Arabian Journal of Chemistry (2021) **14**, 103303

King Saud University

Arabian Journal of Chemistry

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REVIEW ARTICLE

A review on the determination heavy metals ions using calixarene-based electrochemical sensors

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Received 10 April 2021; accepted 30 June 2021
Available online 3 July 2021

KEYWORDS

Calixarene;
Heavy metals;
Electrochemical sensor;
Electrochemical techniques;
Modified electrode

Abstract In aquatic environment, the presence of heavy metal in excess than permissible limits set by the World Health Organization (WHO) can cause problems to human being and aquatic life. Hence, various analytical methods have been developed to monitor the water quality by tracing different heavy metal ions in water samples. The present review summarizes the body of work (143 studies) on heavy metal determination in the past 20 years using electrochemical sensors and calixarene derivatives. The potential of calixarene derivatives to sense heavy metal ions using different electrochemical techniques were discussed. The review begins with the introduction of various electrochemical methods including potentiometry, amperometry, voltammetry and electrochemical impedance spectroscopy along with the general setup. This review provides an overview of the mechanism, main parameters of studies and application of calixarene derivatives in selective and sensitive detection. The detection of various target analytes, concentration range, and detection limit using calixarene derivative-based sensors, with different electrochemical techniques, are presented. The strengths and weaknesses of different electrochemical techniques based on calixarene derivatives are also discussed. The review shows that calixarene derivatives have great potential in sensing technology applications, specifically in heavy metal ion determination. In the end, present challenges and future prospects for translating developed sensors into portable sensing in commercial purposes is highlighted.

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Peer review under responsibility of King Saud University.

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https://doi.org/10.1016/j.arabjc.2021.103303
1878-5352

Contents

1. Introduction

In supramolecular chemistry, cyclodextrins and crown ethers, calixarenes also serve as macrocyclic host molecules. Calixarenes are synthesized by the base-catalyzed reaction of phenol derivatives and formaldehyde. Their basket shape enables them to form a complex with small ions and molecules, leading to their wider applications as extractors of metal ions and as carriers in liquid membranes (Toutianoush et al., 2005). Calixarenes are useful basic skeletons. They can provide superior platforms for the design and synthesis of receptors for guest recognition (Adhikari, 2011). Calixarenes act as receptors for anionic, cationic, or neutral substrates by providing a rigid concave surface at their lower or upper rim or by using the bowl-shaped arrangement of the aromatic groups as a hydrophobic cavity (Satheeshkumar, 2004). Since calixarenes possess a high level of preorganization and cooperative functional groups, the modification of calixarenes with suitable ligating arms have recently proven to be powerful extractants for many elements (Adhikari, 2011). The selectivity and efficiency of metal ion bonds with calixarene ligands depend on the nature of the binding groups attached to the calixarene, as well as the macrocycle conformation and the size of the calixarene skeleton (Torma, 2009).

Calixarenes, the third generation of supramolecules, have been used as receptors to identify guest molecules and various ions due to theirs remarkable properties (Chen, 2001). Calixarenes are easy to synthesize at a large scale and can be selectively functionalized at theirs upper rim (non-polar) and lower rim (polar) (Bhat et al., 2004). Moreover, calixarenes have electron-rich interior cavities and can form complexation with metal ions of compatible dimension through dipole–dipole interaction (Kumar, 2012).

Calixarenes, also known as metacyclophanes, exist in different ring sizes ranging from 4 to 8 aromatic residues (Gutsche et al., 1985). The phenolic residue number in this macrocycle is designated an n-value (4, 6, or 8) following the term calix [n]arene (Moran, 1994). The cavity sizes in calixarene can be varied according to the requirements of different size molecular guests (Dernane, 2013). Calix[4]arenes exist in several conformations, as validated using space-filling (Corey-Pauling-Koltun) molecular models. Hence, increased calixarene ring size might increase the calixarenes' conformational flexibility (Gutsche et al., 1985). In the calixarene family, calix[4]arenes have been studied more intensively compared to calix[8]arenes in solid state due to the latter's poor control over stereoselective substitution reactions at the two rims; that limit its solubility and the flexibility of the molecule from forming various structural conformations and thus hindering long-range orders in the solid state (Bergougnant et al., 2007).

2. The overall problem with heavy metals ions

Heavy metals are naturally occurring substances that exist in the environment at low levels (Martin and Griswold, 2009). The term "Heavy" commonly refers to high density while the term "Metals" implies a pure element or an alloy of metallic elements (Duffus, 2002). Heavy metals are referred to as any high-density metallic element that is poisonous or toxic even at very low concentrations (Nagajyoti et al., 2010). These metals have a density greater than 5 g cm^{-3} and have an adverse effect on both living organisms and the environment (Jaishankar, 2014; Barakat, 2011). Heavy metals are classified as environmental pollutants because they have toxic effects on living organisms, including animals, humans, and plants. These metals persist in the environment, as they cannot be destroyed or degraded (Gupta, 2014). The water pollution caused by hazardous heavy-metal-based ions has been an increasing concern, as heavy metal causes diverse health problems such as those related to the hematopoietic, gastrointestinal, kidney, and nervous systems (Sayin, 2020).

Our environment nowadays is increasingly exposed to heavy metal toxins because of modern agricultural practices and rapid industrialization. These days, routine pharmaceutical, hydrometallurgical, and electronic activities have seriously contributed to water pollution. These activities have led to the accumulation of heavy metal ions including, chromium(III), copper(II), lead(II), and nickel(II) ions, in the aquatic environment (Priastomo, 2020). The speedy toxic heavy metal ion contamination of earth water channels is alarming for both water consumers and aquatic life (Sultan, 2019).

In this regards, a number of studies have been conducted for the removal and detection heavy metal ions based on the calixarenes-based derivatives from aqueous systems. Several removal methods applied in the systems such as solvent extraction, transport across liquid membrane and adsorption were described and discussed in the following works (Xie, 2019; Wang, 2016; Wu, 2019; Wang, 2016; Eddaif et al., 2019; Al-Trawneh, 2015) which shows the possibility to work in industrial applications. In addition to this, it is as well essential to firstly identify the presence of heavy metal in the samples. Hence, this review is mainly focused and explored on the detection of heavy metal ions using calixarene-based compounds.

3. Detection methods for heavy metal ions

Conventional detection techniques for heavy metals ions are based on analytical and physicochemical techniques, such as fluorescence spectrophotometry (FL) (Yarur et al., 2019), inductively coupled plasma-optical emission spectrometry (ICP-OES) (Massadeh et al., 2020), inductively coupled plasma-coupled to mass spectrometry (ICP-MS) (Kılıç Altun, 2017) or atomic absorption spectrometry (AAS) (Zhong et al., 2016). Although these analytical techniques provide complete information of selectivity and sensitivity, they still offer some drawbacks, including tedious sample preparation, the need for expert knowledge, high operational costs, and lengthy analysis time (calibration, pre-concentration, preparation, sampling) (Eddaif, 2020). Hence, electroanalytical techniques are more promising alternatives (Sultan, 2019).

4. Electrochemical detection of heavy metal ions

Various electrochemical techniques using calix[n]arene (n = 4, 6, 8) have been demonstrated to detect heavy metal ions. These methods include potentiometry, amperometry, differential pulse voltammetry (DPV), square wave voltammetry (SWV), differential pulse anodic stripping voltammetry (DPASV), square wave anodic stripping voltammetry (SWASV), cyclic voltammetry (CV), and electrochemical impedance spectroscopy (EIS). These electrochemical methods are illustrated in the flow chart of Fig. 1. Electrochemical techniques have gained much attention recently because of their fast response, easy operation, cost efficiency, and on-site application (Stoytcheva, 2019), providing inherent sensitivity and selectivity (Xiao-bo, 2004). Syehla et al. (Torma, 2009) established the use of calix[n]arenes for heavy metal recognition in the electroanalysis field at the end of the 80 s, mainly for the development of ion-selective electrodes. The use of calixarenes was then extended on variety of electrodes using various electroanalytical techniques.

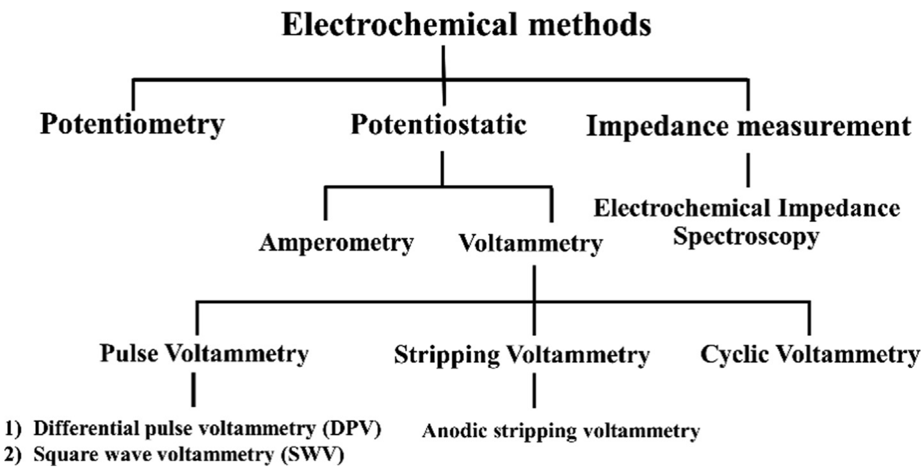

Fig. 1 A flow chart of the electrochemical methods used to detect heavy metal ions.

This review paper presents the calixarene-based detection of heavy metal ions using different analytical techniques such as potentiometry, amperometry, voltammetry (differential pulse voltammetry, square wave voltammetry, anodic stripping voltammetry, and cyclic voltammetry) and electrochemical impedance spectroscopy.

4.1. Potentiometric technique

Potentiometry is a static interfacial technique used in diverse practical applications such as in environment tests involving 'in field measurement' (Abdalla, 2019), and healthcare and clinical tests (Tymecki et al., 2004). In this technique, the electromotive force (emf) measurement is based on the difference in the potentials of two half-cells at zero current (Hulanicki and Głąb, 2005; Bansod, 2017). In potentiometry, both a reference electrode of constant potential and an indicator electrode that respond to the target analyte are required to complete the electrochemical cell (as shown in Fig. 2) (Tymecki et al., 2004; Hulanicki and Głąb, 2005). This method requires selective electrodes to quantitatively analyze ions in a solution (Bansod, 2017).

Potentiometric detection based on ion-selective electrodes (ISEs) is a simple technique, with advantages such as simple instrumentation, cost effectiveness, rapid response, a simple procedure and preparation, reasonable selectivity, and a broad dynamic range (Lu, 2004; Demirel, 2006). In the sample analysis, chemical or ion-sensors are commonly used because they provide rapid results and are convenient and suitable for all minimum concentrations and "on-line" monitoring without requiring any sample pre-treatment. These sensors are also selective, accurate, and non–destructive (Gupta, 2014; Gupta, 2012; Tyagi et al., 2010). Although researchers have put in a lot of effort in developing ion-selective electrodes to detect ions such as Ni^{2+} (Kumar, 2012), Pb^{2+} (Alva, 2019), Na^{+} (Nielsen, 2017), and Cu^{2+} (Brinić, 2012); these sensors still exhibit a long response time, poor reproducibility, and a narrow working concentration. Besides, competitive metal ions can still interfere with the process (Kumar, 2012). Therefore, a more powerful sensor must be developed to address these drawbacks.

There is evidence that the selectivity of ISE towards analytes can be enhanced when incorporated with ionophores. Such a synthetic receptor has analyte binding ability afforded by selective host–guest interactions (Guinovart, 2017). The selected ionophores must contain properties of rapid exchange kinetics, an adequate complexation formation constant in the membrane, good solubility in the membrane matrix, and sufficient lipophilicity to prevent leakage from the membrane into the sample solution (Bhat et al., 2004).

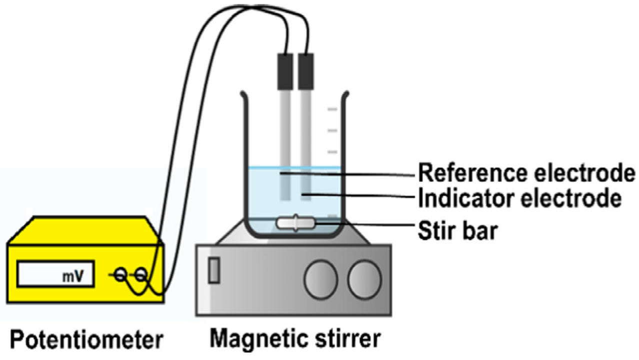

Fig. 2 Potentiometric titration setup (Hulanicki and Głąb, 2005; Ma'mun et al., 2018).

4.1.1. Calixarenes as ion selective electrodes

In 1986, for a time, calix[4]arenes were first reported in detecting Na^{+} and used as ionophores or ligands in ion selective electrodes (Duncan and Cockayne, 2001). The selectivity and complexation efficiency of calixarenes in ions and molecular binding depend on the nature of the binding groups attached to the calixarenes and the calixarene ring size (Chen, 2001; Mahajan, 2004). Derivatives with various functional groups exhibit different levels of ionophoric receptor activity (Lu et al., 2003). Calixarenes also possess high lipophilicity, thermostability, and conformational flexibility that cause the fast exchange of metal ions (Kumar, 2012). Many studies have also determined metal ions (silver ions (Ag^{+}), cadmium ions (Cd^{2+}), mercury ions (Hg^{2+}), nickel ions (Ni^{2+}), lead ions (Pb^{2+}), strontium ions (Sr^{2+}), and uranium ions $(UO_2)^{2+}$ via the potentiometric technique using calixarene derivatives as an electrode modifier. The influence of plasticizers, pH, internal filling, and different amounts of the anionic sites solution are the main factors that affect the detection of analytes using potentiometric technique (Chen, 2001; Demirel, 2006; Mahajan, 2004; Chen, 2000).

4.1.1.1. Potentiometric analysis of Ag^{+}. Ion-selective electrodes based on calixarene have been widely employed in the potentiometric detection of Ag^{+}. Calixarene derivatives **1**, **2**, **3**, **4**, **5**, and **6** (as shown in Fig. 3) were found selective toward Ag^{+}. Glassy carbon electrode (GCE) based on calix[4]arene **1** has good long-term stability, with only less than 5 % fluctuation in potential response when detecting silver ions after the electrode was stored in air for 1 month. This sensor also showed good response performance and properties, and hence can be used to detect silver ions at the sub-micromolar level. Ag^{+}-ISE was developed by directly coating the surface of GCE with tetrahydrofuran solution containing PVC, 25,27-dihydroxy- 26,28-bis[5-(4-methyl-6-hydroxypurimidine)thiaamyloxy] calix[4]arene, sodium tetraphenyl borate and dioctyl phthalate (Lu, 2004).

Calix[4](arene derivative **2** containing N-atoms of modified electrodes displayed good selectivity and sensitivity, a good detection limit, and a good linear response in detection. The electrode retained its performance even after it was repeatedly calibrated (7 times in 1 month). Calixarene derivative **2** containing N-atoms was used to detect Ag^{+} because the soft heavy metal ions (Ag^{+}, Pb^{2+}, and Hg^{2+}) demonstrated a great affinity toward soft coordination centers such as nitrogen, sulfur and selenium atoms. For electrode preparation, a calixarene carrier, poly(vinyl chloride) (PVC), plasticizer, and potassium tetrakis (4-chlorophenyl-borate) (KTClPB) were mixed and dissolved in tetrahydrofuran (THF) to form a PVC-THF syrup. The syrup was poured into a glass mold and evaporated at room temperature overnight. A flexible,

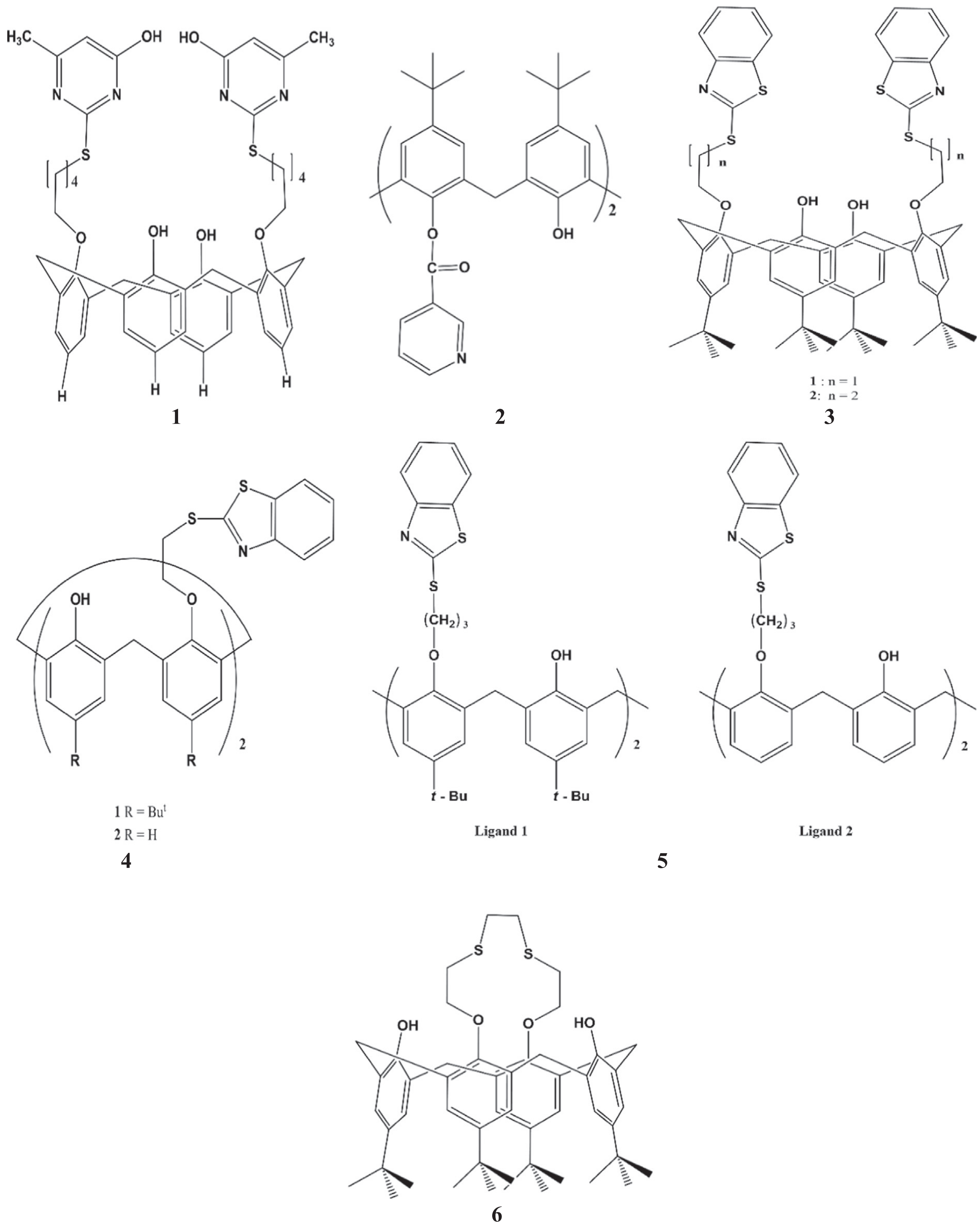

Fig. 3 The structure of **1)** 25,27-dihydroxy- 26,28-bis[5-(4-methyl-6-hydroxypurimidine)thiaamyloxy] calix[4]arene (Lu, 2004) **2)** calixarene derivative (Chen, 2000) **3)** 1,3-Bis(2-benzothiazolyl)thioalkoxy-p-*tert*-butylcalix([4]arenes (Zeng, 2000) **4)** calix[4]arene derivatives functionalized by two hydroxy and two benzothiazolylthioethoxy groups (Chen et al., 2000) **5)** 25,27-dihydroxy-26,28-bis(3-benzothiazolyl -thiopropoxyl)-5,11,17,23-tetra-*tert*-butylcalix[4]carene (Ligand 1, L1), 25,27-dihydroxy-26,28-bis(3-benzothiazolylthio-propoxyl)-calix[4]arene (Ligand 2, L2) (Chen, 2001) and **6)** 5,11,17,23-tetra-*tert*-butyl-25,27-dihydroxy-calix[4]arene-thiacrown-4 (Demirel, 2006).

transparent membrane (0.2–0.4 mm thick) was obtained and cut into a disk (6 mm diameter) using a cork borer, and then pasted onto the PVC tip clipped at the end of electrode body, while the Ag-AgCl wire was immersed in a 0.01 M silver nitrate, internal solution. Lastly, the modified electrodes were pre-conditioned by immersion in 0.01 M silver nitrate solution for 2 h prior to detection purposes (Chen, 2000).

