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A simple membrane with the electroactive [Sulfapyridine-H]$^{+}$[Co($C_2B_9H_{11}$)$_2$]$^{-}$ for the easy potentiometric detection of sulfonamides

Abhishek Saini [a, b], Isabel Fuentes [a], Clara Viñas [a], Nadia Zine [b], Joan Bausells [c], Abdelhamid Errachid [b, **], Francesc Teixidor [a, *]

[a] Institut de Ciència de Materials de Barcelona (CSIC), Campus de la U.A.B, 08193, Bellaterra, Spain
[b] Université de Lyon, Institut des Sciences Analytiques, UMR 5280, CNRS, Université de Lyon 1, ENS Lyon-5, 5 Rue de La Doua, F-69100, Villeurbanne, France
[c] Barcelona Microelectronics Institute IMB-CNM (CSIC), Bellaterra, Spain

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ABSTRACT

The detection of a drug belonging to the Sulfonamide class of compounds, namely Sulfapyridine, is reported in this work using an in-*situ and* fast potentiometric method. The strategy employed for this detection is based on the novel ion pair complex, [Sulfapyridine-H]$^{+}$[Co($C_2B_9H_{11}$)$_2$]$^{-}$ acting as the active site for highly selective recognition of Sulfapyridine. This enables the sensor's selectivity to be improved by incorporating the target molecule to the selective membrane. In this work, all solid state Sulfapyridine selective microelectrodes based on PVC-type membranes were prepared using three different plasticizers and the aforementioned ion pair complex. The sensors developed have provided quick and accurate response within the range of 10^{-6} mol/dm^3 to 10^{-3} mol/dm^3 of Sulfapyridine concentration and showed a Nernstian slope between 47 and 61 depending upon the type of plasticizer used. The lowest limit of detection achieved was 4 μmol/dm^3. The potentiometric coefficient of selectivity, $K_{A,Bpot}$, has shown that the Sulfapyridine-selective microsensors were highly selective towards Sulfapyridine even when compared to other members of the Sulfonamides class of compounds. In addition, from the Reilley diagram it can be observed that the sensor signal is stable for a working pH interval between 6.00 and 8.00.

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1. Introduction

Sulfonamides are a class of antibacterial agents that have found widespread use in livestock for prevention of infections and treatment of diseases [1,2]. The residues of these sulfonamides are known to find their way into the food chain through residues of meat and milk products and are dangerous as they have been found to be responsible for causing of cancer [3,4].

Various methods have been employed for the detection of Sulfonamides like Thin layer chromatography, Gas Chromatography coupled to Electron Ionization Mass Spectroscopy, Gas Chromatography with Atomic Emission Detection, Capillary zone electrophoresis coupled with nano-electrospray Mass Spectroscopy, Liquid Chromatography interfaced with fluorescence detection [3–11]. But all these techniques have been found to have their respective drawbacks as well, such as, being prone to interferences and inadequate for quantitative analysis in the case of Thin Layer Chromatography, requiring complex preconditioning techniques in case of Gas Chromatography coupled to Electron Ionization Mass Spectroscopy, and Capillary Zone Electrophoresis require a pre detection clean up procedure. In the case of Liquid Chromatography interfaced with fluorescence detection, detection is non-specific and resolution is poor.

In the past decade some electrochemical methods have also been reported for the detection of Sulfonamides [12–14]. These methods have been known to show fast detections, low detection limit, high accuracy and being cost effective [15,16]. Sulfapyridine is an antibacterial agent belonging to the Sulfonamide class of medications and recently a Differential Pulse Voltammetry method was

* Corresponding author.
** Corresponding author.
E-mail addresses: asaini@icmab.es (A. Saini), ifuentes@icmab.es (I. Fuentes), clara@icmab.es (C. Viñas), nadia.zine@univ-lyon1.fr (N. Zine), joan.bausells@imb-cnm.csic.es (J. Bausells), abdelhamid.errachid@isa-lyon.fr (A. Errachid), teixidor@icmab.es (F. Teixidor).

