilic diamide, N-N'-diheptyl-N,N'-5,5-tetramethyl-3,7-dioxanonane diamide (VIII) was evaluated as a sensor with TEHP [19,21] in a PVC mode but the selectivity for sodium is poor (Table 2). Nonetheless, this lithium sensor has been employed to measure lithium in snail neurones [20], the intra- and extracellular cortex [20, 32] and the central nervous system [33]. Its lifetime is substantial and no change of characteristic whatsoever has been detected in such membranes despite 8 months of permanent contact with water and intermittent use in different analytical problems [19].

Subsequent research with acyclic diamide materials has produced a spectrum of selectivity coefficients,  $k_{Li,Na}^{pot}$ , from poor, 0.4 to at best  $3.16 \times 10^{-3}$  and the subtle influence of the structures of just side chains on sodium selectivity is exemplified by ligands X and XI using the same o-NPOE solvent mediator [22].

To date, the best acyclic sensor is based on XII with 30% KTpClPB relative to sensor, but it must be emphasised that its most useful selectivity performance could hardly be predicted ( $k_{Li,Na}^{pot} = 3.16 \times 10^{-3}$ ). A very fair comparison between the performances of PVC ISEs with sensors VIII and IX is possible since the mediators are common and the concentrations of the three components are similar and their sodium selectivities are essentially identical. The slight changes in selectivity coefficients  $k_{Li,Na}^{pot}$  of 0.063-0.085 for sensor IX with three different solvent mediators must be considered in the context of the considerable spread of sensor levels in the PVC membrane namely from 3.9-19.4 mass% (Table 2).

### 2.3 Polypropoxylate adducts

Poly(alkylenoxy) compounds also provide a flexible array of donor oxygen atoms based on  $-CH(R)-CH_2O-$  units and may also be regarded as acyclic ethers. A tetraphenyl borate (TPB) - barium complex of PPG-1025, a poly(propyleneglycol), in conjunction with various mediators, eg, di-n-octylphenyl phosphonate (DOPP) constitutes the basis of a very useful barium ISE [34]. For one of them  $k_{Ba,Li}^{pot}$  was 3400 while in other cases, even at 5mM lithium levels, the ISEs were completely insensitive to barium. This interesting feature initiated a study of the clinical utility of microelectrodes based on poly(propyleneglycol) adducts of barium and lithium in a microconduit flow injection analysis (FIA) system [7,8].



The response of this PVC Ba (PPG-1025)<sub>0.69</sub>·(TPB)<sub>2</sub>-DOPP electrode was studied using 0.14M sodium chloride as carrier in the FIA mode when lithium could be identified down to 0.1mM, the linear range being 56mV decade<sup>-1</sup>.

Lipophilic salts, such as potassium tetrakis(p-chlorophenyl)borate (KTPClPB) incorporated into PVC sensor membranes are reported to reduce electrical membrane resistances and interferences by lipophilic anions [35]. Results for such KTPClPB-Ba (PPG-1025) electrodes were disappointing in that the selectivity was either essentially unaltered or considerably impaired. Even the best of these polyalkoxylate sensors is inferior to electrodes based on sensors IV, X and XII (Table 3) but they are extremely easy to prepare and together with alternative mediators may yet provide enhanced lithium selectivity.

### 3. PROBLEMS IN THE APPLICATION OF ISES TO SERUM LITHIUM ANALYSIS

The selectivity required of a lithium ion-selective electrode for just 1% interference by sodium in blood is easily calculated at to be  $<10^{-4}$  [22]. Only a few of the many neutral carrier ionophores studied, eg, IV and XII, can be considered as approaching this goal. Moreover, the contribution of the other common cations, K<sup>+</sup>, Ca<sup>2+</sup> and Mg<sup>2+</sup>, to the "total selectivity coefficient" cannot be overlooked.

Lithium ISE electrodes have been used in intracellular and cortex studies [20,32,33]. Otherwise their use has been restricted for example, to measurements in artificial sera based on LiCl/NaCl/KCl/CaCl<sub>2</sub>/MgCl<sub>2</sub>/urea/glucose [11]; this is somewhat unrealistic since proteins and virtually all the known organic materials present in blood were excluded.

Xie et al employed an electrode based on crown ether IV to measure lithium in thirteen sera samples of manic patients with an FIA system; agreement with atomic absorption results averaged  $\pm 5\%$  for the range 0.67 - 1.46 mM lithium [16]. A PVC electrode incorporating diamide XII with o-NPOE/KpClTPB has also been used in a static system for measuring lithium in spiked sera at levels between 0.79 and 1.83 mM [25, Table 4].