In the work of Weng et al. (Zeng, 2000); calix[4]arene derivative **3** came with functional groups containing S and N atoms. The study expected the derivative to improve selectivity towards soft heavy metal ions such as Ag^+, Pb^{2+} and Hg^{2+} over alkali metal ions. Then, 1,3-Bis(2-benzothiazolyl)thioalkoxycalix[4](arenes **1** (n = 1) and **2** (n = 2) as ISEs ionophores were found to be selective toward Ag^+ with little interference from Hg^{2+} and had better Nernstian response, 58 mV/decade^{-1} as compared to the membrane without ionophores with slope less than Nernstian, 41 mV/decade^{-1}. The study introduced benzothiazolyl units into a calix[4]arene because the introduction of heterocyclic groups (pyridyl, bipyridyl, bithiazolyl) in both the upper and lower rims improved cation selectivity, enzyme mimicking abilities, and other physical properties.

Calix[4]arene derivative **4** functionalized by two hydroxy and two benzothiazolylthioethoxy groups-based polymeric membranes showed more selectivity towards Ag^+ and against Hg^{2+}, with a selectivity coefficient of ($\log K_{Ag/Hg} < -2.6$) compared to Ag_2S-based electrodes, and a selectivity coefficient of ($\log K_{Ag/Hg} > 0$) (Ma'mun et al., 2018). Of the calix[4]arene derivatives substituted by the benzothiazolyl unit, ligand **1** (**L1**) and **2** (**L2**) in **5** (as shown in Fig. 3) incorporated with the Ag^+ membrane electrodes, showed a better Nernstial slope. **L1** and **L2** consisting of two (benzothiazolyl)thioproxy groups substituted calix[4]arene and had better sensitivity due to the good coordination geometrical arrangement of N or S atoms in **L1** and **L2** that affected the complexing ability towards Ag^+, followed by the potential response of these electrodes. Therefore, dithia macrocycles-based electrodes have a high selectivity toward Ag^+, not only because of their macrocyclic cavity size but also because of the coordination geometrical arrangement of sulfur group. In the pH study, the modified electrode possess drastic drop in current response at pH outside the range of pH 2.5 – 7.0, which is likely due to the formation of silver hydroxides and response to hydrogen ions at high and low pH, respectively (Chen, 2001).

A new 5,11,17,23-tetra-*tert*-butyl-25,27-dihydroxy-calix[4]arene-thiacrown-4-based PVC membrane potentiometric sensor **6** was found to increase electrode performance. However, this sensor depends on the stoichiometry of the complex formed between the neutral carrier and the target analytes. In this study, these electrodes containing 8.6 mg of calix[4]arene in the membrane demonstrated better performance than those containing 4.3 mg of the neutral carrier, and those containing the same mass ratio of PVC to plasticizer. The modified electrode was highly selective towards Ag^+ (with a soft acid character) and exhibited the most potential response. The intermediate acid character of the metal ions showed negligible response. Hard acid character metal ions (alkali and alkaline earth ions), also known as soft bases, have negligible response because of their weak interaction with sulfur atoms (Demirel, 2006).

4.1.1.2. Potentiometric analysis of Cd^{2+}, Cs^+, Hg^{2+}, Ni^{2+}. A cadmium-selective sensor containing p-*tert*-butylcalix[6]arene **7** (as shown in Fig. 4) showed a fast response time of 35 s in detecting cadmium ions (Cd^{2+}) and had a good lifetime; it can be used for 4 months and more without undergoing any significant change in potential response. Based on the literature, the loss of ionophores from the membrane while in contact with aqueous solution is the main factor contributing to a sensor's limited lifetime. This research revealed that sufficient amounts of plasticizer and lipophilicity of ionophores could ensure long lifetimes and stable potentials. This sensor was successfully applied to industrial waste water samples, with the results showing good agreement with standard atomic absorption spectroscopy (AAS) technique (Gupta, 2014).

Calix[6]arene tetraester I **8** (as shown in Fig. 5) displayed better detection of Cs^+ with a detection limit below 10^{-6} M. The membrane (0.3 mm) for cesium ion detection was developed via a mixture of poly(vinyl chloride) (PVC): plasticizer in the ratio of 1:2, 1 mg ionophore and potassium tetrakis(p-chlorophenyl)borate (KTpClPB) (50 mol.% of ionophore if needed) in an appropriate volume of tetrahydrofuran (THF) followed by mechanical stirring. Lastly, the tetraester was casted in glass rings and dried at room temperature for 24 h. Calix[6]arene tetraester I without para t-butyl substituents was found to have superior characteristics in comparison to those containing para t-butyl substituents. Hence, this study concludes that, in PVC membrane electrodes, the ionophore structure is the major factor determining selectivity aside from the type of plasticizer used (Oh, 2000).

Fig. 6 shows that calixarene derivatives **9**, **10**, and **11** have been found to be highly selective toward Hg^{2+}. Calix[4]arene

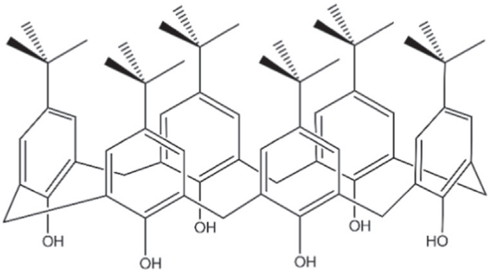

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Fig. 4 The structure of p-*tert*-butylcalix[6]arene (Gupta, 2014).

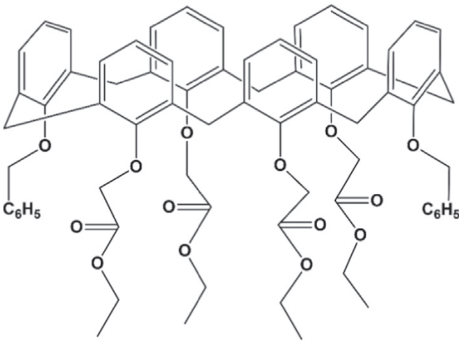

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Fig. 5 The structures of calix[6]arene tetraester I (Oh, 2000).

derivative **9** was synthesized through the condensation of calixamine and a Schiff base product. The response time of sensor **9** towards Hg^{2+} was rapid—within 20 s. In the pH study, the potential was maintained from pH 1.3 to pH 4 and dropped after pH 4 because of the formation of $Hg(OH)^{+}$ ions. This work reported p-*tert*-butyl calix[4]crown with imine units, as the mercury (II) ion-selective electrode is superior in slope, response time, selectivity values, linear concentration range, and has a lifetime of more than 3 months. However, Ag^{+} with a high selectivity coefficient value strongly interferes with the detection of Hg^{2+} ions (Mahajan, 2004).

Calix[4]arenethioether derivative **10** acts as an ionophore for the ISE and displayed high selectivity towards Hg^{2+} ions, with advantages such as fast response, simplicity, low detection limit, reproducibility, and fair stability. The mechanism of the electrode response to Hg^{2+} involves the interaction of Hg^{2+} (electron acceptor) with O and S atoms in the calix[4]arenethioether derivative molecule (electron donor). This sensor showed a high response time of 14 s and could work satisfactorily in both aqueous and partially non-aqueous media up to 40 % (v/v) acetone, ethanol, and methanol, with a long lifetime of up to 7 – 9 months. The electrode was also successfully applied in real applications, including in amalgam samples, industrial wastewater, and a solder sample, displaying satisfactory agreement with the result obtained from atomic absorption spectroscopy (Tyagi et al., 2010).

In the detection of Hg^{2+} using calix[6]arene derivative **11**, two Nernstian responses were obtained, at a slope of 61.1 mV per decade (at pH 6.5) and 28.7 mV per decade (at pH 4), due to the different forms of Hg^{2+} at different pH values. At pH 5.5 to pH 7.0, the ISE showed a twice Nernstian response typical for a monovalent cation, i.e., a slope of 55 mV per decade. At pH 3.0 to pH 5.0, ISE showed a Nernstian response with a slope of 25.6 mV per decade, which is a typical value for a divalent cation. Ionophore **11** is rich in intermediate donor atom-groups (nitrogen atom and azo group) and soft donor atoms; therefore, interferences from Ag^{+}, Cu^{2+} and Pb^{2+}, which are soft and intermediate acidic ions, are more likely to form complexation with donor N and S atoms attached to the calixarene. This proposed electrode proved applicable for real samples, such as in the detection of mercury ions in industrial wastewater, lake water, and synthetic solution (Lu et al., 2003).

p-(2-thiazolazo)calix[4]arene **12** (as shown in Fig. 7), an ionophore with an azo group on the upper rim of calixarene is an excellent neutral carrier for the solid state Ni (II) sensor and is applicable for determining Ni^{2+} ion concentration in environmental analysis (electroplating waste), and food samples (chocolate), where the results exhibited close agreement with those analyzed using atomic absorption spectroscopy (AAS). When the sensor was equilibrated with Ni^{2+} ions, the highest emf response was obtained. This result reveals that the ionophore is more selective towards Ni^{2+} in comparison with other metal ions, and the resulting ligand–metal ion com-

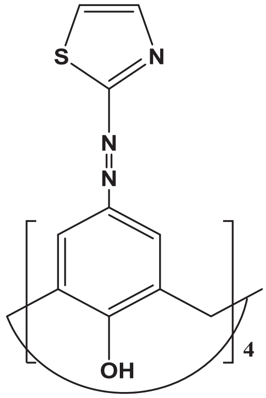

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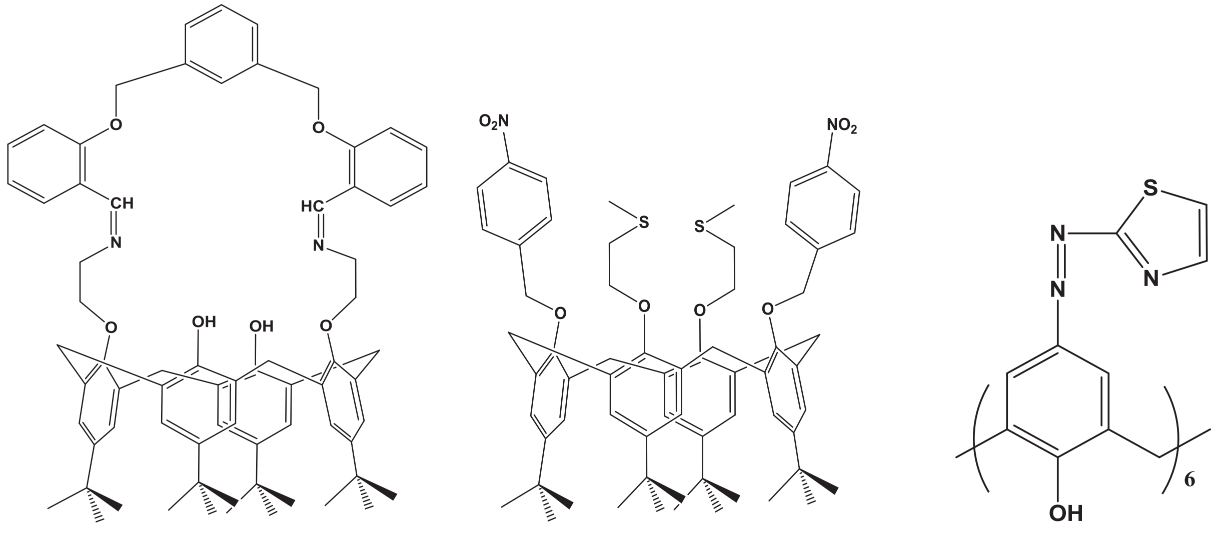
Fig. 7 The structure of *p*-(2-thiazolazo)calix[4]arene (Kumar, 2012).

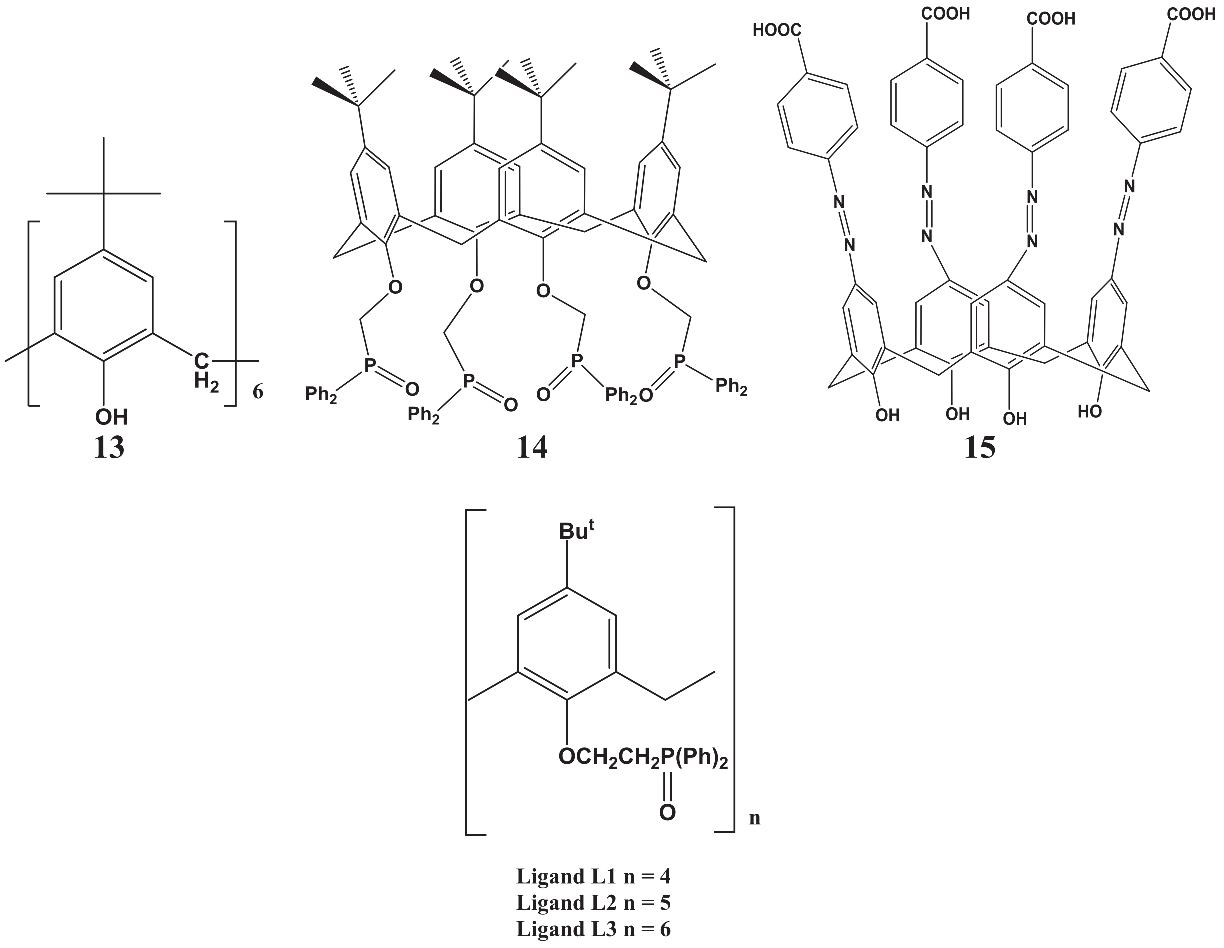


9 **10** **11**

Fig. 6 The structures of **9)** *p-tert*-butyl calix[4]crown with imine units (Mahajan, 2004) **10)** p-*tert*-butyl-calix[4]arenethioether derivative (Tyagi et al., 2010), and **11)** 5,11,17,23,29,35-Hexa[(1-thiazole) azo]-37,38,39,40,41,42-hexahydroxy calix[6]arene (Lu et al., 2003).

plex experienced fast exchange kinetics. This sensor fabrication is different from the conventional ISE, where 10 μL of the membrane solution was directly modified on a cleaned and polished graphite electrode, and then evaporated at room temperature. This research found that the addition of plasticizers shortened the response time, returning best results of 10–15 s in comparison with the response time of 180 s (at high concentration level) and 300 s (at low concentration level) of the membrane without any plasticizer (Kumar, 2012).

4.1.1.3. Potentiometric analysis of Pb^{2+}. Calixarene derivatives **13**, **14**, **15,** and **16** (as shown in Fig. 8) are selective toward Pb^{2+}. To prepare an electrode with ionophore **13**, platinum wires were used as substrates to coat the slurries calix[6]arene, PVC poly(vinylchloride) and anion excluder NaTPB (sodium tetraphenyl borate) dissolved in THF (tetrahydrofuran). Sensor **13** could be used for over 5 months without exhibiting any remarkable effect on the membrane potential, but the electrode response dropped after 5 months, possibly due to the aging of the PVC ionophore, the matrices, and the plasticizers. The sensor was successfully used in determining Pb^{2+} in synthetic samples such as alloy samples, battery waste samples, effluent water, and in electroplating bath solutions. The results acquired using this proposed sensor are in good agreement with both AAS and titrimetric techniques. The coated-wire ISE was selected in this work because it requires a very small volume of sample. It is also low cost, simple in design, and allows for the possibility of microfabrication and miniaturization. It also has mechanical flexibility in which the electrode can be used at any angle and in the absence of an internal solution (Bhat et al., 2004). 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(diphenylphosphinoylmethoxy)calix[4]arene **14** used as an ionophore, was directly coated on a graphite electrode to detect lead ions. In the graph of the potential response of the electrode for the Pb^{2+}-ion-selective electrode, a plateau was observed at high concentrations, possibly due to the saturation of test solution/membrane interface by the lead complexes. The sensor exhibited a lifetime of over eight weeks. Additionally, the slope of the potential versus lead ion concentration remained constant throughout the assessment period. This sensor was tested in various synthetic water samples; however, there was some inaccuracy in measurement that could have been due to the presence of calcium. The electrode could be successfully used to determine Pb^{2+} when performing the


13 **14** **15**

Ligand L1 n = 4
Ligand L2 n = 5
Ligand L3 n = 6

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Fig. 8 The structure of **13)** 5,11,17,23,29,35-*hexa*-tert-butyl-37,38,39,40,41,42-hexahydroxycalix[6]arene (Bhat et al., 2004) **14)** 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(diphenylphosphinoylmethoxy)calix[4]arene (Yaftian, 2006) **15)** 5,11,17,23-tetrakis[(*p*-Carboxyphenyl)azo]-25,26,27,28-tetrahydroxy calix[4]arene (Lu et al., 2002), and **16)** general structures of butylcalix[*n*]arene ethyleneoxydiphenylphosphine ($n = 4$, 5 and 6 for ligands L1–L3, respectively) (Cadogan, 1999).

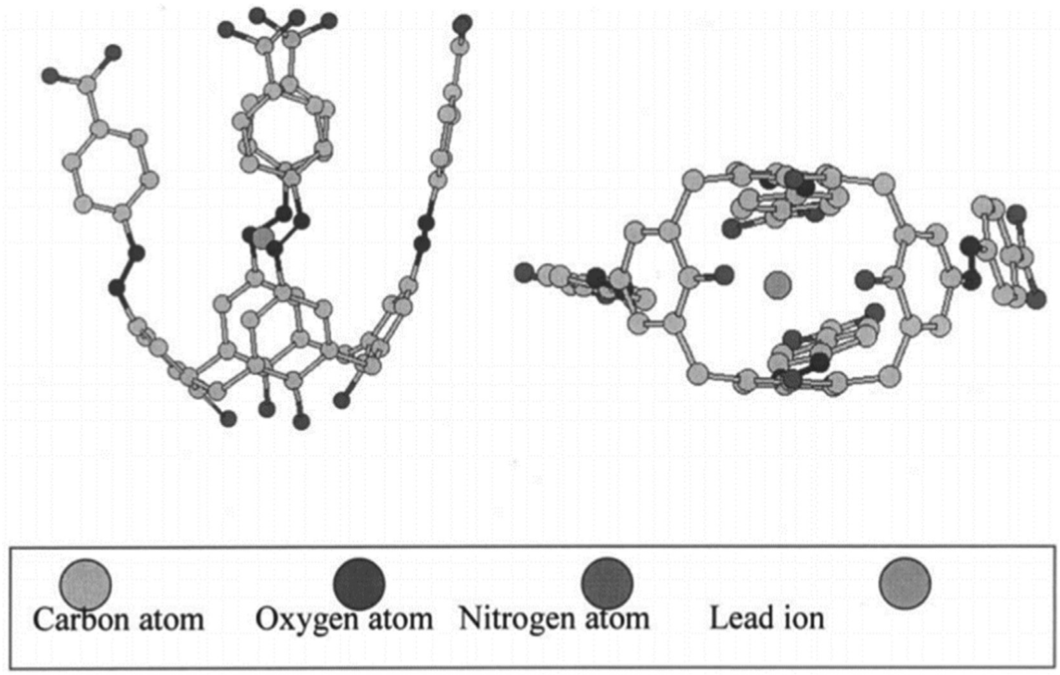

Fig. 9 Side view of the 3D structure of the ligand, i.e., the Pb^{2+} complex. The energy-minimized structure suggests that the lead ion is located in a medium cavity (hydrogen atoms omitted for clarity) (Lu et al., 2002).

potentiometric titration of lead solution with EDTA (Yaftian, 2006).