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reported for the detection of Sulfapyridine in human plasma [17]. But there is a need for a simpler and cheaper method for the detection of these Sulfonamides like Sulfapyridine especially in sea water where they find their way through the food chain. In this work we propose an Ion Selective micro Electrode (μISE) for the detection of Sulfapyridine in water which is simple to generate, has the advantage of being able to withstand repeated usage without degradation in quality and does not entail any complex chromatography or extraction procedures. This technique also does away with the usage of any antibodies or expensive equipment.

Polymeric membrane (especially Polyvinyl Chloride (PVC) based μISEs have seen a massive growth in the last few decades mainly due to their simple and low cost nature as instruments for electroanalytical detection [18–20]. μISEs based on polymeric membranes containing neutral or charged carriers (ionophores) are widely used in the detection of many Organic and Inorganic ions [21,22]. They have also been used extensively in pharmaceutical analysis [23]. This has led to a big upgrade in the implementation of potentiometric analysis using μISEs with respect to their most important parameters, namely, limit of detection and selectivity [24,25].

The purpose of using the organometallic anion [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2]^-$ in PVC membrane based μISEs is due to its properties as an electroactive ion-generator of the interactions within the components of the membrane that leads to a stable entity. This has already been reported in our previous works [26–29]. These studies have shown that solid membrane based μISEs having ion-pair complexes such as [cation- NH]$^{n+}$ n [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2]^-$can be assimilated in PVC membranes and are suitable for detection of bioactive nitrogen containing compounds [cation-NH]$^{n+}$. Fig. 1 demonstrates the different compounds that have been detected using this ion-pair complex technique [26–30]. There are no examples of Sulfonamides in the aforementioned list of compounds. Since the Sulfonamide functional group is the basis of many types of drugs, here we report a long lasting Sulfonamide μISE based on the anion [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2]^-$ necessary for the stability of the components of the membrane and its counterion [Sulfapyridine-H]$^+$ that is the electroactive part. This ion pair complex can also be the model example for the determination of Sulfapyridine derivatives in drugs containing the sulfonamide functional group.

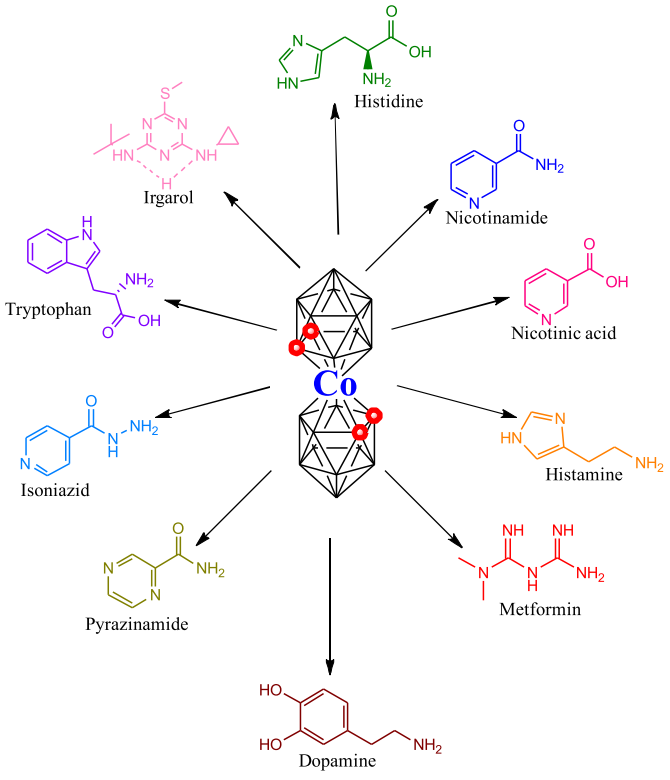

Fig. 1. Existing Ion Pair complexes using 3,3'-[Co(1,2-*closo*-$C_2B_9H_{11})_2$] anion: The reported ion pair complexes made using 3,3'-[Co(1,2-*closo*-$C_2B_9H_{11})_2]^-$ in conjunction with Histidine, Nicotinic Acid, Histamine, Metformin, Dopamine, Pyrazinamide, Isoniazid, Tryptophan and Irgarol.