A more detailed investigation has dealt with the prospects of three different types of lithium ISEs presented in Table 3 regarding the behaviour in neat and ionic mixtures of LiCl/NaCl/KCl/MgCl<sub>2</sub>/CaCl<sub>2</sub>; proteins, fats as well as real lithium loaded blood sera [8]. Each ISE was calibrated with 0.1mM - 0.1M lithium chloride standards in the artificial serum A whose composition is listed in Fig.1.

#### 3.1 Serum analysis procedure

Serum samples (Nos 1-10) were first analysed for the common cations listed in Table 5 at the University Hospital of Wales and then injected into the carrier stream of artificial serum A and the emf recorded (Fig. 2).

Table 4. Assay of lithium in normal sera (Ref. 25)

[Lithium] added to normal sera <sup>a</sup> /mM	[Lithium] found with two sensors (sd) /mM	Relative accuracy/%
0.77	0.79(0.00)	+3
0.99	0.96(0.02)	-3
1.32	1.31(0.04)	-1
1.48	1.37(0.02)	-7
1.96	1.83(0.02)	-7

<sup>a</sup> [Li] < 10<sup>-5</sup> M by flame photometry

Table 5. Cation concentration in real serum samples previously analysed at the University Hospital of Wales (Ref.8)

Serum Sample number	Cation/mM			
	Li	Na	K	Ca
1	0.21	105.3	1.77	1.62
2	0.40	110.7	2.36	1.78
3	0.61	116.1	2.95	1.97
4	0.79	122.0	3.57	2.16
5	1.00	126.9	4.17	2.35
6	1.20	132.3	4.78	2.53
7	1.40	137.7	5.38	2.72
8	1.58	143.5	6.03	2.90
9	1.75	148.7	6.60	3.09
10	2.00	153.9	7.18	3.27
Analysis Technique	Flame Photometry	Ion-Selective Electrode	Ion-Selective Electrode	Spectrophotometry

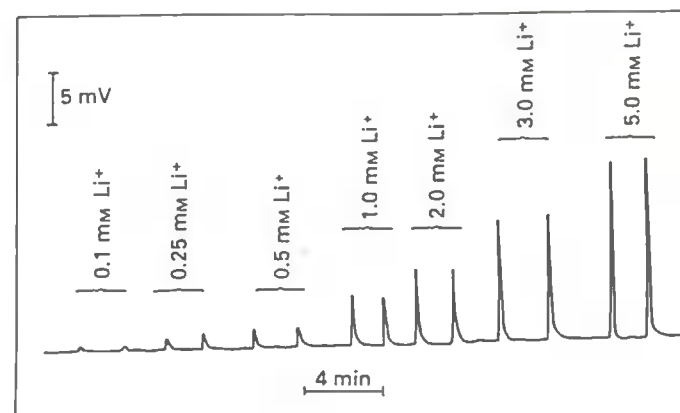


Fig. 1 FIA profiles of Type 1 electrode for lithium standards in artificial serum electrolyte A  
Carrier A: NaCl (140mM); KCl (2.8mM); KH<sub>2</sub>PO<sub>4</sub> (1.3mM); CaCl<sub>2</sub> (2.5mM); MgSO<sub>4</sub> (2.3mM); pH (7.1)

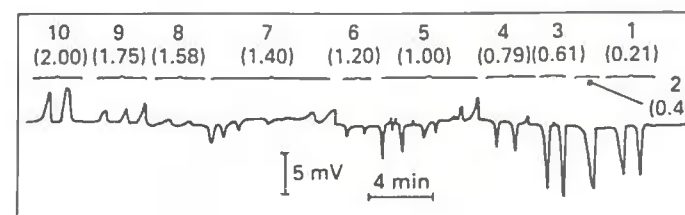


Fig. 2 FIA profiles of Type 1 electrode for 10 lithium serum samples (Carrier A). Lithium levels determined by flame photometry are parenthesised

Despite its relatively poor sodium selectivity the Type 1 electrode responds quite reproducibly, even at 0.1mM lithium, in an artificial serum A (Fig. 1). Results for the 10 real serum samples were unexpected in that either positive or negative FIA profiles were obtained for some samples while Nos. 4,5 and 7 gave both positive and negative peaks (Fig. 2).

These patterns could relate to parameters like pH, anions, proteins, lipoproteins, nature of sensor and/or the varying electrolyte concentrations seen in Table 5. However, the negative peaks are unlikely to relate to chloride or phosphate since similar levels of both anions were present in the artificial carrier A. Again the Type 1 PVC electrode suffers little hydrogen ion interference [7] and in any case the pH values of the carrier and sera are ~7.1. Further investigations were thus undertaken regarding some common natural products, type of sensor and variation of electrolyte.