The ionophore of a calix[4]arene derivative containing carboxyphenyl azo group **15**, with a polymeric membrane, was found selective towards lead ions. The binding mechanism was studied using molecular modeling in which lead ion complexed with the heteroatom group (N = N) on the upper rim of the calixarene derivatives and displayed a cone conformation. The molecular modeling was studied using Hyperchem molecular modeling package (version 6.01), and a 3D energy-minimized structure recommend that lead ions possible to accommodate medium cavity calixarene as shown in Fig. 9. The lead ions were found to bind electrostatically to the polar cavity containing four azo-bond rings (Lu et al., 2002).

Three difference ring sizes of calixarene phosphine oxide deriviative **16** were used to fabricate ion-selective electrodes with selectivity towards Pb^{2+} ions. An increase in the number of repeating units, n, in macrocycles, was found to enhance the selectivity. Ca^{2+}, the most important interfering element, experienced decreased impact with increased cavity size from tetramer (n = 4), pentamer (n = 5), and then to hexamer (n = 6). All these calixarenes were found to have similar

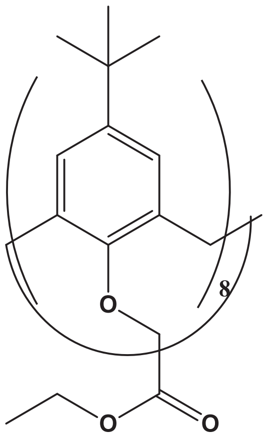

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Fig. 10 The structure of 4-*tert*-butylcalix(8)arene-octaacetic acid octaethyl ester (Jain et al., 2004).

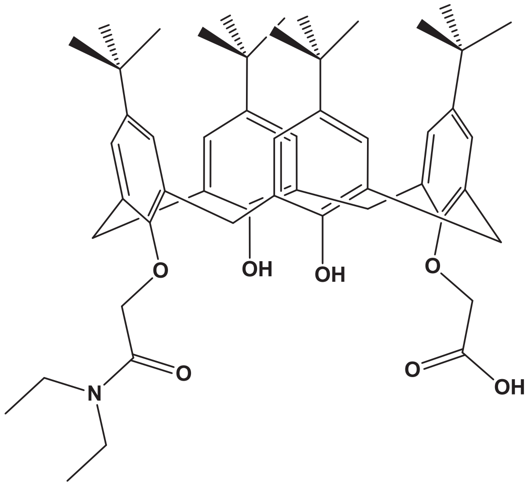

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Fig. 11 The structure of 5,11,17,23-tetra-*tert*-butyl-25,27-bis (hydroxy)-26-(ethoxycarbonylmethoxy)-28-(diethyl carbamoylmethoxy) calix[4]arene (Duncan and Cockayne, 2001).

modes of complexation. The models obtained using Monte Carlo conformational searches indicated that the ions were complexed within the medium region between two types of oxygen atoms, namely, phosphine oxide and the phenoxy in all cases (Cadogan, 1999).

4.1.1.4. Potentiometric analysis of Sr^{2+}, $(UO_2)^{2+}$. A strontium (II)-selective sensor based on 4-*tert*-butylcalix(8)arene-octaacetic acid octaethyl ester **17** (as shown in Fig. 10) in a poly(vinyl chloride) (PVC) matrix showed greatly improved selectivity towards strontium ions in comparison with existing sensors. This sensor is an extended work from 4-*tert*-butylcalix(8)arene which exhibited improved pH range, selectivity, and response time. Based on the literature, the ester derivatives of calix[n]arenes (n = 4, 6) revealed better selectivity compared to the parent calixarene because of the change in conformation, cavity size, and also increased binding sites. In the pH study, the sensors displayed constant potential in detecting Sr^{2+} ions from pH 3 to pH 10. The changes in potential at pH lower than pH 3 and higher than pH 10 are due to the cofluxing of hydrogen ions and the formation of $SrOH^+$ ions. The response time for this electrode to detect Sr^{2+} was 10 s. This electrode has a lifetime of 4 months. This electrode could be used as an indicator electrode in Sr^{2+} ion sensing via potentiometric titration (Jain et al., 2004).

Calixarene derivative **18** (as shown in Fig. 11) was incorporated in a poly(vinyl chloride) (PVC) membrane for uranium complexation. The extraction process was first carried out by

Table 1 List of various calixarene derivative electrochemical sensors and the associated potentiometric method used for heavy metal ion detection.

No.	Modifier	Analyte	Detection range	Limit of detection (LOD)	Reference
1	25,27-dihydroxy- 26,28-bis[5-(4-methyl-6-hydroxypurimidine) thiaamyloxy] calix[4]arene	Ag^+	10^{-8} – 10^{-1} M	1.0 × 10^{-8} M	(Lu, 2004)
2	calixarene derivative	Ag^+	5.0 × 10^{-6} – 10^{-2} M	$10^{-5.3}$ M	(Chen, 2000)
3	1,3-bis(2- benzothiazolyl)thioalkoxy-p-*tert*-butylcalix[4]arenes	Ag^+	5.0 × 10^{-6} – 10^{-1} M	$10^{-5.5}$ and $10^{-5.8}$ M	(Zeng, 2000)
4	calix[4]arene derivatives functionalized by two hydroxy and two benzothiazolylthioethoxy groups	Ag^+	5.0 × 10^{-6} – 10^{-1} M	$10^{-5.8}$ M	(Chen et al., 2000)
5	25,27-dihydroxy-26,28-bis(3-benzothiazolylthiopropoxyl)-5,11,17,23-tetra-tert-butyl calix[4]arene (Ligand 1, L1), 25,27-dihydroxy-26,28-bis(3-benzothiazolylthiopropoxyl) calix[4]arene (Ligand 2, L2)	Ag^+	5.0 × 10^{-6} – 1.0 10^{-1} M	2.5 × 10^{-6} and 3.2 × 10^{-6} M	(Chen, 2001)
6	5,11,17,23-tetra-*tert*-butyl-25,27-dihydroxy-calix[4]arene-thiacrown-4	Ag^+	1.0 × 10^{-2} – 1.0 × 10^{-6} M	8.0 × 10^{-7} M	(Demirel, 2006)
7	p-*tert*-butylcalix[6]arene	Cd^{2+}	9.7 × 10^{-5} – 1.0 × 10^{-1} M	–	(Gupta, 2014)
8	calix[6]arene tetraester I	Cs^+	1.0 × 10^{-6} – 1.0 × 10^{-1}M	< 10^{-6} M	(Oh, 2000)
9	p-*tert*-Butyl calix[4]crowns with imine units	Hg^{2+}	5.0 × 10^{-5} – 1.0 × 10^{-1} M	2.24 × 10^{-5} M	(Mahajan, 2004)
10	p-*tert*-butylcalix[4]arenethioether derivative	Hg^{2+}	7.2 × 1.0^{-8} – 1.0 × 10^{-1} M	1.0 × 10^{-8} M	(Tyagi et al., 2010)
11	5,11,17,23,29,35-Hexa[(1-thiazole) azo]-37,38,39,40,41,42-hexahydroxy calix[6]arene	Hg^{2+}	7.5 × 10^{-6} – 5.0 × 10^{-2} M (at pH 6.5) 5.0 × 10^{-6} – 10^{-2} M (at pH 4)	8.0 × 10^{-7} M (at pH 6.5) 4.5 × 10^{-7} M (at pH 4)	(Lu et al., 2003)
12	*p*-(2-thiazolazo)calix[4]arene	Ni^{2+}	1.0 × 10^{-6} – 1.0 × 10^{-1} M	9.0 × 10^{-7} M	(Kumar, 2012)
13	5,11,17,23,29,35-*hexa*-*tert*-butyl-37,38,39,40,41,42-hexahydroxycalix[4]arene	Pb^{2+}	1.0 × 10^{-6} – 1.0 × 10^{-1} M	6.0 × 10^{-7} M	(Bhat et al., 2004)
14	5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis-(diphenylphosphinoylmethox)calix[4]arene	Pb^{2+}	1.0 × 10^{-5} – 1.0 × 10^{-2} M	1.4 × 10^{-6} M	(Yaftian, 2006)
15	5,11,17,23-tetrakis[(p-Carboxyphenyl)azo]-25,26,27,28-tetrahydroxy calix[4]arene	Pb^{2+}	10^{-6} – 10^{-2} M	$10^{-6.1}$ M	(Lu et al., 2002)
16	butylcalix[n]arene ethyleneoxydiphenylphosphine (n = 4, 5, and 6 for ligands L1 — L3, respectively)	Pb^{2+}	–	1.0 × 10^{-6} M	(Cadogan, 1999)
17	4-*tert*-butylcalix(8)arene-octaacetic acid octaethyl ester	Sr^{2+}	3.2 × 10^{-5} – 1.0 × 10^{-1} M	–	(Jain et al., 2004)
18	5,11,17,23-tetra-*tert*-butyl-25,27-bis(hydroxy)-26-(ethoxycarbonylmethoxy)-28-(diethyl carbamoyl-methoxy) calix[4] arene	UO_2^{2+}	–	3.7 × 10^{-6} M *	(Duncan and Cockayne, 2001)

The value is converted from unit ppm* to M using molar mass of metal.

immersing the membrane in uranyl species for 65 h, and then followed by uranium analysis. Extraction in this project entailed the ability of the membrane-bound calixarene to complex with the UO_2^{2+}. This study showed that the presence of plasticizer (2-nitrophenyl octylether (NPOE)) did not interfere with the ISE measurement, as there was no extraction of ions when no calixarene was present. The selectivity of sensor **18** to uranium in simulated waste solution was also studied. The preparation of diluted uranium solution with waste solution generated a response at lower concentration; however, no response was observed when the uranium solutions were prepared directly using waste solution. Under these conditions, this experiment showed that calix[4]arene might have reacted with other background ions, as the electrode was not selective towards $(UO_2)^{2+}$ prepared directly using waste solution (Duncan and Cockayne, 2001).

Table 1 lists a summary of various calixarene derivative electrochemical sensors and the associated potentiometric method used for heavy metal ion detection.

4.2. Amperometric technique

Ampertometry is a technique that maintains a constant potential in the working electrode after which the changes in current resulting from the gradual addition of analytes are measured (Vyas et al., 2019). In this technique, the electrical current response is directly proportional to the concentration of analytes—a similar concept to the voltammetric technique. Moreover, the selectivity of the detector can be varied according to the electrode potential (Wilke, 1996). Amperometric detection normally involves three electrodes, namely the counter electrode, the reference electrode, and the working electrode, to complete the electrochemical detector cell (Fig. 12). A potentiostat is used to control the applied voltage and to measure the current (Kappes and Hauser, 1999). The amperometric technique has seen a lot of uses, as it is easier to implement experimentally and gives good sensitivity (Wen and Cassidy, 1996). Amperometric detection has been reported to yield lower detection limits (usually 10^{-7} M) for electroactive substances (Kappes et al., 1999). The determination of metal ions (cobalt ions (Co^{2+}) and mercury ions (Hg^{2+})) via amperometric analysis with calixarene derivatives as the electrode modifier has also been reported.

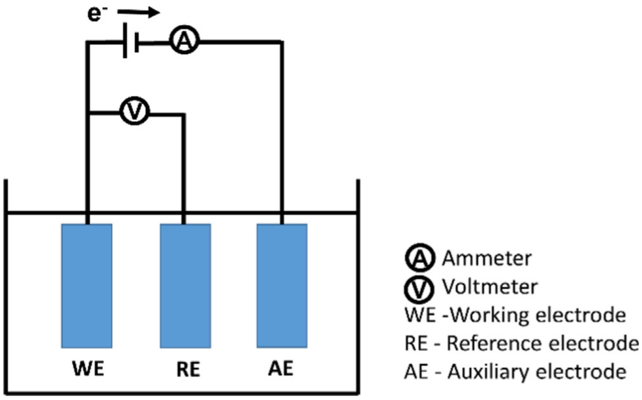

Fig. 12 Amperometric technique setup (Zhang, et al., 2014).

4.2.1. Amperometric determination of Co^{2+} and Hg^{2+}

An amperometric response was observed when modified sensor calix[4]arene **19** functionalized gold nanoparticles (as shown in Fig. 13a) bonded to cobalt ions. The current measured also correlated with the analyte concentration. This result may be explained by the equilibrium potential, which is a function of analyte concentration, so the current of the indicator electrode will change according to the cobalt ion concentration (as shown in Fig. 13 b). The concentration range for Co^{2+} was 10^{-12} M to 10^{-9} M, since above a concentration of 10^{-9} M, all sites of the receptors will become unavailable for further binding of Co^{2+} ions, thus the current underwent no further change and caused the sensor response curve to plateau. The observation from this work revealed that the gold nanoparticles had no direct role in electrochemical measurement; however, there increased current in Co^{2+} detection was observed when calixarene-modified nanoparticles (CFAuNPs) were used. The anchoring of calixarene moiety onto the AuNPs surface yielded a rigid ionophore that was appropriate for selectively coordinating the cobalt ions (Maity, 2014).

One study carried out the detection of Hg^{2+} and observed high sensitivity with the aid of calix[4]arene-functionalized sil-

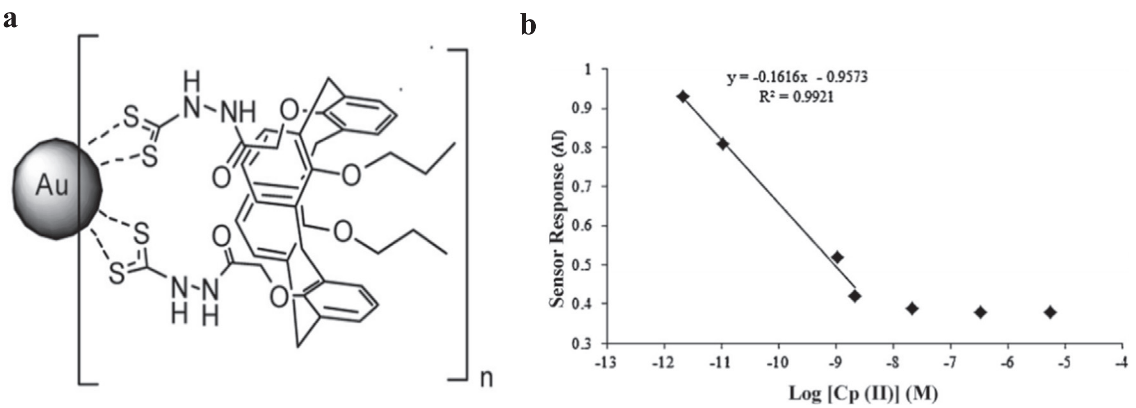

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Fig. 13 **a)** The structure of the dithiacarbamide derivative of calix[4]arene and its anchoring on the surface of AuNPs (CFAuNPs). **b)** The amperometric sensor response as a function of Co (II) concentration (Maity, 2014).

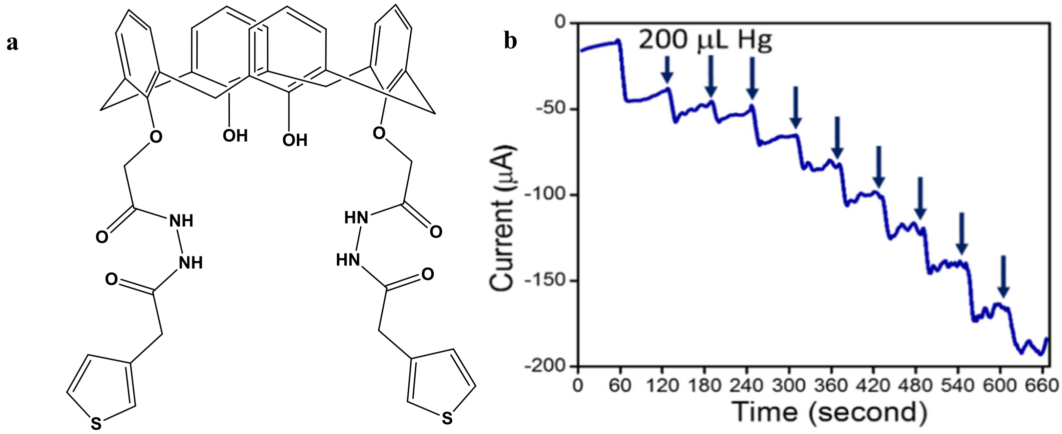

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Fig. 14 **a)** The structure of thiophene-substituted calixarene derivative (ThC). **b)** The amperometry of ThC-AgNPs with the incremental addition of Hg^{2+} showing dynamic stairs due to a decrease in the current with each addition of Hg^{2+} at a time interval of 60 s (Vyas et al., 2019); https://pubs.acs.org/doi/abs/10.1021/acsomega.8b03299, further permissions related to the material excerpted should be directed to the ACS.

ver nanoparticles, **20** (as shown in Fig. 14 a). Silver was chosen not only because it is more cost-effective than gold but also because silver nanoparticles have been predicted to perform as well as gold nanoparticles. The amperometry curve was obtained via the separate, successive addition of Hg^{2+} ions in a homogenously-stirred solution (ThC-AgNPs solution in 0.1 M PBS (pH 5.8)) at an applied potential of – 0.035 V. A decrease in current was observed for every addition of Hg^{2+}, with a 60 s time interval, observed as dynamic stairs (as shown in Fig. 14 b). The detection limit obtained for Hg^{2+} was 10 nM (2 ppb). This sensor was found applicable for real sample analysis, as the steady-state current was acquired in just a few seconds (Vyas et al., 2019).

Table 2 lists a summary of various calixarene derivative electrochemical sensors and the associated amperometric method used for heavy metal ion detection.

4.3. Differential pulse voltammetry (DPV) technique

Voltammetry is a method that obtains information about analytes by measuring the current in an electrochemical cell as a function of applied potential. The electrochemical cells contain three electrodes, including a working electrode, a counter electrode, and a reference electrode immersed in supporting electrolytes (in analytes and a non-reactive electrolyte solution) together with a potentiostat instrument (Yadav and Sharma, 2019).

Differential pulse voltammetry (DPV) is a technique that is immune to the residual current which offer rapid and sensitive measurement (Vilas-Boas, 2019; Aravindan and Sangaranarayanan, 2017). It is a controlled potential technique that applies the pulse of the potential with a constant amplitude while increasing the potential with time. Although the size of the pulse is the same, the potential of each subsequent pulse is slightly higher than the previous pulse (Harris, 2012). For the current sampling of this technique, the current is measured just before the start (*T*) and at the end (*T'*) of a potential step in which $\Delta i = i_{\tau'} - i_{\tau}$ where Δi is the differential current, $i_{\tau'}$ is the current at time τ', and i_{τ} is the current at time τ, as shown in Fig. 15 (Islam and Channon, 2020). From the formula, by subtracting the second current measurement with the initial current, the concentration of analytes can be determined more accurately (Harris, 2012).

DPV can enhance the selectivity of targets by observing different redox processes in comparison with linear sweep voltammetry (LSV) and cyclic voltammetry (CV) (Scott, 2016). This technique is found to produce better defined and less noisy signals as compared to linear sweep voltammetry (LSV) (Pérez-Ràfols, 2017). Hence, DPV provides better detection limits than other electrochemical methods due to its high signal-to-noise ratio and the rapid decay of the charging current at a constant potential pulse (Islam and Channon, 2020; Laborda, 2012). Heavy metals such as chromium ions (Cr^{2+}), copper ions (Cu^{2+}), ferum ions (Fe^{2+}), zinc ions

Table 2 List of various calixarene derivative electrochemical sensors and the associated amperometric methods used for heavy metal ion detection.