2. Experimental

2.1. Chemicals

All reagents used in this study were analytical grade. Cesium Cobaltabis(dicarbollide) (Cs [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2$]) was purchased from Katchem. o-Nitrophenyl Octyl Ether (NPOE), Bis (2-ethyl hexyl) Sebacate (DOS) and Di-Octyl Phthalate (DOP) were purchased from Sigma Aldrich. High molecular weight Poly (vinyl chloride) was purchased from Fluka while Sulfapyridine, Pyrrole, Acetonitrile (ACN), Tetrahydrofuran (THF) and Hydrochloric Acid (HCl) were purchased from Sigma Aldrich. Solutions of lower concentrations were freshly prepared with deionized water by dilution steps.

2.2. Apparatus

Cyclic voltammetry (CV) and electropolymerization of Polypyrrole [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2$] were studied using a multichannel potentiostat (Biologic-EC-Lab VMP3) analyser. All electrochemical experiments were done by using a three-electrode electrochemical cell. It consists of a saturated calomel reference electrode, a platinum wire counter electrode and working microelectrode made of platinum substrate. IR spectra were obtained on PerkinElmer® Universal ATR Accessory spectrophotometer. The ^{1}H- and ^{1}H{^{11}B}-NMR (300.13 MHz), ^{13}C{^{1}H}-NMR (75.47 MHz) and ^{11}B- and ^{11}B{^{1}H}-NMR (96.29 MHz) spectra were recorded on a Bruker ARX 300 instrument equipped with the appropriate decoupling accessories. All NMR spectra were performed in acetone deuterated solvent at 22 °C. The ^{11}B- and ^{11}B{1H}-NMR shifts were referenced to external $BF_3 \cdot OEt_2$, while the ^{1}H, ^{1}H{^{11}B}, and ^{13}C{^{1}H}-NMR shifts were referenced to $SiMe_4$. Chemical shifts are reported in units of parts per million downfield from reference, and all coupling constants in Hz. The mass spectra were recorded in the negative ion mode using a Bruker Biflex MALDI-TOF-MS [N2 laser; λexc 337 nm (0.5 ns pulses); voltage ion source 20.00 kV (Uis1) and 17.50 kV (Uis2)].

2.3. Complex formation

The [Sulfapyridine-H]$^+$[Co($C_2B_9H_{11})_2]^-$, alternatively [$C_{11}H_{12}N_3O_2S$][3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2$] salt (Fig. 2), was synthesized in open vessels in aerobic conditions:

Cs [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2$] (300 mg, 0.657 mmol) was extracted with aqueous HCl 1 M (15 mL) and diethyl ether (20 mL). The organic layer was shaken three times with fresh HCl 1 M (15 mL 3x). Then, the diethyl ether was evaporated and the residue was diluted with water to generate 0.05 M solution of H [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2$ (solution 1). Sulfapyridine was dissolved in water by adding the minimal quantity of HCl 1 M to prepare 0.05 M acid solution (solution 2). Next, 15 mL of solution 1 and 15 mL of solution 2 were mixed and after stirring a yellow precipitate was obtained. This was filtered off, washed with HCl 0.1 M and dried in vacuum. The composition of [$C_{11}H_{12}N_3O_2S$][3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2$] salt

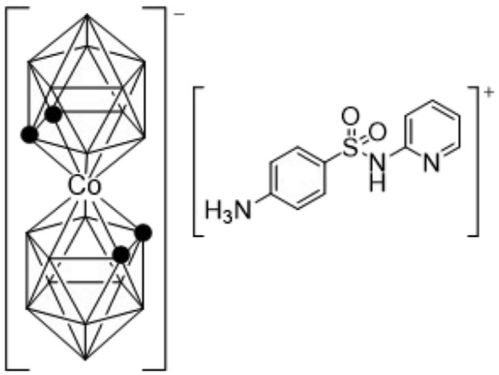

Fig. 2. Ion pair Complex: Chemical structure of the 3,3'-[Co(1,2-closo-$C_2B_9H_{11})_2]^-$[Sulfapyridine]$^+$ ion pair complex.

was analyzed by ^{1}H NMR integrating the C–Hs of metallacarborane resonances and comparing them with the aromatic ^{1}H- resonances due to Sulfapyridine. The integration provided 4:8, these for metallacarborane C–H (4) and aromatic Sulfapyridine protons (8) indicating a 1:1 salt.