### 3.2 Effect of natural products on the electrodes

The electrode response was unaffected by  $\alpha$ -globulin,  $\beta$ -globulin,  $\gamma$ -globulin, bovine albumin or glucose both individually or collectively. The same applied to cholesterol (free and total), triglyceride, phospholipids and  $\beta$ -lipoproteins both singly and in admixture, again in artificial serum A.

For clinical purposes protein exclusion membranes are usually attached to sensor surfaces to offset large molecule effects. The effect of dialysis polycarbonate and cellulose acetate membranes respectively on the response of Type 1 electrodes was thus examined. This resulted in 50%, 0% and 26% of the normal FIA response shown in Fig. 1 when injecting 0.1M lithium chloride in artificial serum A.

The behaviour of the polycarbonate covered lithium ISE - no reduction in the expected signal of the artificial lithium serum - appears ideal but unfortunately when employed with real sera peaks were irreproducible and often showed negative profiles. Thus the polycarbonate membrane was either inefficient in excluding large molecules from the sensor surface or the effects relate to one, or more, unidentified low molecular mass organic components of the serum. This anomalous behaviour was only temporary and the FIA base line was rapidly restored after passage of sample plugs and the PVC ISEs established their usual Nernstian responses in lithium/serum A standards (re Fig. 1).

### 3.3 Nature of sensor

The responses of Types 2 and 3 electrodes to artificial and real serum lithium samples resembled those for Type 1 electrode (Figs. 1 and 2). Therefore, these irregular FIA patterns seem to relate to components in serum rather than to the sensors.

### 3.4 Effect of varying electrolyte levels in serum samples

The sodium content of the real serum samples varied from 105.3 -153.9mM (Table 5); the typical literature average content being 140mM and the carrier artificial serum electrolyte A was accordingly set at 140mM (re Fig. 1). Serum samples containing lower and higher amounts of sodium than the carrier serum A generally gave negative and positive FIA peaks (Fig.2).

This aspect was further investigated by injecting mock serum samples (but free of all organic compounds) containing just lithium, sodium, potassium and calcium, in amounts equivalent to those in the real serum samples Nos 2, 6 and 10 (Table 5) into the carrier electrolyte stream A. As suspected, the low sodium systems, eg, Nos. 2 and 6, gave negative FIA peaks supporting the idea that the variable sodium in the serum samples is partly the cause of the strange response of Type 2 electrode as well as Types 1 and 2. It should be emphasised, however, that the responses obtained using the three mock serum samples are reproducible in extent and direction unlike the variable cases when running real serum samples (Fig. 2). Evidently parameters other than the sodium effect must be responsible for these FIA signals portrayed in Fig. 2.

### 3.5. Serum electrolyte correction

To attempt a correction for the variation in sodium content on the lithium responses (re Fig. 2) the real serum samples (1cm<sup>3</sup>) were spiked with appropriate volumes of sodium chloride (1M) to bring the concentration of sodium in every serum (except of course No. 10) to the same level as that set for the modified carrier electrolyte B, namely, 153.9mM. Carrier B, which functioned as an alternative carrier for the pretreated real sera, differed from carrier A only in its higher sodium content. These sodium elevated sera were then injected into the non-protein based artificial carrier serum electrolyte B. Results with each type of lithium electrode were improved compared with the previous analysis, but statistically were unsatisfactory.

Only 3 results out of 10 samples attempted with Type 3 electrode (Fig. 3) show any agreement with the actual flame photometry values (Table 5), while no response was obtained for samples 2, 3 and 4. Sample No. 10 containing 2mM lithium is to be compared with 2.3mM (sd = 0.49mM, n=4).

For the Type 1 electrode, 6 results out of 10 samples examined show a relatively close agreement (Fig. 3) but no response was obtained for samples 1,2 and 3. Only 5 serum samples were run with Type 2 electrode due to lack of samples but only one result showed some agreement.

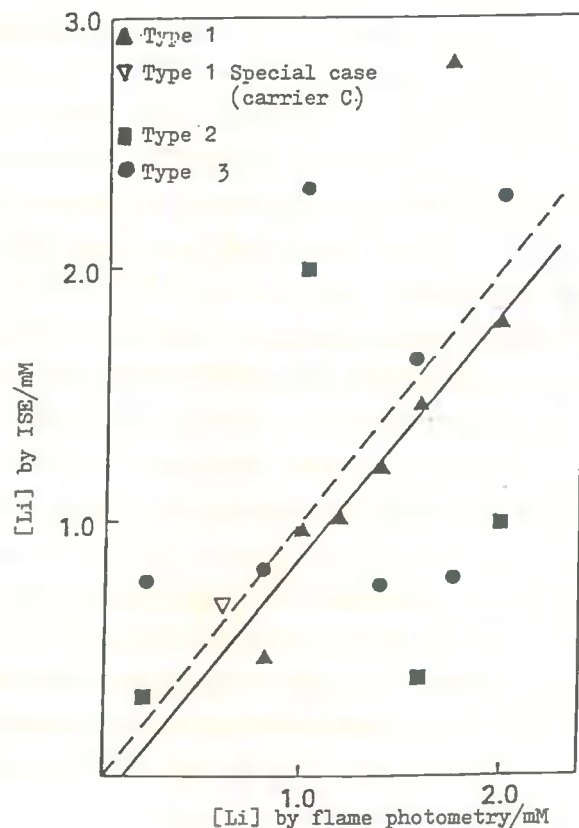


Fig. 3 Analysis of real serum samples by types 1, 2 and 3 electrodes and flame photometry