No.	Modifier	Analyte	Detection range	Limit of detection (LOD)	Reference
19	dithiacarbamide derivative of calix[4]arene	Co^{2+}	$10^{-12} – 10^{-9}$ M	10^{-12} M	(Maity, 2014)
20	thiophene-substituted calixarene derivative	Hg^{2+}	$45 \times 10^{-9} – 105 \times 10^{-9}$ M	10×10^{-9} M	(Vyas et al., 2019)

(Zn^{2+}), mercury ions (Hg^{2+}), and lead ions (Pb^{2+}) were successfully detected using a calixarene-derivative-based sensor and DPV. In general, the factors that influence the detection of metal ions using DPV are supporting electrolytes, pH, deposition time, and deposition potential (Aziz et al., 2018).

4.3.1. Differential pulse voltammetry analysis of Hg^{2+}, Pb^{2+}

The interaction between Hg^{2+} and this calix[4]arene **21**-based sensor (as shown in Fig. 16 a) occurred by means of the benzothiazole azo groups at the upper rim. From the voltammo-

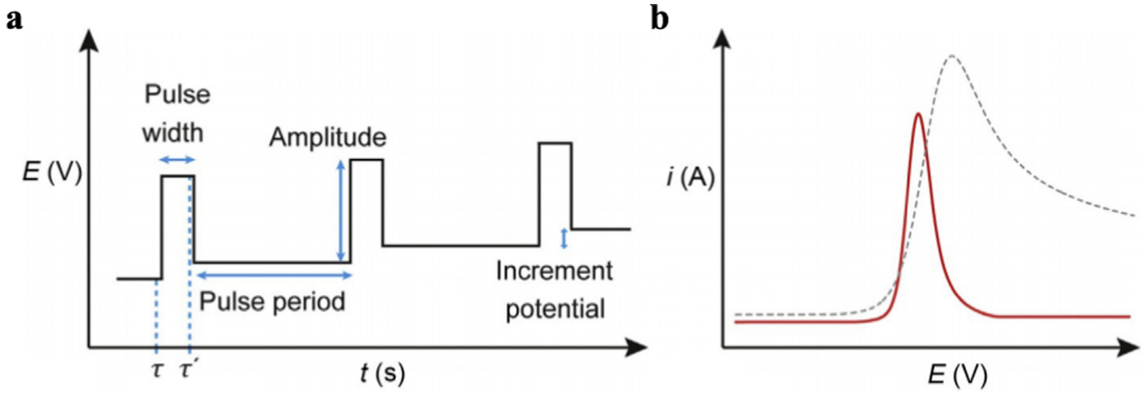

Fig. 15 **a)** Potential staircase and **b)** current–potential plot for an oxidation via Differential Pulse Voltammetry (—) at a macroelectrode overlaid with the corresponding Linear Sweep Voltammogram (– – –) (Islam and Channon, 2020).

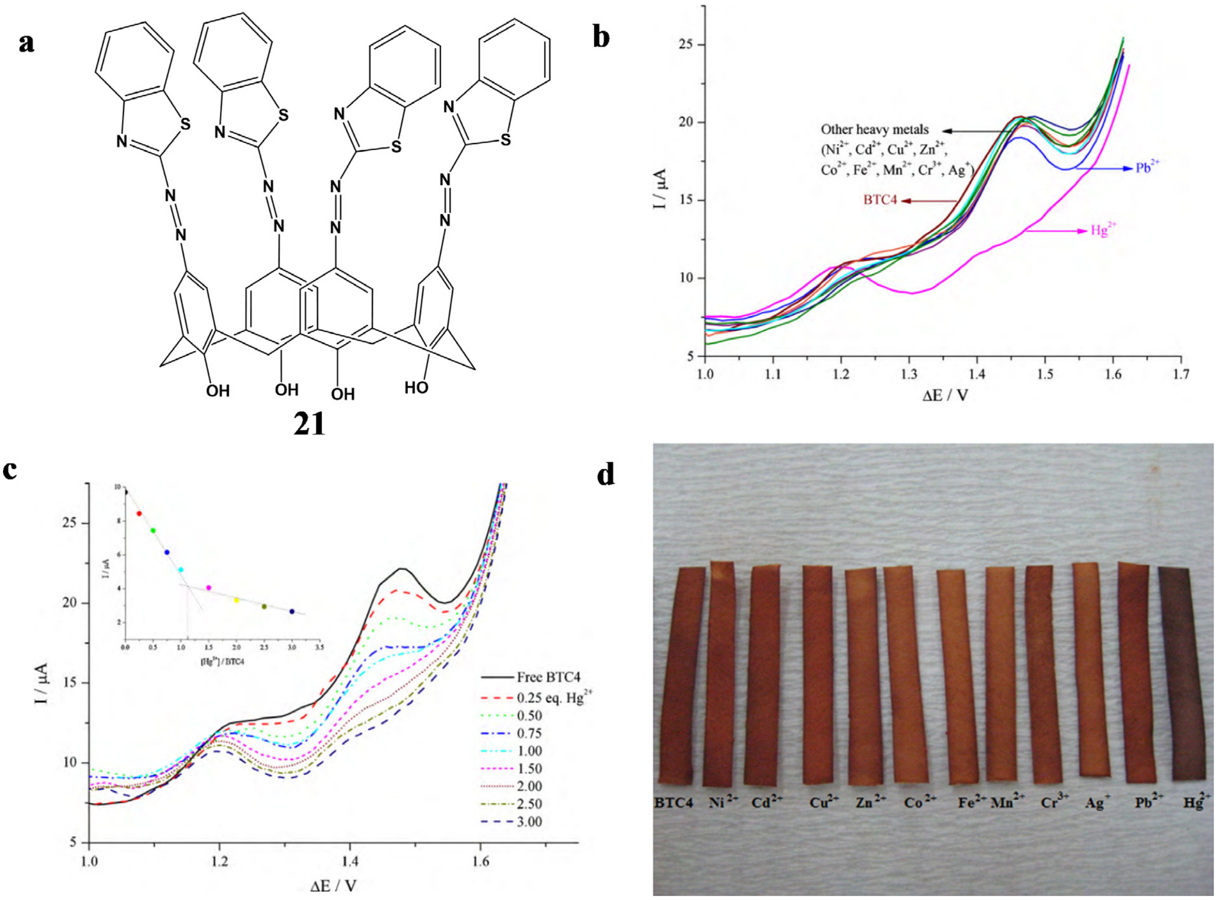

Fig. 16 **a)** The structure of benzothiazole azocalix[4]arene (*BTC4*). **b)** The DPVs of BTC4 (1×10^{-3} M) and BTC4 with different heavy metal ions (3 equivalent) in DMF at GCE. Pulse amplitude 50 mV. **c)** The DPVs of BTC4 upon increasing amounts of Hg^{2+} ions in DMF including 0.1 M TBAP; a pulse amplitude of 50 mV. The inset shows the amperometric titration curve at 1.42 V. and **d)** The color changes were observed after the test strips were dipped for 30 s in 1×10^{-3} M aqueous solutions of the indicated metals (Bingol, 2010).

gram, in the presence of Hg^{2+}, the potential and the current of the first peak (at around 1.2 V) showed little changes whereas the second peak current (at around 1.45 V) almost disappeared (as shown in Fig. 16 b). This change is due to Hg^{2+} interacting with the benzothiazole azo groups at the upper rim of BTC4 (benzothiazole azocalix[4]arene), proving that Hg^{2+} accommodates the medium calixarene cavity. The peak current decreased at the second peak with an increase in Hg^{2+} concentration (as shown in Fig. 16 c). A rapid test kit was developed to detect Hg^{2+} in aqueous solution, with a concentration range between 1×10^{-4} and 1×10^{-2} M. The test strips were immersed in a solution with different metal ions and concentrations, 1×10^{-3} M for 30 s, where the test strips changed from orange to dark brown in the presence of Hg^{2+} (1×10^{-4} M) (as shown in Fig. 16 d) (Bingol, 2010).

A simple selective electrochemical sensor was developed to determine Pb^{2+} in water samples via the modification of dicarboxyl-calix[4]arene **22** (as shown in Fig. 17 a) on gold electrode and via the chemical linkages of 3-mercaptopropionic acid (MPA), resulting in electrocatalytic activity enhancement and higher current response towards lead ions than MPA/Au and bare Au electrodes. This result indicates that the electrode has a better barrier to electron transfer than MPA/Au and the bare Au electrodes. The attachment between dicarboxyl-calix[4]arene and MPA/Au enhanced the electroanalytical performance. For the fabrication mechanism, the MPA with thiol groups were modified on gold surface using self-assembly method. The well-ordered monolayers were formed after dipping the electrode into MPA solution for overnight. Then, the chemical attachment of dicarboxyl-calix[4]arene **22** on MPA/Au was completed through drop-casting modifier solution on electrode surface. In the optimization study, among the supporting electrolytes, KCl was used in the Pb^{2+} detection because it offered the highest current response in detection. The interaction mechanism was investigated in which host–guest interactions occurred between Pb^{2+} ions and the oxygen donor atoms attached at the lover rim of calixarene (as shown in Fig. 17 b). This developed sensor was successfully applied in real sample analysis, yielding sufficient precision, relative standard deviation, and acceptable recovery (Aziz et al., 2018).

In the work of Mei et al. (Mei et al., 2021), thiolated calix[4]arene-modified screen-printed carbon electrode **23** (as shown in Fig. 18 a) was fabricated for Pb^{2+} and Cu^{2+} detection. The sensing platform was found to be more selective towards Pb^{2+} rather than Cu^{2+}. In the study, the highest current response in detecting Pb^{2+} was achieved when the deposition potential was at –1.2 V and deposition time was at 120 s. The current response was dropped at the deposition potential more negative than –1.2 V, which due to hydrogen evolution. Moreover, the reduced of peak current after 120 s of deposition time was because of the surface saturation of the developed electrode. The interaction mechanism was demonstrated in Fig. 18 b in which Pb^{2+} coordinates with the hydroxyl groups located at the lower rim of thiolated calix[4]arene (TC4) through electrostatic interaction and induce complex formation. The innovative developed sensor was successfully applied in Pb^{2+} detection in river water with good recovery value.

4.3.2. Multiple detection of Cr^{3+} and Hg^{2+} using differential pulse voltammetry analysis

The selectivity of **24** (as shown in Fig. 19 a) for heavy metal ions was investigated using both spectroscopic and voltammetric techniques. During the electrochemical measurement, the solutions calix[4]arene derivatives (*NAC4*) solution with metal solution were purged with nitrogen gas for 30 min, and then the analysis was carried out at room temperature while the solution was maintained under a nitrogen atmosphere. The detection was performed using a glassy carbon electrode (GCE). Two peaks were observed on the DPV voltammogram with the addition of Cr^{2+} to the *NAC4* (5,11,17-tris[(1-naphtyl)azo]-25,26,27,28-tetrahydroxy-calix[4]arene) solution, as indicated in Fig. 19 b. The first peak showed almost negligible change, whereas the second peak experienced a quantitative decrease. The current experienced a more significant decrease

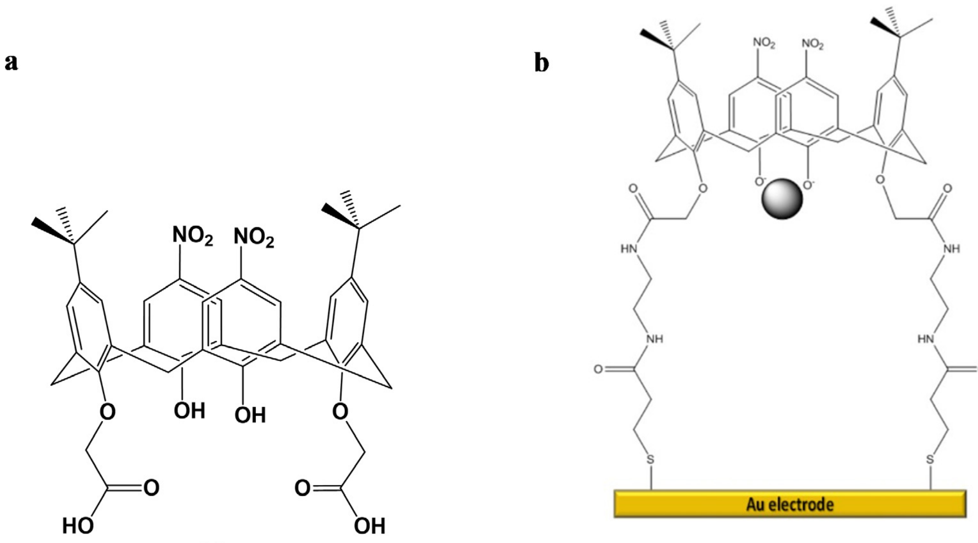

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Fig. 17 **a)** The structure of dicarboxyl-calix[4]arene. **b)** The proposed binding interaction of the COOH–C4 electrode with Pb (II) ion (Bingol, 2010). Copyright Wiley-VCH GmbH. Reproduced with permission.

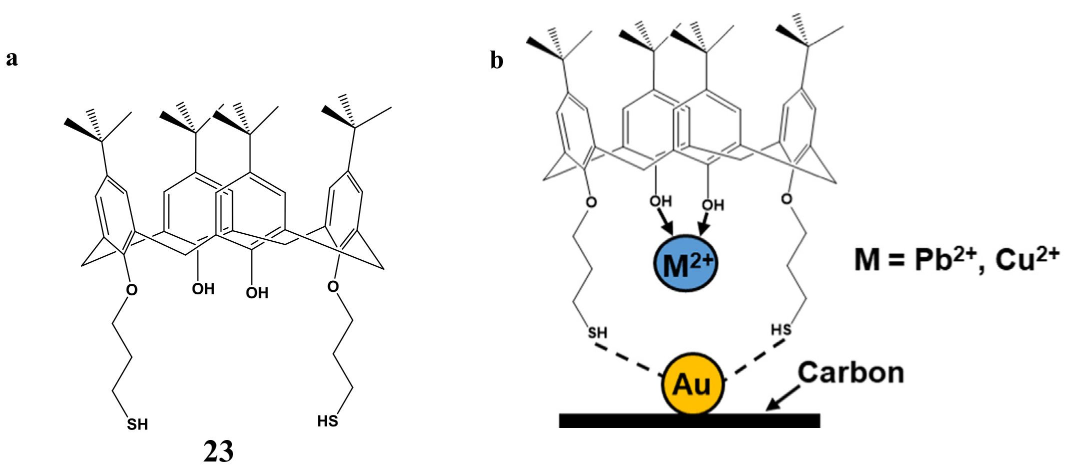

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Fig. 18 **a)** The structure of thiolated calix[4]arene (TC4). **b)** Schematic representation of the binding and complexation mode of TC4/AuNPs/SPCE with Pb^{2+} and Cu^{2+} (Mei et al., 2021).

in the presence of Cr^{3+} (5 eq.) as compared to Hg^{2+} (5 eq.). Hence, calix[4]arene derivative **24** displayed excellent selectivity towards Cr^{3+} in comparison to the other metal ions (Bingol, 2011).

4.3.3. Multiple detection of Cu^{2+}, Fe^{2+} and Zn^{2+} using differential pulse voltammetry analysis

The functionalization of dicarboethoxy-calix[4]arene (EtC4) **25** (as shown in Fig. 20 a) on APTMS/ITO served as a chemical sensor for the simultaneous detection of Cu^{2+}, Fe^{2+} and Zn^{2+}. APTMS/ITO was fabricated via the self-assembly of APTMS on ITO electrodes under nitrogen atmosphere. Then, EtC4 was functionalized on APTMS/ITO electrode by immersing the working electrode into EtC4 solution in room temperature. In the optimization study, NaCl solution was used as supporting electrolytes in comparison with other supporting electrolytes because it has the lowest background current. The effect of immersion time of EtC4 was investigated from 25 to 300 min, and the highest current response was obtained at 180 min. A pronounced peak was observed when EtC4/APTMS/ITO (dicarboethoxy-calix[4]arene/3-aminopropylsilane/indium tin oxide) were used to detect the target ions, while bare ITO only slightly detected the analytes (as shown in Fig. 20 b) because of the weak binding between the metal ions and the negatively charged hydroxyl groups of ITO. In the calibration plot, the anodic peak current increased with increased metal ion concentration. This sensor's detection limit towards individual target analytes (Zn^{2+}, Cu^{2+}, Fe^{2+}) was found to be below the WHO (World Health Organization) permissible value for drinking water, proving that dicarboethoxy-calix[4]arene (EtC4) is a promising electrochemical sensor candidate. In simultaneous detection, the results showed EtC4/APTMS/ITO's pronounced selectivity toward Zn^{2+} compared to Cu^{2+} and Fe^{2+} (Ruslan, 2017).

Table 3 lists a summary list of various calixarene derivative electrochemical sensors and the associated DPV method used for heavy metal ion detection.

4.4. Square wave voltammetry (SWV) technique

Square wave voltammetry (SWV), a special form of DPV, is an advanced technique among the family of pulse voltammetric

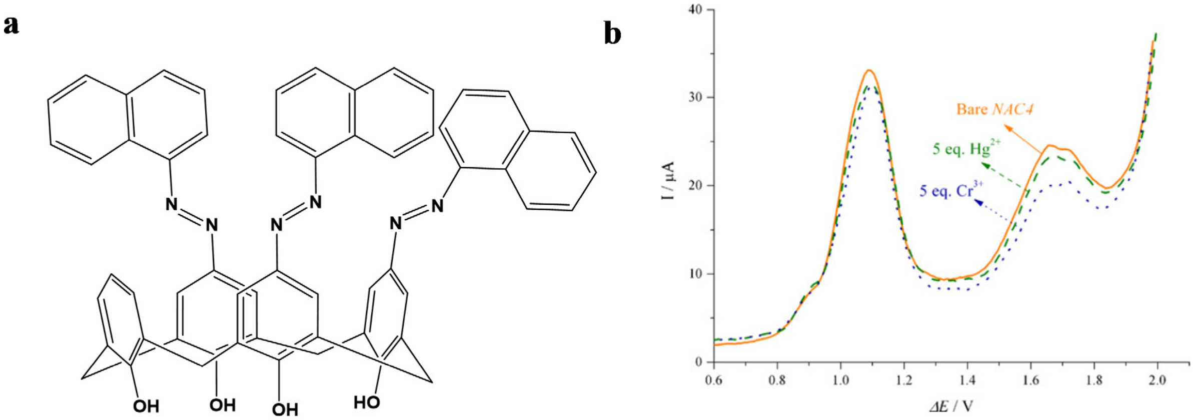

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Fig. 19 **a)** The structure of 5,11,17-tris[(1-naphtyl)azo]-25,26,27,28-tetrahydroxy-calix[4]arene (NAC4). **b)** The differential pulse voltammograms of *NAC4* (1.0×10^{-3} M) and *NAC4* in the presence of Cr^{3+} and Hg^{2+} (5 equivalent) at the GCE with a pulse amplitude of 50 mV (first scan) (Bingol, 2011).

techniques, designed to improve the sensitivity and speed of the analytical measurement (Mirceski, 2019). Moreover, it is the most applicable technique due to its selectivity, accuracy, precision, portability, and low cost (Petovar et al., 2018). Square wave voltammetry (SWV) involves the superimposed repetition of square-shaped potential pulses on a staircase potential sweep, which is efficient for differentiating both faradaic and charging currents. It is a sensitive electroanalytical approach that can determine electroactive analytes up to nanomolar or even picomolar concentrations (Dauphin-Ducharme, 2017). However, as with any technique, SWV also has several drawbacks. First, this technique is fairly complex