2.4. Microelectrode preparation

The microelectrodes were fabricated using the process already well reported [31]. A P-type ⟨100⟩ silicon 100 mm diameter wafer with a nominal thickness of 525 μm was used, upon which an oxide layer 0.8 μm was deposited by thermal oxidation. The microelectrode also consists of double metal layer (50 nm Ti plus 150 nm Pt) which is deposited on top. Each μISE consists of 4 working microelctrodes. Polypyrrole [3,3′-Co(1,2- closo-$C_2B_9H_{11})_2$] is galvanostatically grown by electropolymerization on the platinum microelectrodes to enhance the conductivity of the microelectrode. This generates a solid internal contact layer on the microelectrode which is conductive. The solution for the electropolymerization was made of 0.035 M Cs [3,3′-Co(1,2- closo-$C_2B_9H_{11})_2$] and 0.1 M Pyrrole in acetonitrile with 1 wt% in water. After polymerization, the micro-electrodes were rinsed with water and dried under Nitrogen before electrochemical measurements [32].

To prepare the PVC membranes, we used the same composition that had shown remarkable success in our previous work [30]. The composition was 30 wt% of PVC, 63 wt% of Plasticizer (in this study 3 different plasticizers were used, NPOE (o-Nitrophenyl Octyl Ether), DOP (Di-Octyl Phthalate) and DOS (Bis (2-ethyl hexyl) Sebacate), and hence 3 different membranes were prepared each with a different plasticizer) and 7 wt% of [$C_{11}H_{12}N_3O_2S$][3,3′-Co(1,2-closo-$C_2B_9H_{11})_2$] ion pair complex in 1.5 mL THF. This membrane solution was deposited directly on top of the active area of the microelectrode. The solvent was allowed to evaporate overnight at room temperature.

2.5. Potentiometric measurements

A personal computer equipped with four microelectrodes simultaneously connected along with a data procurement system was used to carry out the measurements. A saturated calomel reference electrode having KCl as inner solution was used as the reference electrode. The measurements were carried out at room temperature under constant magnetic stirring.

Sulfapyridine solutions with a concentration range of 10^{-5} to 10^{-1} M were prepared to obtain the calibration curves. Successive aliquots of these solutions were added to 25 ml of distilled water for the potentiometric measurements. The measurements were made between the concentration range of 10^{-8} to 10^{-3} M, following the Generalized Standard Addition Method [33].

The Debye-Huckel equation is used in an aqueous solution for the measurement of the activity of an organic cation. This activity was reflected by the potential variations recorded whose value was plotted as a logarithmic function of Sulfapyridine activity. The Fixed Interference Method was used to determine the selectivity coefficient by testing the best performing μISE against interferences [34]. The pH working range was also measured by increasing the pH of a 10^{-3} M solution of Sulfapyridine with NaOH 1 M from 1 to 12.5 (pH-meter: Mettler Toledo FE20/EL20).

3. Results and discussion

3.1. Electrochemical polymerization of polypyrrole[3,3′-Co(1,2-$C_2B_9H_{11})_2$] as conductive-solid-contact layer

The formation of conducting polypyrrole may be intuitively made of two steps, first the oxidation of pyrrole leads to the formation of the PPy backbone, that upon further oxidation leads to the formation of positive charges in bipolar states and stabilization by resonance in the conjugated polymer chain. Due to this property, Polypyrrole is grown onto a platinum substrate doped with [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2]^-$ to improve the mechanical and electrical contact between the electrode surface and sensing polymer membrane [35]. The porous polypyrrole layer formed enables the polymeric membrane to establish full contact between the sensing membrane and the electrode contributing to the long shelf life of the sensors as it prevents the appearance of air and liquid bubbles between the flat transducer surface and the polymeric membrane, avoiding partial detachment. This leads to an enhancement in the electrical properties of the electrode [29]. The introduction of Cobaltabis (dicarbollide) is responsible for neutralizing of charges. There are various other reasons for using Cobaltabis (dicarbolide) for this purpose and they have already been reported [31]. It is well documented that the cyclic voltammograms of the platinum microelectrode in redox probe K_3 [$Fe(CN)_6$]/K_4 [$Fe(CN)_6$] 5 mM in phosphate buffer solution, before and after electrochemical polymerization of PPy [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2$] show a marked increase in current intensity due to the presence of a conducting polymer that enhances the electrical properties of the electrode [30]. The improved response to the test with K_3 [$Fe(CN)_6$]/K_4 [$Fe(CN)_6$] may also be influenced by an increased surface area as a consequence of the electropolymerization of the pyrrole.