From Fig. 3, it appears that Types 2 and 3 electrodes are more affected by serum components than Type 1 electrodes despite their better selectivity coefficients. This modified procedure is based on a prior knowledge of sodium serum levels in order to increase the sodium to that of the carrier B before injection and not on a correction via selectivity coefficients. Nevertheless the quality of the data even for Type 1 electrode is still poor, mainly because of the low lithium content of certain samples and the fixed, rather high sodium level in carrier B.

The analysis procedure was accordingly further modified for just sample No. 3 using a Type 1 electrode and another artificial protein free carrier, C, containing the same quantities of sodium, potassium and calcium as the chosen sample (Table 5). Thus the lithium standards were prepared in an all-ionic medium of sodium chloride (116.1 mM), potassium chloride (2.95mM), calcium chloride (1.97mM) and magnesium chloride (1.01mM). This tedious procedure gave 0.68mM lithium compared with 0.61mM by flame photometry (Fig. 3).

#### 4. CONCLUSION

Low levels of lithium can be measured using ion-selective electrodes with different artificial carrier solutions for each sample. Such a procedure is, however, too laborious and clinically impracticable. Xie et al have stated that it will be necessary to measure the sodium and make a suitable correction [16]. Potentiometric analysis for serum lithium



requires further research to developing a lithium ion-selective electrode with  $k_{Li,Na}^{pot} < 10^{-4}$  so as to offset the need for sample pretreatment with sodium. Nevertheless, recent work indicates a second requirement of such lithium sensors, namely, minimal interference from other, as yet, unidentified serum components [8].

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## CONSTRUÇÃO E AVALIAÇÃO DE UM ELÉCTRODO SELECTIVO PARA ANIÃO BROMETO COM SENSOR DE $Hg_2Br_2/HgS$ APLICADO SOBRE RESINA CONDUTORA

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**RESUMO:** Descreve-se a construção de um eléctrodo selectivo para anião brometo com sensor formado por uma mistura de brometo de dimercúrio(I) e sulfureto de mercúrio (II) (2:1 em massa) aplicada sobre um suporte de resina epoxi condutora e os resultados da avaliação das suas características de funcionamento em resposta ao anião brometo e ao catião dimercúrio(I). Em resposta a brometo, o eléctrodo comporta-se como um eléctrodo de segunda espécie. O eléctrodo tem qualidade superior ao eléctrodo marca Graphic Controls, ref. PHI 91300, que usa o mesmo tipo de sensor.

**ABSTRACT:** BROMIDE ELECTRODE BASED ON  $Hg_2Br_2/HgS$  MIXTURE APPLIED TO ELECTRICALLY CONDUCTIVE EPOXY. A bromide selective electrode based on mercury salts applied to a support of electrically conductive epoxy has been prepared and tested. A 2:1 (by weight) mixture of mercurous bromide and mercuric sulphide was used as sensor. Response characteristics to bromide and mercurous ion were determined by standard procedures, showing that the electrode responds to bromide as a second kind electrode. The electrode shows a better performance than the PHI 91300 Graphic Controls commercial electrode, which uses the same type of sensor.

## INTRODUÇÃO

No âmbito de um projecto cujo objectivo é o desenvolvimento de processos de construção de eléctrodos selectivos de iões que sejam fáceis de concretizar e possam ser utilizados em laboratórios não especialmente vocacionados ou apetrechados para a montagem de eléctrodos, desenvolveu-se, neste Departamento, um processo de construção de eléctrodos de membrana cristalina que consiste em aplicar o sensor sobre um suporte de resina condutora. Este processo foi utilizado, com êxito, na obtenção de eléctrodos com sensores baseados em misturas de sulfureto de prata(I) com outros sais de catião prata(I) ou com sulfuretos de catiões bivalentes [1-6]. Posteriormente, o processo foi aplicado à construção de eléctrodos selectivos de membrana cristalina com sensores constituídos por misturas de sulfureto de mercúrio(II) com sais de catião dimercúrio(I), introduzidos por SEKERKA E LECHNER [7-9],