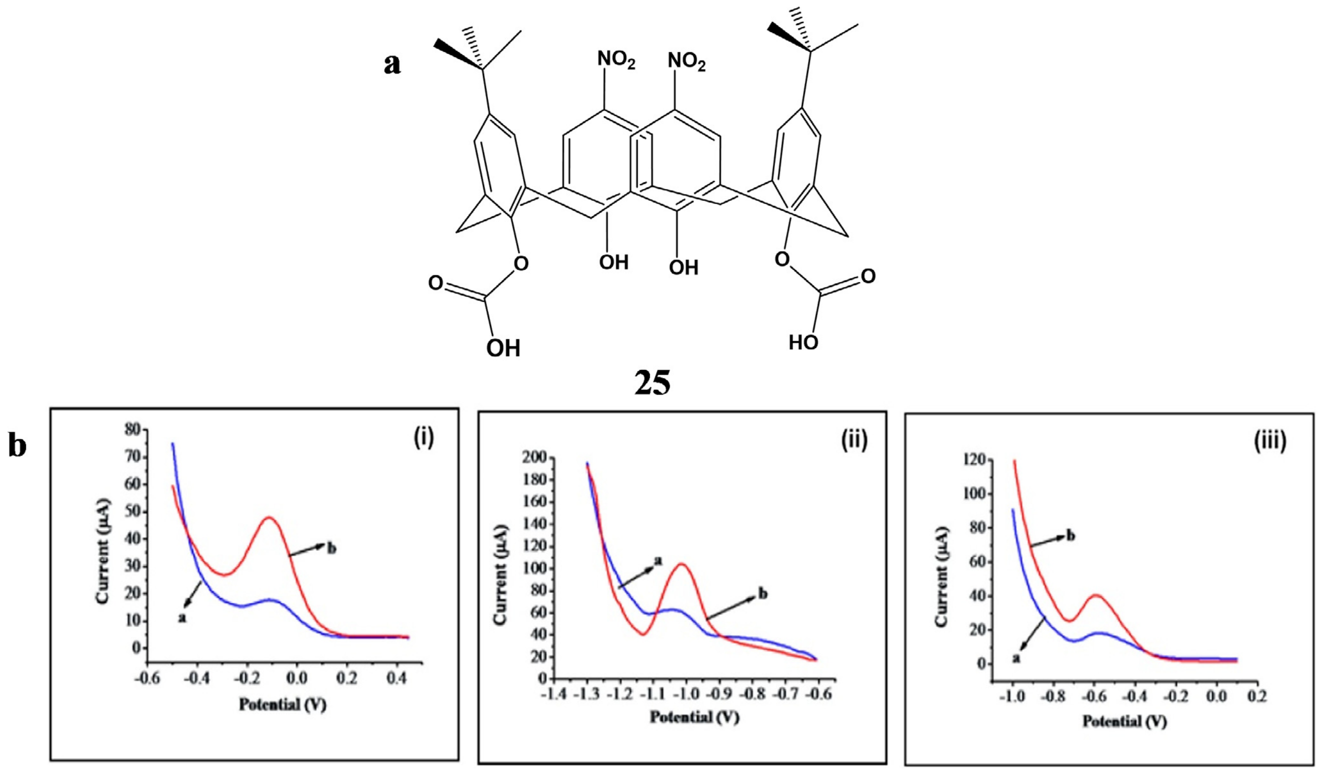


Fig. 20 **a)** The structure of 5,17,dinitro-11,23-ditert-butyl-25,27diethoxycarbonyl-methoxyleneoxy-26,28-dihydroxycalix[4]arene (EtC4). **b)** A comparison of the DPV voltammograms for (a) bare ITO and (b) EtC4/APTMS/ITO in 8 μM of i) Cu^{2+} ii) Zn^{2+} and iii) Fe^{2+} in 0.1 M NaCl, potential vs Ag/AgCl at a scan rate of 100 mV/s (Ruslan, 2017).

Table 3 A list of various calixarene derivative electrochemical sensors and the associated DPV method used for heavy metal ion detection.

No.	Modifier	Analyte	Detection range	Limit of detection (LOD)	Reference
21	benzothiazole azocalix[4]arene (*BTC4*)	Hg^{2+}	1.0×10^{-4} – 1.0×10^{-2} M	–	(Bingol, 2010)
22	dicarboxyl-calix[4]arene	Pb^{2+}	1.35×10^{-6} – 1.21×10^{-5} M *	3.0×10^{-8} M *	(Aziz et al., 2018)
23	thiolated calix[4]arene (TC4).	Pb^{2+}, Cu^{2+}	4.83×10^{-7} M –4.83×10^{-6} M (Pb^{2+}), 1.57×10^{-6} M 1.57×10^{-5} M (Cu^{2+}) **	3.85×10^{-8} M (Pb^{2+}) and 2.1×10^{-7} M **	(Mei et al., 2021)
24	5,11,17-tris[(1-naphtyl)azo]-25,26,27,28-tetrahydroxycalix[4]arene (*NAC4*)	Cr^{2+}, Hg^{2+}	10 – 100 eq	–	(Bingol, 2011)
25	5,17,dinitro-11,23-ditert-butyl-25,27diethoxycarbonyl-methoxyleneoxy-26,28-dihydroxy-calix[4]arene (EtC4)	Cu^{2+}, $Fe^{2+}$and Zn^{2+}	20×10^{-6} M – 800×10^{-6} M	1.50×10^{-13} M (Zn^{2+}), 1.31×10^{-7} M (Cu^{2+}) and 2.06×10^{-8} M (Fe^{2+}) * simultaneously detection of Cu^{2+}, Zn^{2+} and Fe^{2+} ions 9.74×10^{-11} M, 4.62×10^{-5} M and 5.00×10^{-5} M *	(Ruslan, 2017)

and the voltammetric data is more difficult to understand compared to cyclic voltammetry (Mirceski, 2019). Some research works have analyzed heavy metals (cadmium (Cd^{2+}), ferum ions (Fe^{3+}) and lead ions (Pb^{2+})) using calixarene derivative-based sensors and SWV. In general, the pH and incubation times of analytes are the main factors that influence the detection of metal ions using SWASV (Göde, 2017).

4.4.1. Simultaneous detection of Cd^{2+}, Fe^{3+}, Pb^{2+} using square wave voltammetry analysis

Glassy carbon electrode modified with calix[4]arene derivative **26** (as shown in Fig. 21 a) functionalized reduced graphene oxide (CA/RGO/GCE), was found to be highly selective, sensitive, and rapidly detected multiple metal ions and displayed stable performance for long-term usage. This CA/RGO modified GCE demonstrated practicality in the determination of three metal ions in pharmaceutical formulations. As seen in Fig. 21 b, the peak signal (μA) in the voltammogram was proportional to the metal ion concentration between 1.0×10^{-10} M and 1.0×10^{-8} M, with a limit of detection of 2.0×10^{-11} M for all metal ions. Graphene/Graphene-oxide was used for the nanosensor development because it enhances mechanical and electrical properties; while calixarene improves the sensor selectivity towards metal ions via complexation with the metal ions. The synergistic effect between graphene/graphene-oxide and calixarene resulted in high peak signals in the simultaneous detection of metal, such as Cd^{2+}, Fe^{3+}, and Pb^{2+} on CA/RGO/GCE (Göde, 2017).

4.5. Anodic stripping voltammetry (ASV)

Anodic stripping voltammetry (ASV) is a common method to detect heavy metal ions at very low concentrations (Finšgar et al., 2019). Electrochemical stripping techniques incorporated with various electrodes and are acknowledged as one of the powerful tools used in trace analysis (Torma, 2009). This technique can determine several elements simultaneously with concentration levels down to the fractional parts per billion range, using relatively inexpensive and portable instrumentation (Copeland and Skogerboe, 1974; Wang, 2000). Fig. 22 shows the two steps in anodic striping voltammetry measurement. Firstly, the analytical species are electrodeposited on a working electrode, and then oxidized back into the supporting electrolytes. The rate for metals to be deposited reach the electrode surface is determined by the area of electrode used, their respective concentration, and the diffusion properties of the electrolytes solution (Copeland and Skogerboe, 1974). The subsequent stripping step is a crucial step in this analytical procedure that generates the analytical signal (Finšgar et al., 2019). Faradic current was produced after oxidation and measured at the oxidation potential of each analytical species (Copeland and Skogerboe, 1974).

4.5.1. Differential pulse anodic stripping voltammetry (DPASV)

Differential pulse anodic stripping voltammetry (DPASV) is a fine detection technology for trace-level heavy metals, as it

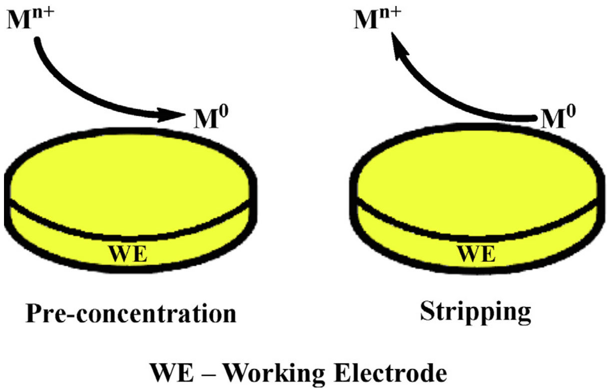
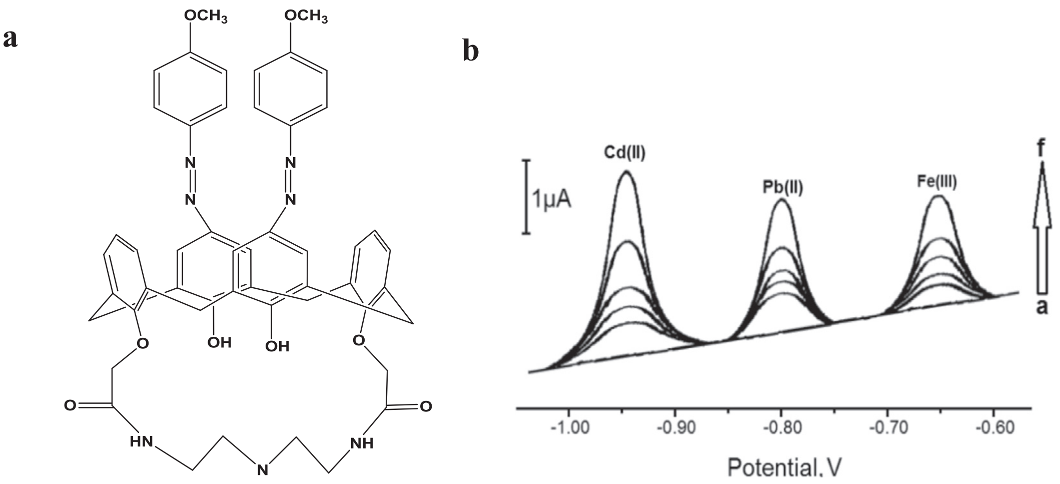


Fig. 22 The principle of anodic stripping voltammetry (ASV) (March et al., 2015).



26

Fig. 21 **a)** The structure of calixarene (CA). **b)** Square wave voltammograms of different heavy metals in ABS (pH 6.0 and incubation time 25 min) at varying concentrations of the blank **(a)** 1.0×10^{-10} M **(b)** 5.0×10^{-10} M **(c)** 1.0×10^{-9} M **(d)** 2.0×10^{-9} M **(e)**, and 1.0×10^{-8} M **(f)** at CA/RGO/GCE (Göde, 2017).

engenders the unique accumulation or preconcentration of analytes species present in the solution. According to these unique advantages, the surface modification of the electrode could result in the increased performance of chemically-modified electrodes (Zhu, 2017). A vast number of research works have determined heavy metals using DPSV as compared to other techniques, not only for individual detection but also for simultaneous detection. The heavy metal ions that were successfully quantified by calixarene derivative-based sensors using this technique involved silver ions (Ag^+), cadmium ions (Cd^{2+}), copper ions (Cu^{2+}), mercury ions (Hg^{2+}), lead ions (Pb^{2+}), and thallium ions (Tl^+). The main factors such as supporting electrolytes, accumulation time, reduction potential, and reduction time are significant for stripping techniques. These parameters influence the detected sensitivity and efficiency of preconcentration (Wang, 2009; Prashanth and Pandurangappa, 2016). Others effect such as modifier suspension volume and pulse amplitude also affect the current signals of analytes (Adarakatti et al., 2019).

4.5.1.1. Differential pulse anodic stripping voltammetry analysis of Ag^+, Cd^{2+}, Cu^{2+}, Hg^{2+}, Pb^{2+}. Glassy carbon electrode coated with Langmuir-Blodgett film of p-*tert*-butylthiacalix[4]arene, LB-TCA/GCE **27** (as shown in Fig. 23) was investigated and found highly selective towards Ag^+ using differential pulse anodic stripping voltammetry. An LB film modified electrode was used in this work, as it enhances the measuring sensitivity of Ag^+. Langmuir-Blodgett technique is useful for forming sequential layers of ultrathin organic films and able to precisely control the thickness and order of a film at the molecular scale. The GCE was modified using direct coating method. The effect of accumulation time of Ag^+ was studied. The result shows peak current increased from 0 to 20 min, and remain constant after 20 min because of the surface saturation. This sensor (LB-TCA/GCE) demonstrated good repeatability. Besides, the response of Ag^+ on LB-TCA/GCE poses little effect after 30 days. A 50-fold Pb^{2+} and Cu^{2+} concentration was found to interfere with the detection of Ag^+ as they competed with Ag^+ to form complexes with TCA at the GCE surface. This research suggested adding a shelter reagent to eliminate the interference from Cu^{2+}, Hg^{2+} and Pb^{2+}. Real samples, including tap, lake, and synthesized water, were analyzed via the standard addition method and the result showed a good recovery percentage (Wang, 2009).

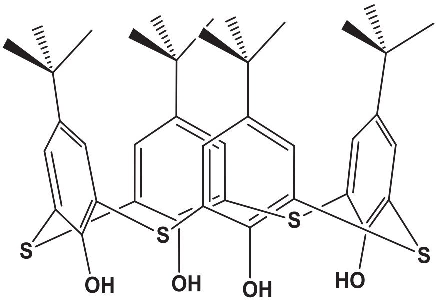


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Fig. 23 The structure of p-*tert*-butylthiacalix[4]arene (TCA) (Wang, 2009).

Calix[4]arene **28** (as shown in Fig. 24), labelled as CAL, was modified on SPCEs for cadmium ions determination by anodic stripping voltammetry using open circuit accumulation. The CAL-SPCEs were developed by dropping 2 μL, 10 mg mL^{-1} of CAL in dichloromethane (DCM) solution onto the electrode surface via micropipette, followed by solvent evaporation at room temperature. The principle of the method comprises the chelation of Cd^{2+} ions with calixarene modified SPCE at the open circuit. At the closed circuit, the accumulated Cd^{2+} ions are reduced to Cd^0 and form a thin film on SPCE surface. Finally, reduced Cd^0 undergo electrochemically strip back into the solution in the form of Cd^{2+} using differential pulse waveform. The resulting oxidation peak current was then displayed as the analytical signal. This sensor successfully accumulated Cd^{2+} at pH 8, 15 min accumulation time with a detection limit 2.8 ng mL^{-1}. Furthermore, it is the first report calixarene-based sensor for the trace determination of cadmium ions in real environmental water samples, namely river water (Honeychurch, 2002).

Calix[4]arene **29** (as shown in Fig. 25) modified carbon paste electrode was used to determine Cu^{2+} by the accumulation of Cu^{2+} ions at an open circuit in the stirred solution with 10 min preconcentration time. The results revealed that an increase in calix[4]arene ligand percentage increases the accumulated amount of metal ions. However, poor reproducibility was observed in higher percentage of ligand. The increase in accumulation time led to an increase in analytical signals, thus resulting in lower detection limits of Cu^{2+}. The copper signals also increased with stirring rate, and slow down until maximum accumulation of Cu^{2+} reached. The sensitivity of the sensor is retained for three months without significant changes, proving the chemical stability of the calixarene ligand. To prevent oxidative or hydrolytic cleavage of the ligand in atmospheric conditions, it was recommended that the sensor be stored in a desiccator. In a real application, a standard addition method was applied to tap water samples. The dilution of the samples gave a closer response to the pure aqueous solution as the matric effects and ionic strength of the solution had

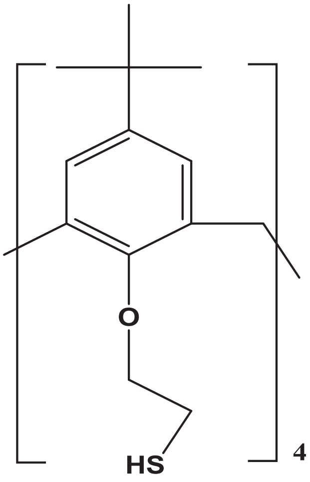

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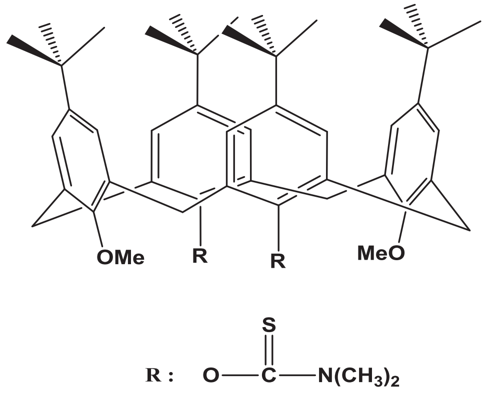
Fig. 24 The structure of (5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(2-mercaptoethoxy)-calix[4]arene) (Honeychurch, 2002).



29

Fig. 25 The structure of *p-tert*-butyl-2,4-dimethoxy-1,3 [(dimethyl-thiocarbamoyl)oxy] calix[4]arene (Canpolat, 2007).

decreased, thus enhancing the accumulation of Cu^{2+} (Canpolat, 2007).

Calixarene derivatives **30**, **31**, and **32** (as shown in Fig. 26) are selective toward Hg^{2+}. Amino-thiacalix[4]arene **30** modified graphitic carbon on screen-printed graphite electrodes was developed using a microwave-irradiation process. The carboxylic groups were induced on the electrode via microwave-irradiation process, providing an ease platform for the anchoring of amino-thiacalix[4]arene via amide bond formation on screen-printed electrodes. Amino-thiacalix[4]arene was synthesized as mercury sensing due to the potential of carbonyl oxygen and amide nitrogen as donor atoms. The interaction mechanism is predicted to be through the thiolate ion and the lone pairs of electrons present on the nitrogen and oxygen atoms (as shown in Fig. 27). Hence, due to its features, the covalently modified amino-thiacalix[4]arene interface was able to detect mercury at trace level concentrations (pico molar). In the recovery study, known concentrations of standard solution were spiked into the samples and the results validated the employment of the proposed sensors in real applications (Adarakatti et al., 2017).

Amino-calix[4]arene **31** modified a graphitic composite glassy carbon electrode as a sensing probe for Hg^{2+}. The graphite material was underwent microwave irradiation to induce COOH functional groups on its surface in the presence of low concentrated nitric acid. Therefore, the introduction of carboxyl groups on graphite materials are easier for further immobilization of amino-calixarene moieties to graphite surfaces through amide bond formation. Preconcentration time was studied in this work to obtain better current response because it promotes the accumulation of mercury ions on the modified electrode interface, known as the chelating phenomena. This proposed interface was successfully applied to real sample matrices such as chrome plating, lake water, and industrial effluents. Moreover, this proposed interface was validated as an alternative sensor, which displayed better results compared to other existing sensors (Prashanth and Pandurangappa, 2016).

The fabricated electrode of Langmuir-Blodgett film with calixarene **32** showed superior sensitivity and reproducibility for both preconcentration and stripping analysis of Hg^{2+} ions in water. The various steps involved in analysis process are as follows:

i) Preconcentration step:

$\text{allyl (surface)} + Hg^{2+} \rightarrow \text{allyl-}Hg^{2+}$

ii) Reduction step:

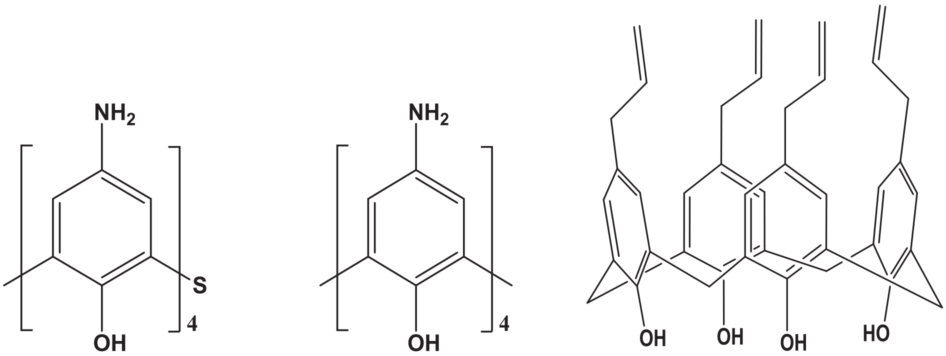
$\text{allyl-}Hg^{2+}\text{ (surface)} \rightarrow \text{allyl} + Hg^{0}\text{ (surface)}$

iii) Stripping step:

$Hg^{0}\text{ (surface)} \rightarrow Hg^{2+}\text{ (solution)} + 2e$

In mercury detection, the LB film coated electrode was found to give higher peaks compared to the direct coating method of calixarene **32**. This may occur because the number of active groups outside of the surface of the electrode is higher than the electrodes in the direct coated method. The allyl groups at the upper rim of calixarene **32** is important in mercury ion recognition. This is because this study found that the modification of *p-tert*-butylcalixarene on LB film is not be able to recognize soft metal ions, meaning that benzene rings were not involved in the mercury recognition process. This fabricated electrode has great potential for practical sample analysis such as tap, lake, and river water with good recoveries for the determination of mercury (Dong, 2006).