3.2. Role of plasticizers

Plasticizers play a significant function in the performance of the polymeric membranes. The most important requirement that a plasticizer should fulfil is to be well matched with the other components in the polymeric membrane to provide stability. This is even more imperative when using $[Co(C_2B_9H_{11})_2]^-$ as the company ion of the electroactive cation, due to the strong non-bonding interaction between the $[Co(C_2B_9H_{11})_2]^-$ and the oxygen lone pairs of the plasticizer. Having high molecular weight and high lipophilicity are also necessary qualities for a plasticizer. Due to the aforementioned properties the nature of the plasticizer used heavily influences the dielectric constant of the membrane, the mobility of the ionophore molecules and state of the ligands. The choice of plasticizer is influenced by the use of the ISE. In polar solvents like water, deposits of charged species may cause potential drifts and hence non polar plasticizers like DOS and DOP are preferred. Expectedly, they showed better results when used in the polymeric membrane when compared to the highly polar NPOE [36,37]. In this study we used the composition: PVC – 30 wt %,

Plasticizer- 63 wt%, Ion Pair Complex – 7 wt% to make 3 different membranes based on the respective plasticizer used.

3.3. Response characterstics

The most important parameters for judging the performance of the μISEs prepared for detection of Sulfapyridine are summarized in Table 1.

All μISEs were calibrated following the GSAM and characteristic response curves are shown in Fig. 3.

The limit of detection is the most important parameter that characterizes the performance of an μISE. As can be seen from Table 1, the plasticizer used affects the performance parameters of the μISE. From Table 1 it is clear that the membrane with DOS showed the best response with a lowest detection limit of 1×10^{-6} mol/dm^3 and an almost Nernstian slope of 61.29 mV/decade. This slope indicates the presence of a single charged species which acts as the electro-active component of the electrode. This yields a calibration curve with an almost perfect Nernstian slope. Thus, the membrane with DOS was chosen for further interference and pH response studies.

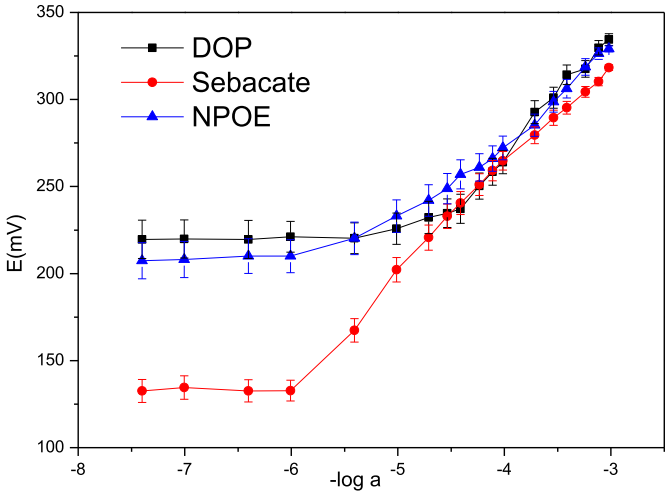

Fig. 3. ISE response: Potentiometric response of Sulfapyridine selective μISE with different plasticizers in the membrane.

3.4. Selectivity of μISE

Selectivity of an μISE is what determines its real life applicability as it indicates the ability of the μISE to detect the target molecule in the presence of interfering species. Due to the electronegativity difference between B and C relative to H, we can say the B–H and C–H bonds have inverted polarities. This causes the B–H bond to have tendency to generate hydrogen and dihydrogen bonding. On the other hand, the C–H bonds in the $[Co(C_2B_9H_{11})_2]^-$ are also more polarized than usual in organic compounds. This also facilitates hydrogen and dihydrogen bonding. This is what leads us to commonly say that $[Co(C_2B_9H_{11})_2]^-$ acts as a thistle, particularly with molecules having the opportunity to generate hydrogen bonding and their interaction with amines and protonated amines is very strong. This is, what makes to our point of view, quite remarkable that this anion provides stability to all participating agents in the membrane. In principle the anion $[Co(C_2B_9H_{11})_2]^-$ is not the sensing part, but the cation in this case the sulfapyridine-H^+ that leads to the selectivity.

In 1976, upon IUPAC's recommendation, the Nikolsky Eisenman equation has become the method determine the potentiometric selectivity coefficient, $K_{A,Bpot}$. [38,39] To determine this potentiometric selectivity coefficient, the Fixed Interference Method (FIM) was used which involves measurement of solutions of constant activity, in this case having concentration 10^{-3} mol/dm^3 of the interfering ion while varying the activity of Sulfapyridine from 10^{-8} to 10^{-3} mol/dm^3.

Compounds belonging to the Sulfonamide class of compounds which are structurally related to Sulfapyridine were chosen for study as interfering ions, namely, Sulfamethizole, Sulfamethoxazole, Sulfanilamide and Sulfisoxazole (Fig. 4). The electrochemical cell used was based on a reference and a working electrode immersed in 25 ml of 1 mM solution of an interference. The response of Sulfapyridine in the presence of interferences is compared to the response of μISE in water.

For the calculation of the $K_{A,Bpot}$, the EMF values obtained are plotted vs the logarithm of the activity of the analyte. The value of the $K_{A,Bpot}$ is extrapolated from the intersection points of the linear portions of the plot. This intersection point indicates the value of the analyte activity and using this value in the Nikolsky-Eisenman equation, we get the $K_{A,Bpot}$. The results obtained from the potentiometric selectivity coefficient measurements are presented in Table 2.

The log $K_{A,Bpot}$ values presented in Table 2 obtained by the FIM reinforce the fact that the μISE for sulfapyridine is not much affected by the presence of other Sulfonamides, despite the fact that these used as interferences have a highly similar molecular structure.

3.5. Lifetime of the μISE

The electroactive part of this sulfapyridine μISE is the [Sulfapyridine-H]$^+$[Co(C$_2$B$_9$H$_{11}$)$_2$]$^-$ ion pair, and the life time of the μISE depends on the ability of the membrane to retain the ion pair concentration constant within the membrane. So the interplay of the forces within the membrane and its lipophilicity determine the lifetime of the sensor. To succeed with this target is the reason behind the use of the cobaltabisdicarbollide [28]. The cobaltabisdicarbollide has two peculiarities: i) the ability to self-assemble through dihydrogen C–H···H–B and N–H···H–B bonds and ii) its amphiphilic character depending on the cation [40–44]. Further through hydrogen bonding C–H···O with the plasticizer the system

Table 1
Characteristic response of the μISE elaborated. Slope, correlation coefficient, concentration range, detection limit, time response and lifetime of different plasticizers for the detection of Sulfapyridine.

Plasticizer	Dioctyl Phthalate (DOP)	Bis(2-ethyl hexyl) Sebacate (DOS)	o-Nitro phenyl octyl ether (NPOE)
Slope (mV/Decade)	61.26	61.29	47.69
Correlation Coefficient	0.9690	0.9936	0.9787
Detection Limit (mol/dm^3)	1×10^{-5}	1×10^{-6}	4×10^{-6}
Time Response(s)	<10	<10	<10
Lifetime (day)	>45	>45	>45