Calixarene **33** and **34** (as shown in Fig. 28) were selective toward Pb^{2+}. Calix[4]arene-tren (Calix-tren) **33** modified glassy carbon (GC) electrode was fabricated for the quantification of lead ions. The modification was performed by immers-



30 **31** **32**

Fig. 26 The structure of **30)** amino-thiacalix[4]arene (Adarakatti et al., 2017) **31)** amino-calix[4]arene (Prashanth and Pandurangappa, 2016) **32)** p-allylcalix[4]arene (Dong, 2006).

ing the clean bare GCE into the modifier solution containing 0.2 mg/mL Calix-tren in chloroform, 10.0 mM ethylene diamine (EDA), 2.0 mM 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC), and 5.0 mM N-hydroxy succinimide (NHS) in dimethyl sulfoxide (DMSO) for 1 h, followed by air drying. The results revealed that this modified sensor pro-

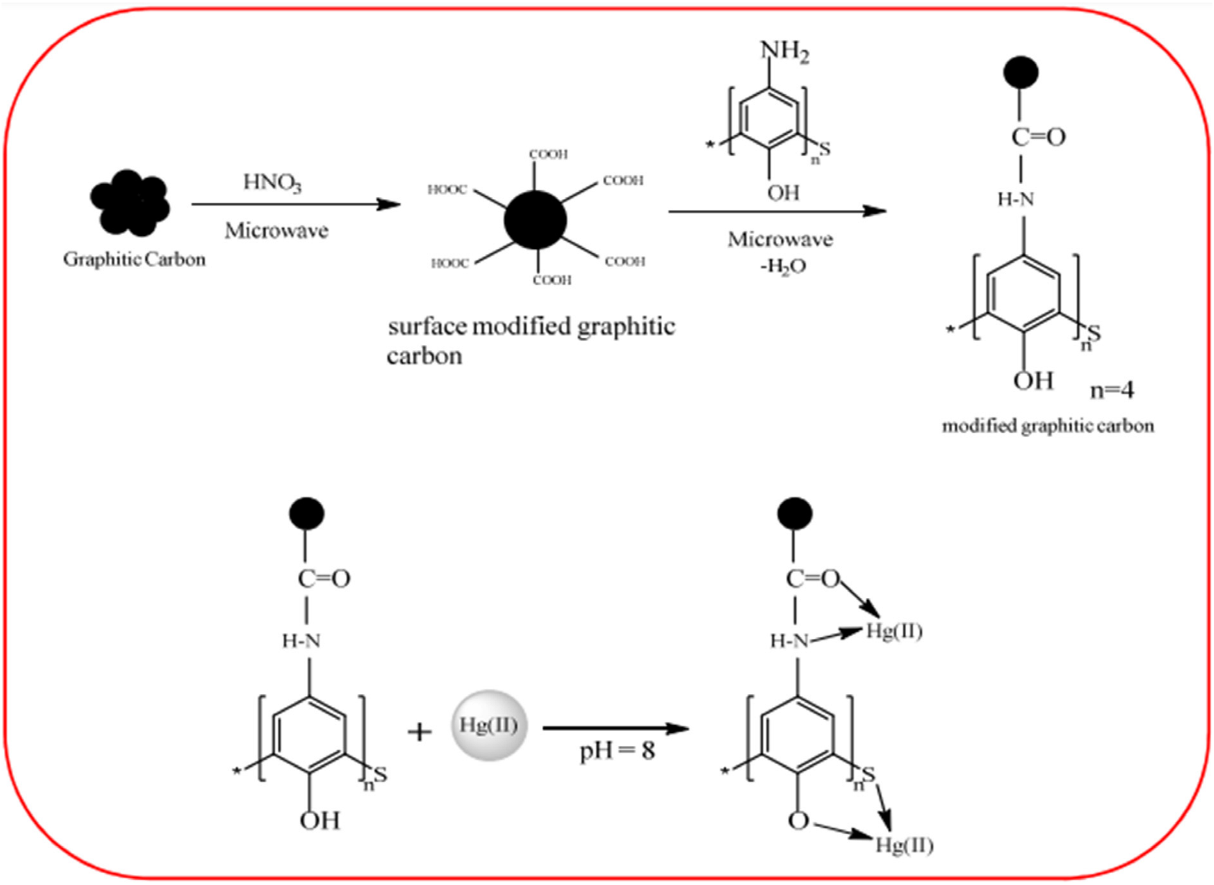
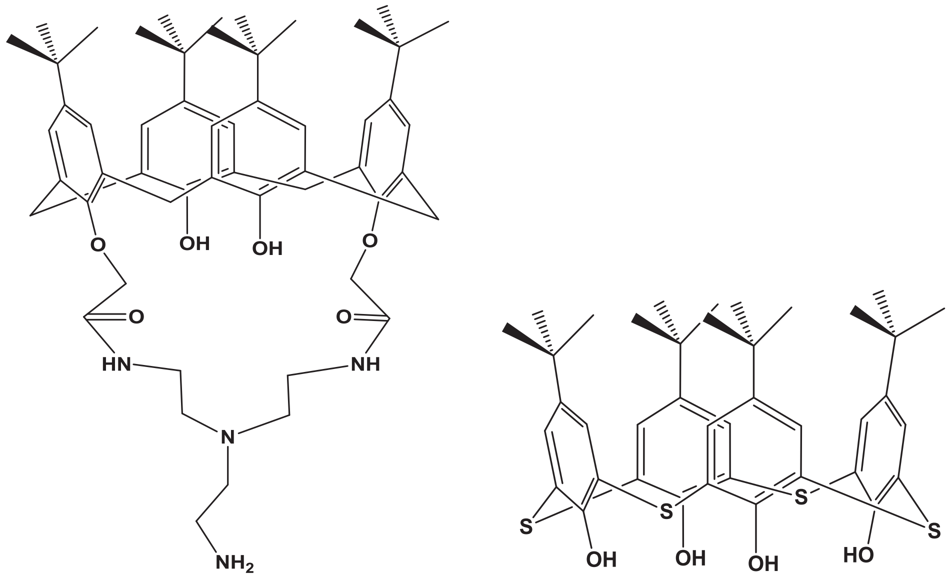


Fig. 27 Schematic representation of the binding and complexation modes of the modifier with the analyte (Adarakatti et al., 2017).



33 **34**

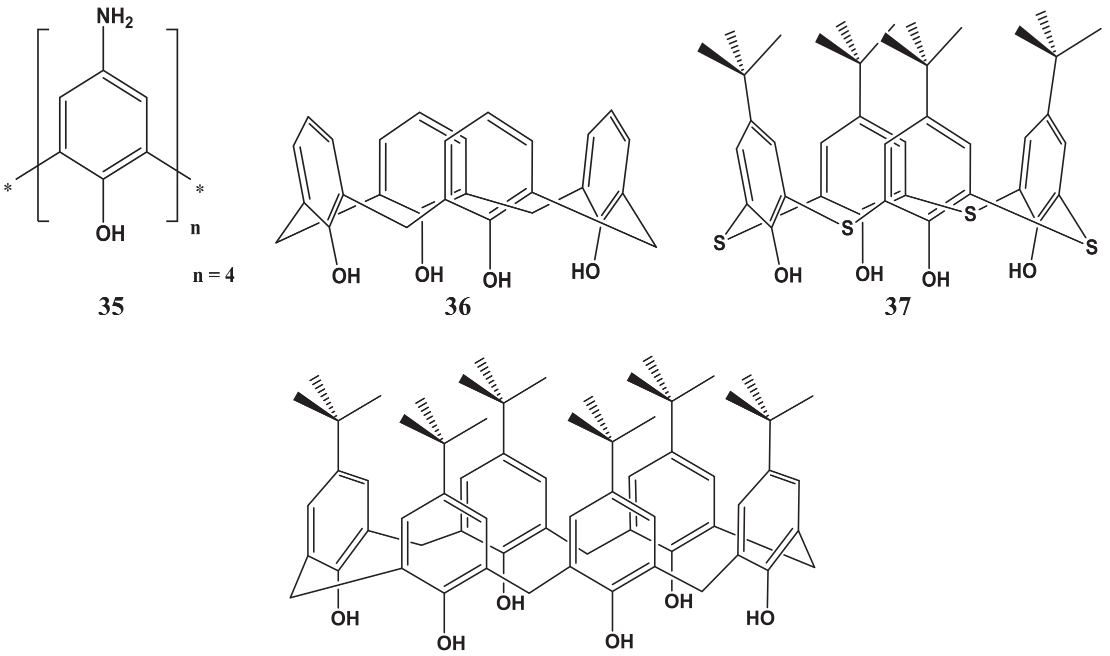
Fig. 28 The structure of **33)** Calix[4]arene-tren (Calix-tren) (Adarakatti et al., 2017) **34)** thiacalixarene (TCA) (Wang, 2012).

vides a better electron transmission pathway compared to bare glassy carbon electrodes. The detection limit of the sensor towards lead ions is 0.11 μM. It was found that the presence of competitive ions caused little effect on lead ion determination. This developed sensor was successfully applied in the analysis of real samples of wastewater. The proposed sensor has advantages of being low cost, good selectivity, and reproducibility in lead ions quantification under the optimum conditions of pH 7, −1.2 V, and 120 s (Kocer, 2019).

The combination of thiacalix[4]arene **34** with superior selective recognition and multi-walled carbon nanotubes (MWCNTs) with outstanding electronic properties in electrode modification displayed outstanding selectivity and sensitivity toward Pb^{2+} ions. The introduction of carbon nanotubes (CNTs) as a new coating material in this study is due to their high conductivity which can counteract the poor conductivity of calixarenes, significantly improving the electrochemical signals, and minimizing the detection limit. The electrode was modified by introducing TCA-MWCNTs into acetone, followed by MCNTs sonication to aid the dissolution of the functionalized MNCTs. In the last step, the sonicated solution was casted directly onto the electrode using micro-injector. The TCA functionalized MCNT-modified electrodes are highly selective towards Pb^{2+} ions with a detection limit of 4×10^{-11} M. The low detection limit may be ascribed to the excellent electronic properties of MWCNT and the outstanding recognition ability of the TCA ligand. The separate signal produced when analysing the solution containing both interfering ions, Sn^{2+} and Pb^{2+} may also be due to the excellent recognition of thiacalixarene **34**. In this study, the mechanism of the stripping voltammetric measurement was proposed. Initially, at open circuit conditions, Pb^{2+} ions are accumulated from the solution phase onto the electrode surface via selective complexation with TCA. Then, the Pb^{2+} on the electrode surface were reduced to Pb^0 at applied voltage. The Pb^{2+} was then electrochemically stripped back into solutions by scanning toward the positive potential (Wang, 2012).

4.5.1.2. Simultaneous detection of Cd^{2+} and Pb^{2+} using differential pulse anodic stripping voltammetry analysis. There are several calixarene derivatives that are selective toward Cd^{2+} and Pb^{2+} including **35**, **36**, **37**, and **38** (as shown in Fig. 29). The amino-calix[4]arene-derivative **35** was modified on a graphitic carbon electrode to perform simultaneous quantification of Cd^{2+} and Pb^{2+} ions at a picomolar level. The selectivity of the amino-calixarene-modified electrode was primarily examined using cyclic voltammetry (CV) to understand the potential affinity of sensors towards Cd^{2+} and Pb^{2+}. The peak potential displayed in the stripping analysis shows that it is located at a more negative potential than the cyclic voltammetry because of the complexation phenomenon between metal ions and ligand molecules (CO-NH groups in the modifier molecule) (as shown in Fig. 30). The excellent detection limits using this developed sensor may be due to the complexation of Cd^{2+} and Pb^{2+} with the hydroxyl groups (lower rim) and amide groups (upper rim) of calixarene during the stripping study. This developed sensor has been successfully applied to determine Cd^{2+} and Pb^{2+} levels in alloy materials, battery effluents, and sewage water sample matrices (Adarakatti and Malingappa, 2016).

Calix[4]arene **36** functionalized Mn_3O_4NPs were used as electrochemical sensors for the simultaneous measurement of Cd^{2+} and Pb^{2+} ions at a nanomolar level by differential pulse anodic stripping voltammetry. In cyclic voltammogram of glassy carbon electrode (GCE), calix[4]arene functionalized Mn_3O_4NPs modified GCE poses a higher peak current than



35 **36** **37**

38

Fig. 29 The structure of **35)** amino-calixarene (Adarakatti and Malingappa, 2016) **36)** calix[4]arene (Adarakatti et al., 2019) **37)** *p-tert*-butylthiacalix[4]arene (Zheng, 2007) **38)** calix[6]arene (Xiao-bo, 2004).

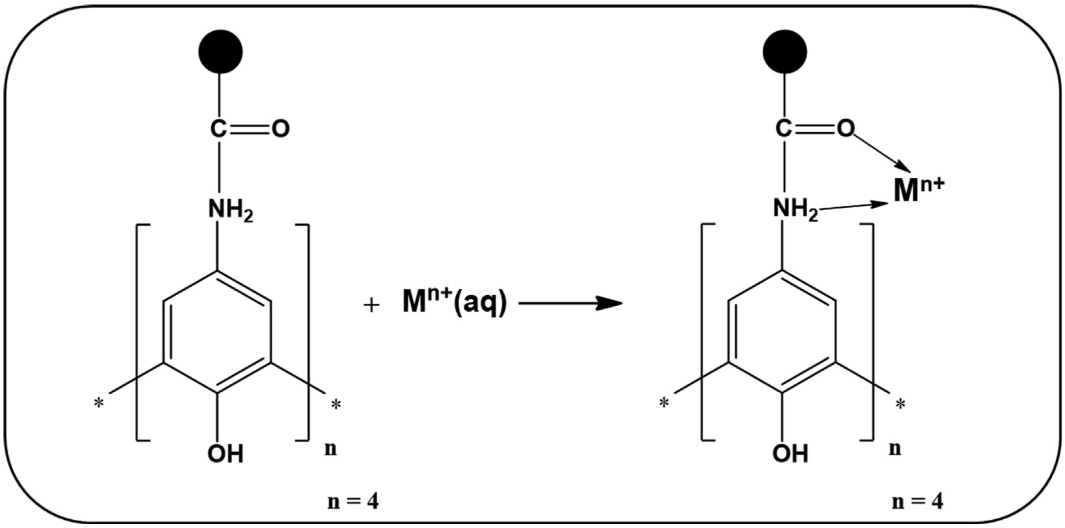


Fig. 30 Schematic representation of binding and complexation mode of modifier with analyte (Adarakatti and Malingappa, 2016).

the calix[4]arene **36** and Mn_3O_4 modified GCE under identical conditions, and at a similar anodic and cathodic peak potential. The improvement in electrochemical response is due to the functional groups with cavity and a high surface to volume ratio. The wide surface area and high porosity of calix[4]arene allow Cd^{2+} and Pb^{2+} ions to access cavities and wide internal surfaces boosted the complexation between Cd^{2+} and Pb^{2+} ions and the surface of the calix[4]arene functionalized Mn_3O_4-NPs. For the electrode modification, 5 µL of modified suspension volume was selected as the optimum volume because higher amount of modifier suspension will increase the resistance of modified film against mass transfer of analytes and electron transfer. In the calibration plot of Pb^{2+}, the result demonstrated an incomplete oxidation process, which may due to the insufficient or incomplete optimized parameter for Pb^{2+} to get oxidized. The application of this sensor to detect Cd^{2+} and Pb^{2+} is verified in the water samples of wood's alloy and lead-acid battery, and it is in good agreement with the standard protocol (Adarakatti et al., 2019).

A disposable sensor, glassy carbon electrode modified Langmuir-Blodgett film of *p*-*tert*-butylthiacalix[4]arene (LB_{TCA}-GCE) **37** was fabricated for quantification of cadmium and lead ions. The voltammogram shows two-well-defined stripping peaks appearing at the LB_{TCA}-GCE. The large difference between Cd^{2+} and Pb^{2+} stripping peak potential (210 mV) proposes LB_{TCA}-GCE suitable to perform simultaneous detection (as shown in Fig. 31). The recognition of metal ions can be explained by the hard and soft acid and base (HSAB) principle. Accordingly, oxygen and sulfur atoms attached to calixarene are soft bases, Cd^{2+} and Pb^{2+} are soft acids, because of that the presence of Cd^{2+} and Pb^{2+} giving notable signals on the LB_{TCA}-GCE electrode. This method holds promise for simultaneous detection of Cd^{2+} and Pb^{2+} in natural water samples with superb average recoveries and good matching with the results obtained using FAAS technique (Zheng, 2007).

In this present work, calix[6]arene modified carbon paste electrodes (CAL-CPEs) **38** were used to detect Pb^{2+} and Cd^{2+} simultaneously with high sensitivity, low detection limit, good reproducibility, and able to determine Pb^{2+} and Cd^{2+} in water samples. The results demonstrated the difference of stripping peak potential between Pb^{2+} and Cd^{2+} is 240 mV, which revealed the potential of this modified electrode to perform simultaneous detection of Pb^{2+} and Cd^{2+} using DPSV. The weight ratio of calix[6]arene (20%) to carbon powder was the optimum loading. The higher loading of calix[6]arene decreased the peak current as higher loading calix[6]arene causing fewer ions to arrive into the inner binding sites for the reduction to M^0. The notable drop in signal is related to the reduction of conductivity of modified electrode because of the rising of resistance at the CAL-CPE. The calix[6]arene

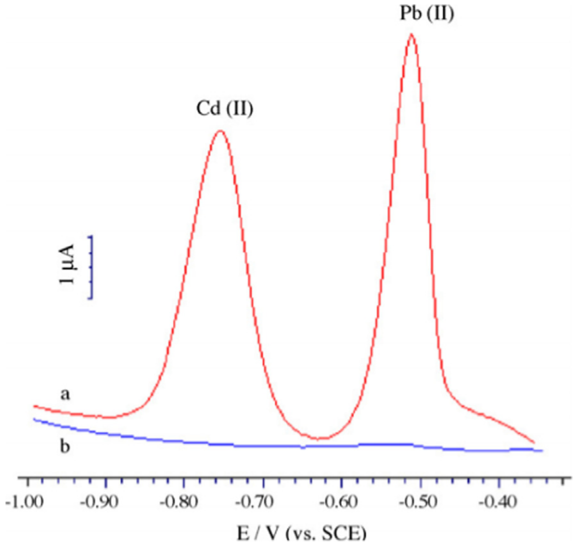
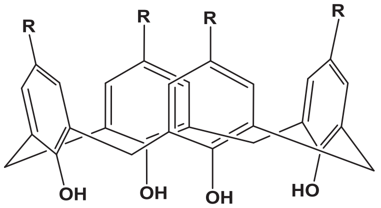


Fig. 31 Differential pulse voltammograms of 1×10^{-6} mol l^{-1} Pb^{2+} and Cd^{2+} in 0.1 mol l^{-1} acetate buffer at different glassy carbon electrodes: **(a)** bare glassy carbon electrode; **(b)** LB_{TCA} modified glassy carbon electrode. Accumulation time, 5 min; accumulation potential, −1.2 V; differential pulse amplitude, 50 mV; scan rate, 50 mV s^{-1}; pulse duration, 40 ms (Zheng, 2007).

modified carbon paste electrode has great potential for practical sample analysis as its recoveries are fine enough for practical use and the results were very close with the results analyzed by atomic absorption spectroscopy (AAS) (Xiao-bo, 2004).

4.5.1.3. Simultaneous detection of Cd^{2+} and Tl^{+} using differential pulse anodic stripping voltammetry analysis. Langmuir-Blodgett film of p-allylcalix[4]arene **39** (as shown in Fig. 32) (AllylCA-GCE) was designed for the simultaneous detection of cadmium and thallium ion traces by using differential pulse anodic stripping voltammetry. LB film was developed by spreading the solution (1–2 mg of compound **39** dissolved in dichloromethane) onto a pure water surface via syringe, followed by 30 min evaporation of spreading solvent. Finally, the LB film was obtained through the horizontal deposition method and coated on a glassy carbon electrode. The mechanism involved in ion detection is the chelation of Cd^{2+} and Tl^{+} ions from solution on the surface of AllylCA-GCE, followed by the reduction of accumulated Cd^{2+} and Tl^{+} ions, and eventually the reductive materials were electrochemically stripped back into the electrolyte solution. KH_2PO_4 buffer (potassium dihydrogen phosphate buffer) was employed throughout the experiment as the highest oxidation peak current was obtained, the lowest background current, and the simultaneous oxidation peak shape was well separated. This research suggested that the sensitivity of detection for low concentrations of analytes can be enhanced by increasing the preconcentration time. The proposed voltammetric sensor can be applied to determine Cd^{2+} and Tl^{+} ions in lake and tap water (Dong, 2006).

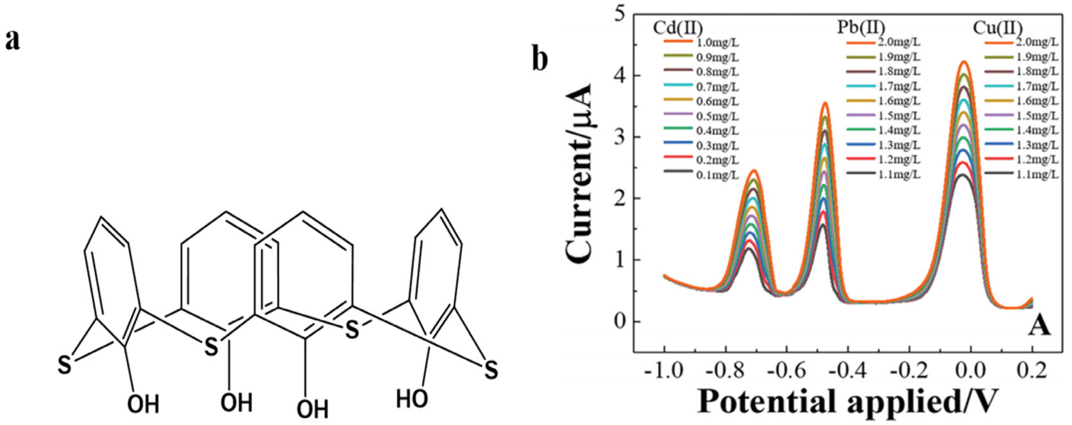


1 R = *tert-Butyl*
2 R = allyl
39

Fig. 32 The structure of p-*tert*-butylcalix[4]arene and p-allylcalix[4]arene (Dong, 2006).

4.5.1.4. Simultaneous detection of Cd^{2+}, Cu^{2+} and Pb^{2+} using differential pulse anodic stripping voltammetry analysis. Thiacalix[4]arene (TC4A) **40** (as shown in Fig. 33 a) modified electrode was successfully applied in the simultaneous detection of Cu^{2+}, Cd^{2+}, and Pb^{2+} in a sample solution and individual detection in a river water sample. TC4A was directly coated onto the glassy carbon electrode and dried at room temperature, forming a continuous uniform film on the electrode surface. The immobilization of TC4A onto the electrode surface is through electrostatic action and Van der Waals force. The coating of TC4A on the glassy carbon electrode was able to detect Cu^{2+}, Cd^{2+} and Pb^{2+} with DPASV curves present at – 0.03 V, – 0.79 V and – 0.55 V, respectively, and the peak current value increased linearly with the concentration (as shown in Fig. 33 b). The complexation ability of TC4A to gather three kinds of heavy metal ions in the solution and deposited it on the TC4A-GCE surface with large quantities may contribute to the simultaneous detection of these target analytes (Cu^{2+}, Cd^{2+}, and Pb^{2+}). The number of heavy metal ions deposited at the TC4A-GCE surface was limited because of the competitive reaction of different heavy metal ions in which complexation priority of this sensor with heavy metal is based on electron arrangement. In a real application, the results obtained by this proposed method and AAS are in good agreement (Liu et al., 2019).

4.5.1.5. Simultaneous detection of Cu^{2+}, Hg^{2+} and Pb^{2} using differential pulse anodic stripping voltammetry analysis. Calix[4]arene bulk **41** (as shown in Fig. 34 a) modified screen-printed electrodes (SPCCEs) as a one-shot disposable electrochemical sensor was successfully applied in the simulta-



40

Fig. 33 **a)** The structure of thiacalix[4]arene (TC4A). **b)** DPASV responses of the TC4A-GCE for the simultaneous determination of different concentrations of Cu (II), Cd (II), and Pb (II) mixed heavy metal ions in a 0.1 mol L^{-1} pH 5.0 acetic acid solution. The concentrations of the heavy metal ions from curve-1 to curve-10 were: 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0 mg L^{-1} for Cu (II) and Pb (II); and 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0 mg L^{-1} for Cd (II), respectively. The experiment was performed under the optimal conditions: deposition potential 1.1 V, deposition time 180 s, pulse amplitude 50 mV (Liu et al., 2019).

neous determination of toxic metal ions including copper, mercury, and lead ions in environmental samples. Multiple peaks were observed in the simultaneous quantification of Cu^{2+}, Hg^{2+} and Pb^{2+} (as shown in Fig. 34 b) due to non complexed analytes trapped on the modified SPCCEs surface or the leaching of the modifier molecule, while the different of intercept of Cu^{2+} and Hg^{2+} in comparison with Pb^{2+} illustrated kinetic limitation. A very tiny volume of real samples (15 – 25 μL) was used in the application study of real sample matrices. This fabricated sensor was tested in sensing target ions present in environmental samples (industrial effluents and wastewater samples) and further validation was conducted using the atomic absorption spectrometric technique. The results verify that this proposed protocol is in good agreement with the standard method (Adarakatti, 2017).

Table 4 illustrates the summary list of various calixarene derivatives electrochemical sensor in relation to differential pulse anodic stripping voltammetry method in heavy metal ion detection.

4.5.2. Square wave anodic stripping voltammetry (SWASV)

Square wave anodic stripping voltammetry (SWASV) is a typical type of ASV with various applications in medicinal and sensing detection. It has the advantages of being cost-effective, has low detection limits, and allows simultaneous analysis (Pizarro, 2019). SWASV employs a similar potential waveform to that of differential pulse voltammetry. It provides high sensitivity and speed of analytical measurement (Mirceski, 2019). This technique differs from differential pulse anodic stripping voltammetry as there are only marginal losses in sensitivity (high detection limit), and it provides faster scanning speeds that lead to faster experiments (30 s vs 3 min) (Islam and Channon, 2020). This technique consists of two steps which are the accumulation of trace elements onto the electrode surface, and the electrochemical stripping of the element that has accumulated on the electrode surface (Li, 2016). By considering these two steps, the modification of the working electrode surface using suitable materials, with properties for the easy adsorption and stripping of heavy metal ions, is crucial for sensitive electrochemical detection (Li, 2016).

There are some heavy metals such as copper ions (Cd^{2+}), lead ions (Pb^{2+}), and thallium ions (Tl^{+}) that were determined by calixarene derivatives-based sensor using square wave anodic stripping voltammetry technique. The main factors such as pH, concentration of modifier agent, accumulation potential, accumulation time, and supporting electrolytes influence the detection of metal ions using SWASV (Torma, 2009; Pizarro, 2019; Zou, 2012; Zou, 2009). Accumulation potential and time are vital in stripping techniques as they have significant effects on the detection sensitivity (Zou, 2012).

4.5.2.1. Square wave anodic stripping voltammetry analysis of Cu^{2+} and Pb^{2+}. Calixarene **42** and **43** (as shown in Fig. 35) are selective toward Cu^{2+}. The modified electrode with calix[4]arene derivative **42** and its optimal experimental conditions was successfully applied in various bivalve mollusks samples with satisfactory results. The modified electrodes were fabricated by drop-coating calixarene derivative **42** on the electrode surface, followed by solvent evaporation at room temperature for 5 min. The preconcentration capacity of the electrochemical sensor was enhanced owing to the chemical linkage of organometallic fragment cyrhetrenyl to lower rim of calixarene macrocycles, thus providing a new platform to carry out rapid and sensitive analyses in quantified Cu^{2+} in marine resources. The increase in current of the modified electrode for Cu^{2+} quantification may be due to the increase in the number of active sites caused by the two OH groups of the calix[4]arene and two imine unsaturated spacers that connect the two fragments, which enhanced the electrostatic interaction with Cu^{2+} ions. In Cu^{2+} detection, the optimum current was observed at pH 4. However, the current decreased at lower pH which probably due to the decomposition of the compound. This proposed method is effective in detecting Cu^{2+} in real bivalve mollusks samples and proposes that the matrix effect does not affect the response of modified electrodes (Pizarro, 2019).

Langmuir-Blodgett film of tetraoxocalix[2]arene[2]triazine (TOCT) **43** was modified on electrodes to analyse traces of copper ions in water samples using a square wave stripping voltammetry (SWSV). From the voltammogram result, a sharp peak was observed using TOCT-GCE. The peak current was further improved when LB_{TOCT}-GCE, Langmuir-Blodgett film of tetraoxocalix[2]arene[2]triazine modified glassy carbon electrode (two layers) was used in the analysis under the same experimental conditions. This may be due to the homogenous

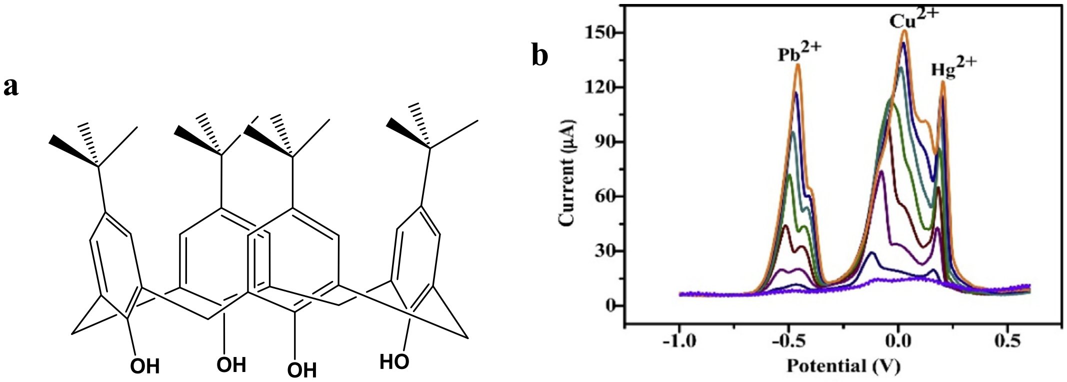


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Fig. 34 **a)** The structure of 25, 26, 27, 28-tetrahydroxy-calixarene. **b)** Overlaid anodic stripping voltammograms of lead (II), copper (II), and mercury (II) with increasing concentration range from 100 to 2400 μg/L. Conditions: accumulation potential – 1.1 V, deposition time 180 s, potential window – 1.0 V to 0.6 V (Adarakatti, 2017).

Table 4 List of various calixarene derivatives electrochemical sensor in relation to differential pulse anodic stripping voltammetry method in heavy metal ion detection.

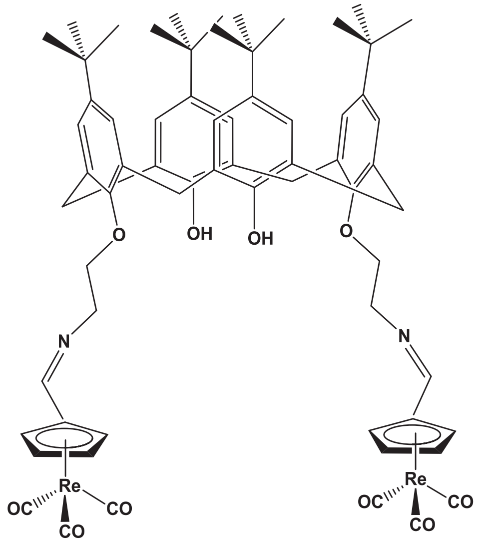
No.	Modifier	Analyte	Detection range	Limit of detection (LOD)	Reference
27	*p*-*tert*-butylthiacalix[4]arene (TCA)	Ag^{+}	5.0×10^{-9}– 2.0×10^{-6} M	3.0×10^{-9} M	(Wang, 2009)
28	(5,11,17,23,tetra-*tert*-butyl-25,26,27,28-tetrakis(2-mercaptoethoxy)-calix[4] arene)	Cd^{2+}	3.11×10^{-9} M *	2.49×10^{-11} M *	(Honeychurch, 2002)
29	*p*-*tert*-butyl-2,4-dimethoxy-1,3 [(dimethyl-thiocarbamoyl) oxy] calix[4]arene	Cu^{2+}	4.72×10^{-8} – 1.57×10^{-6} M *	1.73×10^{-8} M *	(Canpolat, 2007)
30	amino-thiacalix[4]arene	Hg^{2+}	2.0×10^{-12} – 20.0×10^{-12} M	1.0×10^{-12} M	(Adarakatti et al., 2017)
31	amino-calix[4]arene	Hg^{2+}	10.0×10^{-9} – 100.0×10^{-9} M	2.49×10^{-9} M	(Prashanth and Pandurangappa, 2016)
32	p-allylcalix[4]arene	Hg^{2+}	3.49×10^{-10} – 2.00×10^{-7} M *	2×10^{-10} M *	(Dong, 2006)
33	calix[4]arene-tren (Calix-tren)	Pb^{2+}	0.48×10^{-6} – 2.31×10^{-6} M	0.11×10^{-6} M	(Kocer, 2019)
34	thiacalixarene (TCA)	Pb^{2+}	2.0×10^{-10} – 1.0×10^{-8} M	4.0×10^{-11} M	(Wang, 2012)
35	amino-calixarene	Cd^{2+}, Pb^{2+}	10.0×10^{-12} – 120.0×10^{-12} M	3.5×10^{-12} M (Cd^{2+}), 3.3×10^{-12} M (Pb^{2+})	(Adarakatti and Malingappa, 2016)
36	calix[4]arene	Cd^{2+}, Pb^{2+}	4.82×10^{-7} – 8.90×10^{-6} M **	8.01×10^{-8} (Cd^{2+}), 3.38×10^{-8} M (Pb^{2+}) **	(Adarakatti et al., 2019)
37	*p*-*tert*-butylthiacalix[4]arene (TCA)	Cd^{2+}, Pb^{2+}	2.0×10^{-7} – 5.0×10^{-5} M (Cd^{2+}), 1.0×10^{-7} – 2.5×10^{-5} M (Pb^{2+})	2.0×10^{-8} M (Cd^{2+}), 8.0×10^{-9} M (Pb^{2+})	(Zheng, 2007)
38	calix[6]arene	Pb^{2+}, Cd^{2+}	3.0×10^{-8} – 8.0×10^{-6} M (Pb^{2+}), 6.0×10^{-8} – 1.0×10^{-5} M (Cd^{2+})	8.0×10^{-9} M (Pb^{2+}), 2.0×10^{-8} M (Cd^{2+})	(Xiao-bo, 2004)
39	p-allylcalix[4]arene	Cd^{2+}, Tl^{+}	8.90×10^{-8} – 2.67×10^{-6} M (Cd^{2+}), 1.04×10^{-7} – 5.22×10^{-6} M (Tl^{+}) *	1.95×10^{-8} M (Cd^{2+}), 2.09×10^{-8} M (Tl^{+}) *	(Dong, 2006)
40	thiacalix[4]arene (TC4A)	Cu^{2+}, Cd^{2+} and Pb^{2+}	1.57×10^{-5}– 3.15×10^{-5} M (Cu^{2+}), 8.90×10^{-7} – 8.90×10^{-6} M (Cd^{2+}), 4.83×10^{-6} – 9.65×10^{-6} M (Pb^{2+}) *	4.72×10^{-8} M (Cu^{2+}), 3.56×10^{-8} M (Cd^{2+}), 1.21×10^{-8} M (Pb^{2+}) *	(Liu et al., 2019)
41	25, 26, 27, 28-tetrahydroxy-calixarene	Cu^{2+}, Hg^{2+} and Pb^{2+}	4.83×10^{-7} – 3.78×10^{-5} M *	6.29×10^{-7} M (Cu^{2+}), 2.39×10^{-7} M (Hg^{2+}), 1.83×10^{-7} M (Pb^{2+}) *	(Adarakatti, 2017)

The value is converted from unit g/L* and ppb** to M using molar mass of metal.

and stable surface of LB_{TOCT}-GCE that is favorable for the accumulation and selective recognition of copper ions. Furthermore, the cavity and multi-dimensional structure of TOCT on modified electrodes are favorable for copper ion accumulation as TOCT greatly improves the electrode surface area. This proposed method is found to be applicable to quantify copper ions in lake water, drinking water, and city wastewater samples by using a standard addition technique (Zou, 2012).

A calix[4]arene **44** (as shown in Fig. 36) modified sensor was developed by coating calixarene solution and Nafion on a glassy carbon electrode surface, followed by 2 h of solvent evaporation at room temperature. Prior to utilization, this sensor was conditioned in 0.05 M, pH 4.0 potassium phthalate buffer overnight for analytes detection. The modified electrode is applicable for multipurpose usage by cleaning the coating layer of the electrode at a potential of + 0.3 V for 1 min, and then treated in 0.1 M EDTA solution for 2 min to detach the residual metal ions from the polymer layer. In this work with calixarene **44**, ASV contains the accumulation of lead ions onto the electrode surface by complexation with a ligand (ionophore) in an open circuit. Acetate buffer was selected as blank solution in the experiment because the best peak shape and largest stripping current were obtained while performing detection in acetate buffer. In this study, the number of the binding sites on the electrode surface could be enhanced while applying a ligand incorporated-chemically inert polymer. This is the first polymer/ligand modified bismuth-film electrode used to detect Pb^{2+} ions using adsorptive stripping voltammetry. This electrode was successfully used to evaluate the lead concentration in environmental water samples such as tap, and rainwater with good recovery (Torma, 2009).

4.5.2.2. Simultaneous detection of Pb^{2+} and Tl^{+} using square wave anodic stripping voltammetry. The Langmuir-Blodgett film of a p-*tert*-butylcalix[4]arene derivative **45** (as shown in Fig. 37)–modified glassy carbon electrode was fabricated for the simultaneous detection of Pb^{2+} and Tl^{+} using square wave anodic stripping voltammetry. Langmuir-Blodgett film of p-*tert*-butylcalix[4]arene derivative modified glassy carbon electrode (LB_{DCA}-GCE) displayed good response in tracing



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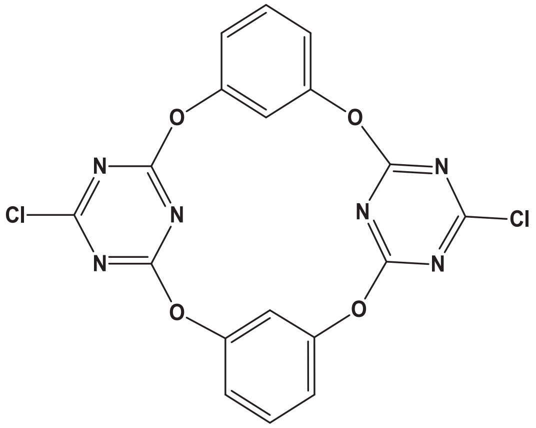

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Fig. 35 The structure of **42)** p-*tert*-butylcalix[4]arene-bis-cyrhetrenylimine (Cy$_2$(Calix[4]) (Pizarro, 2019) **43)** tetraoxocalix[2]arene [2]triazine (TOCT) (Zou, 2012).