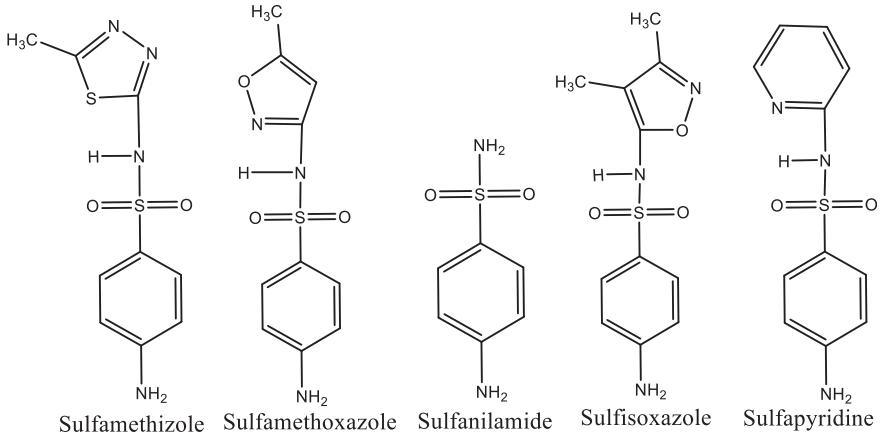

Fig. 4. Interfering Ions: Chemical structures of compounds belonging to Sulfonamide class of compounds which have been used as interferences to measure selectivity of the μISE.

Table 2
Selectivity of μISE against interfering species.

Name of Interference (10^{-3} mol/dm^3)	log $K_{A,Bpot}$
Sulfamethizole	−2.698
Sulfamethoxazole	−3.000
Sulfanilamide	−3.096
Sulfisoxazole	−2.397

metallacarborane plasticizer becomes very stable, with little chance to do leakage. This is highly uncommon with other organic and inorganic anions. In addition, and of great importance is the strong affinity of [3,3′-Co(1,2-*closo*-$C_2B_9H_{11})_2]^-$ anion for amines particularly quaternary, and others in protonated form. All these circumstances lead to a good stability of the membrane throughout its life time [26–28]. The electroactive cation sulfapyridine contains such amines. In this work, life time of the membrane with DOS was studied for 45 days (Table 3) and it showed good response after 45 days.

As is clear from Table 3 and Fig. 5 the response parameters and the calibration curve characteristics of the membrane remain the same over a time period of 45 days.

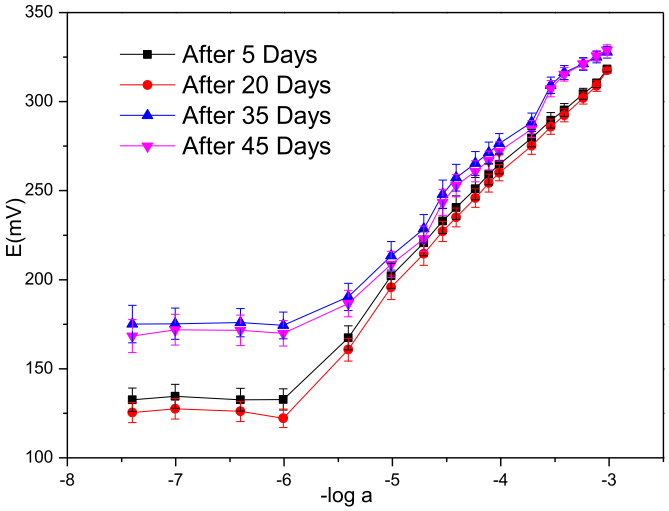

Fig. 5. Lifetime of ISE: Potentiometric response of Sulfapyridine selective μISE over different time periods with Bis (2-ethyl hexyl) Sebacate as plasticizer.

3.6. Response time

The response time is the time taken by the electrode to achieve a stable potential and in this study, it was found to be less than 10 s in all cases.

The response time is strongly dependant on the thickness of the selective membrane and on the thickness of the conducting polymer PPy [$Co(C_2B_9H_{11})_2$]. This is because, more the concentration of anionic sites in the membrane, lesser is the coextraction of the primary ion and, hence, quicker is the response time [36].

3.7. pH response

The influence of pH on the potentiometric response of the microelectrode was examined using a 10^{-3} M Sulfapyridine solution over a pH range from 1.5 to 12 (Fig. 6). For this study the μISE containing DOS as Plasticizer was used since it gave the best performance. The molecular structures of sulfapyridine and the molecules displayed in Fig. 4 corresponding to the interferences studied foresee a dependence of the voltage with the pH and that is indeed what happens. However as shown in Fig. 6 the pH influence on the E value is negligible in the range of pH between pH 6 and 9. This motivated us to avoid buffered solutions to do the testing while adjusting the pH within this interval by addition of NaOH 1 M. Since the purpose of the ISE is to test presence of Sulfapyridine in water bodies, which have pH around 7, the working range of pH 6–9 is appropriate.

In this case, Sulfapyridine-H^+, which is the electroactive part, is in a protonated form within the membrane due to the need for a cation to compensate the negative charge of [$Co(C_2B_9H_{11})_2]^-$ (to provide stability to the membrane). The analyte is not totally in this form, owing to the need for good solubility of the analyte. Thus, there is a difference between the sulfapyridine form within the membrane and in the water solution. This causes a potential change of around 10 mV/decade in the working pH range, but this has not been found to have an appreciable effect on the measurements.

Table 3
Response of Ion Selective membrane over different time periods.

Time Period of Membrane	Slope (mV/Decade)	Limit of Detection (mol/dm^3)
5 days	61.29	1×10^{-6}
15 days	63.95	1×10^{-6}
30 days	59.23	4×10^{-6}
45 days	61.79	4×10^{-6}

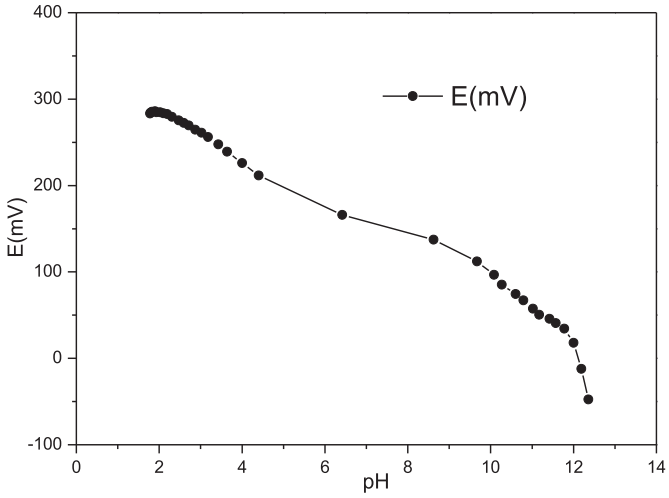

Fig. 6. pH response: Reilley diagram showing the effect of pH variation on the EMF of the Sulfapyridine selective μISE. The μISE gives a stable EMF signal between pH 6 and 8. The pH working range is measured by increasing the pH of a 1 mM solution of Sulfapyridine by titration with small aliquots of NaOH 1 M solution.

4. Conclusions

An unprecedented potentiometric micro Ion Selective Electrode has been prepared for the detection of Sulfapyridine, as an example of the sulphonamide class of compounds, in water using a polymeric membrane made up of the protonated sulfapyridine and the organometallic anion cobaltabisdicarbollide, $[C_{11}H_{20}N_5S][3,3'\text{-}Co(1,2\text{-}closo\text{-}C_2B_9H_{11})_2]$ ion-pair complex, PVC and different plasticizers. The metallacarborane anion $[3,3'\text{-}Co(1,2\text{-}closo\text{-}C_2B_9H_{11})_2]^-$ can be solubilized either in water or non-polar organic solvents depending upon the cation. Its ability to produce weak hydrogen and dihydrogen bonds with O–H or N–H containing molecules and its electroactivity and redox reversibility make it unusually attractive to make reliable sensing membranes for potentiometric detections. Here we aimed at producing a reliable, fast, efficient, reuseable, long lasting and selective potentiometric sensor for sulfonamides of which sulfapyridine is one of the major examples. In this work the μISE prepared for Sulfapyridine detection having composition as 63% Bis(2-ethylhexyl) Sebacate (plasticizer), 30% PVC (polymer matrix) and 7% $[C_{11}H_{20}N_5S][3,3'\text{-}Co(1,2\text{-}closo\text{-}C_2B_9H_{11})_2]$ ion-pair complex shows great sensitivity towards Sulfapyridine with lowest detection limit of 1×10^{-6} mol/dm^3 and is highly selective towards Sulfapyridine when compared with other Sulfonamides, showing to be at least two order of magnitude less permeable to the interfering species in all cases.

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