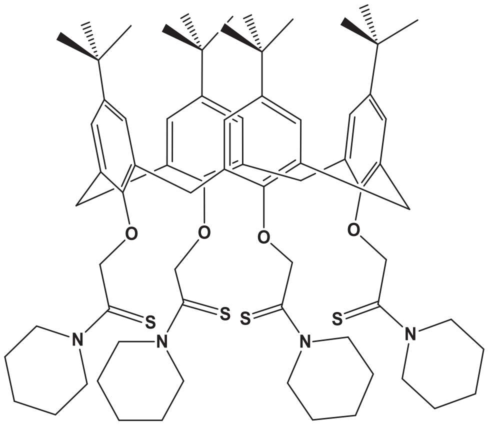
Pb^{2+} and Tl^{+} while no obvious peaks were observed at the bare GCE. One layer of LB$_{DCA}$-GCE showed a higher peak current than two layers of LB$_{DCA}$-GCE in the determination of target ions. This is because LB$_{DCA}$ acts as a bulwark and the R$_{et}$ (reaction resistance) of one layer of LB$_{DCA}$ (1.07 kW) is smaller than that of the two layers (3.02 kW). The DCA attached with LB$_{DCA}$ does not complexation with Pb^{2+} and Tl^{+} but LB$_{DCA}$ functions as a new electrode material by providing a site for Pb^{2+} and Tl^{+} reduction. The mechanisms involved are as follows:

i) Reduction step (accumulation):

$$LB_{DCA}\ (surface) + M^{n+}\ (solution) + n\ e \rightarrow LB_{DCA}\text{-}M^{0}\ (surface)$$

ii) Oxidation step (stripping):

$$LB_{DCA}\text{-}M^{0}\ (surface) \rightarrow LB_{DCA}\ (surface) + M^{n+}\ (solution) + n\ e$$



44

Fig. 36 The structure of calix[4]arene tetrathioamide ligand (Torma, 2009).

The applicability of the proposed method for Pb^{2+} and Tl^{+} detection in tap water and lake water samples was found successful yielding high accuracy and good recovery results (Zou, 2009).

Table 5 provides a summary of electrochemical sensors based on various calixarene derivatives in the determination of Cu, Pb, and Tl metal ions using square wave anodic stripping voltammetry.

4.6. Electrochemical impedance spectroscopy technique

Electrochemical impedance spectroscopy (EIS) is a technique that is used to analyse system and material properties by

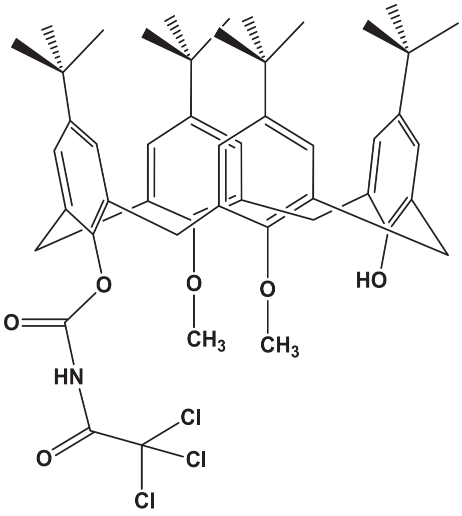


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Fig. 37 The structure of 25,27-Dimethoxy-26-(*N*-trichloroacetyl)carbamoyloxy-*p*-*tert*-butylcalix[4]arene (DCA) (Zou, 2009).

employing alternate electrical signals of different frequencies and measuring the electrical output signals (Alcañiz, 2012). EIS provides information on the electrochemical properties of the surface layers of an individual electrode and other electrochemical phenomena such as the presence of kinetic and/or diffusion control (Finšgar et al., 2019). It is a sensitive and robust technique for investigating the electrical resistance of a system, the sensitivity towards the changes in bulk, and the interfacial properties at the electrode surface (Wu, 2017; Muñoz et al., 2017). EIS is capable of monitoring target substances directly without labeling (Yang, 2012). The modelling of equivalent circuit analogs, also known as the Randles circuit, is shown in Fig. 38. From the equivalent electrical model, the values of the electrical components are obtained using least-squares minimisation fitting of the electrochemical impedance spectroscopy (EIS) spectrum (Hammond, 2016). The variables that are involved in this technique are resistance solution (R_{sol}), charge transfer resistance (R_{ct}), Warburg (Z, considering diffusion processes) and double layer capacitance (C_{dl}) (Islam and Channon, 2020).

This impedance measurement is extensively used in various electrochemistry fields including bio-sensing, solid-state electrochemistry, double-layer studies, electrode kinetics, batteries, and corrosion (Muñoz et al., 2017). Calixarene derivative-based sensor were found to be excellent at quantifying of aluminum ions (Al^{3+}), copper ions (Cu^{2+}), europium ions (Eu^{2+}), mercury ions (Hg^{2+}), nickel ions (Ni^{2+}), and sodium ions (Na^{+}) via electrochemical impedance spectroscopy. In general, factors such as negative overvoltage (electrical parameters), and frequency influence the detection of metal ions using EIS (Sakly, 2002; Ebdelli, 2011).

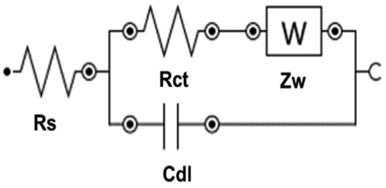
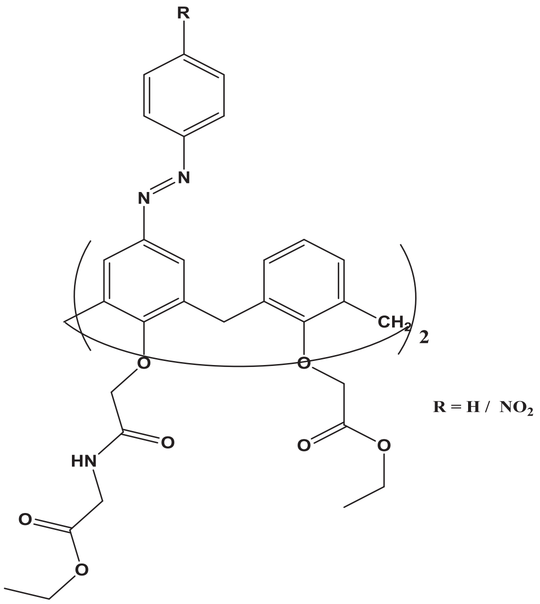


Fig. 38 Equivalent circuit diagram (Randles circuit).



46

Fig. 39 The structure of azo-calix[4]arene (Echabaane, 2017).

4.6.1. Electrochemical impedance analysis of Al^{3+}, Cu^{2+} and Na^{+}

The deposition of azo-calix[4]arene **46** (as shown in Fig. 39)/poly(3,4-ethylenedioxythiophene)/poly-(styrenesulfonate) (PEDOT:PSS) thin film on the indium tin oxide electrode (ITO) surface is highly selective toward Al^{3+}. In the electrode modification, the PEDOT:PSS was spin-casted at 4400 rpm for 30 s from an aqueous solution onto the ITO surface, followed by spin-coating of azocalix[4]arene solution onto the PEDOT:PSS/ITO surface. This study was performed with and without illumination to investigate the effect of light on the amplification of the sensor signal. The light illumination on the electrode with wavelengths shorter than the band gap energy of organic semi-conductors created electron-hole pairs that improved the sensor's reactivity towards target ions. In the impedance spectra of the PEDOT:PSS/ITO and

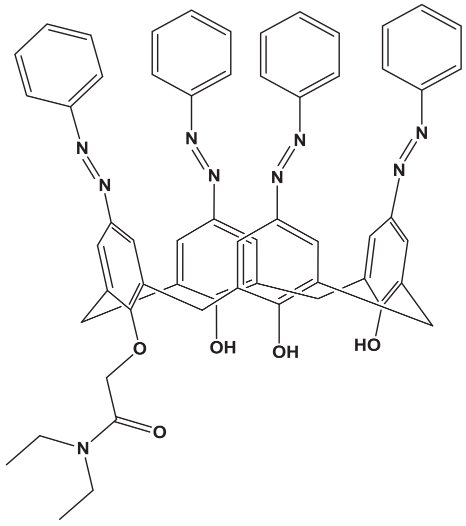
Table 5 List of various calixarene derivatives electrochemical sensor in relation to square wave anodic stripping voltammetry method in heavy metal ions detection.

No.	Modifier	Analyte	Detection range	Limit of detection (LOD)	Reference
42	p-*tert*-butylcalix[4]arene-bis-cyrhetrenylimine (Cy_2(Calix [4])	Cu^{2+}	$1.57 \times 10^{-7} – 2.83 \times 10^{-6}$ M*	4.72×10^{-10} M *	(Pizarro, 2019)
43	tetraoxocalix[2]arene[2]triazine (TOCT)	Cu^{2+}	$2.0 \times 10^{-9} – 1.0 \times 10^{-6}$ M	1.0×10^{-10} M	(Zou, 2012)
44	calix[4]arene tetrathioamide ligand	Pb^{2+}	$0.05 \times 10^{-6} – 0.60 \times 10^{-6}$ M	9.65×10^{-11} M*	(Torma, 2009)
45	25,27-Dimethoxy-26-(*N*-trichloroacetyl)carbamoyloxy-*p*-*tert*-butylcalix [4]arene (DCA)	Pb^{2+}, Tl^{+}	$2.0 \times 10^{-7} – 2.0 \times 10^{-5}$ M (Pb^{2+}), $3.0 \times 10^{-8} – 4.0 \times 10^{-6}$ M (Tl^{+})	8.0×10^{-8} M (Pb^{2+}), 2.0×10^{-8} M (Tl^{+})	(Zou, 2009)

The value is converted from unit g/L* to M using molar mass of metal.

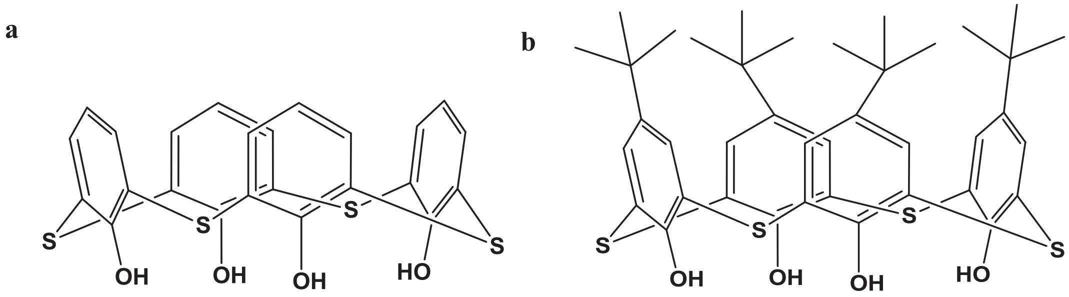
azo-calix[4]arene/PEDOT:PSS/ITO structures, a single semicircle with a large diameter was observed. The broad diameter semicircle shows the overlapping of two semicircles. The first semicircle (at a high frequency range) is due to the thin film bulk. The second semicircle (at a low frequency range) is due to the ion charge transfer at the ITO/aqueous solution interface. From the impedimetric result, the presence of the azo-calix[4]arene film caused a significant decrease in the impedance circle upon the incremental addition of aluminum concentrations. In the presence of light excitation, there was a significant enhancement in the spectra of azo-calix[4]arene/PEDOT:PSS/ITO for Al^{3+} detection as compared to the impedance performed in darkness, thus proving that the sensitivity towards Al^{3+} has been enhanced. Therefore, this study proved that light excitation can amplify signals by enhancing the mobility of the charge transfer and the reaction kinetics and hence resulting in the high sensitivity towards Al^{3+} ion determination (Echabaane, 2017).

A copper chemical sensor was fabricated with thiacalix[4]arene **47** (as shown in Fig. 40 a) thin film using a thermal evaporation technique under vacuum. Thiacalixarene (TCA[4H])-based sensor displayed a large linear range and low detection limit (~10^{-8} M) in copper ion detection as



49

Fig. 42 The structure of 5,11,17,23-tetrakis(phenylazo)-25,27,28-trihydroxy-26-mono[(N,N-diethylaminocarbonyl)methoxy]-calix[4]arene (Ebdelli, 2011).



47

Fig. 40 The structure of **a)** thiacalix[4]arene (TCA[4H]) **b)** *p-tert*-butylthiacalix[4]arene (TCA[4 +]) (Ali, 2006).

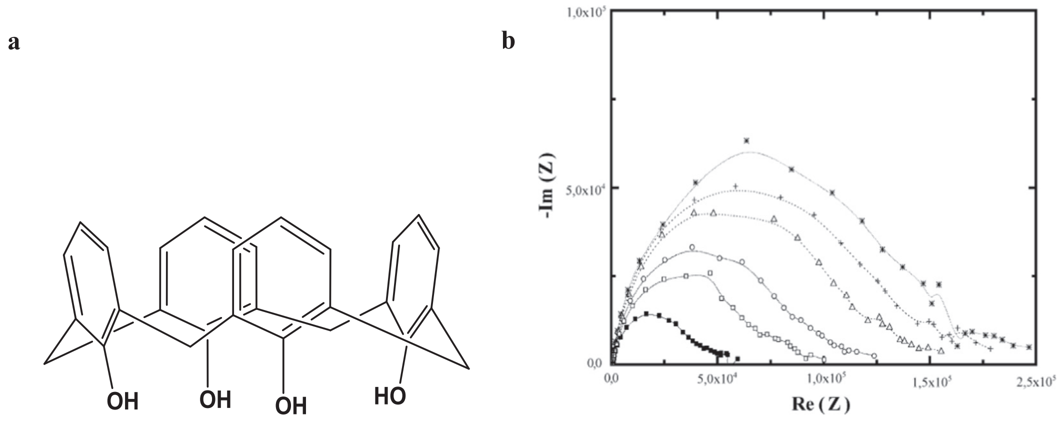


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Fig. 41 **a)** The structure of calix[4]arene. **b)** Evolution of Nyquist spectra vs. concentration of sodium in buffer (Sakly, 2002).

compared to p-*tert*-butylthiacalixarene TCA[4+]-based sensors (as shown in Fig. 40 b). This occurrence may be due to the absence of the *tert*-butyl group contributing to the rigid natural cavity that is able to detect Cu^{2+} ions easily based on the lock and key interaction mechanism (Ali, 2006).

In the work of Sakly et al. (Sakly, 2002), the mode of deposition of the calix[4]arene **48** (as shown in Fig. 41 a) layer on a platinum electrode, and its thickness, produced no effect on sensor sensitivity. A thick and compact enough layer was developed when there was an increase in the ionophore concentration. Platinum was selected for this work because it has good resistance to corrosion, and results in oxidation phenomena in an aqueous media. In the optimal experiment conditions study, it was found that under negative overvoltages 0, − 0.2, − 0.6, and − 0.9 V vs. SCE, the half-circle diameter and Warburg straight line were decreased because of the effect of

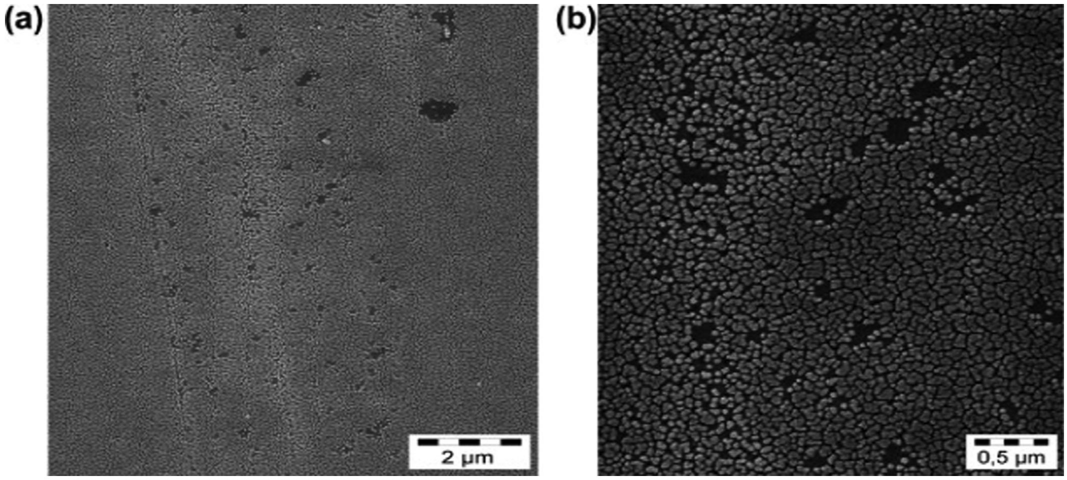

Fig. 43 SEM pictures of azo-calix[4]arene thin film deposited on a gold electrode **a)** at 2 µm, **b)** at 0.5 µm (Ebdelli, 2011).

Table 6 List of various calixarene derivatives electrochemical sensors in relation to electrical impedance spectroscopy method in heavy metal ions detection.

No.	Modifier	Analyte	Detection range	Limit of detection (LOD)	Reference
46	azo-calix[4]arene/poly(3,4-ethylenedioxythiophene)/poly-(styrenesulfonate) (PEDOT: PSS)	Al^{3+}	–	–	(Echabaane, 2017)
47	thiacalix[4] arene (TCA[4H])	Cu^{2+}	over three decades	10^{-8} M	(Ali, 2006)
48	calix[4]arene	Na^{+}	–	10^{-8} M	(Sakly, 2002)
49	5,11,17,23-tetrakis(phenylazo)-25,27,28-trihydroxy-26-mono[(N,N-diethylaminocarbonyl)methoxy]-calix [4]arene	Eu^{2+}, Hg^{2+}, and Ni^{2+}	–	–	(Ebdelli, 2011)

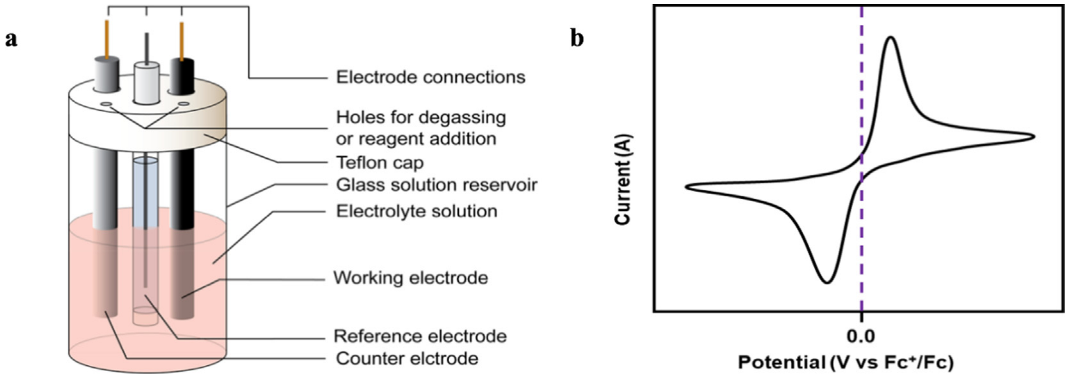

Fig. 44 **a)** Schematic representation of an electrochemical cell for CV experiments. **b)** Voltammogram of the reversible reduction of a 1.0 mM Fc^{+} solution to Fc, at a scan rate of 100 mV s^{-1} (Elgrishi, 2018). https://pubs.acs.org/doi/10.1021/acs.jchemed.7b00361, further permissions related to the material excerpted should be directed to the ACS.

electrical dipole composed by charge-transfer resistance (Rct) and Helmholtz double layer interfacial capacitor (Cdl). In Fig. 41 b, the Nyquist diagram showed that the diameter of the semicircles increased with increased sodium concentration, probably due to the variation in the resistance of the membrane. The half-circles are imperfect because of the different phenomena at the interface of the working and auxiliary electrodes. However, the global appearance was still preserved. This study reveals that the low coverage rates might be due to the bad adhesion of the membrane on the metallic electrode surface besides the poor solubility of calixarene in water. It was also found that the deposition technique causes to weak bonding (Van der Waals) between the ionophores and the transducer.

4.6.2. Multiple detection of Eu^{2+}, Hg^{2+} and Ni^{2+} using electrochemical impedance technique

A new azo-calix[4]arene **49** (as shown in Fig. 42) membrane was fabricated to detect Eu^{2+}, Hg^{2+}, and Ni^{2+} using electrochemical impedance. The electrochemical sensor is fabricated by spin-coating the chromogenic azo-calix[4]arene derivative onto gold electrode. From the optimal experiment, the Warburg impedance was minimized and the diameter of the half circle was reduced when the gold electrode/azo-calix[4]arene structure was polarized at − 400 mV/SCE. After the addition of different cation concentrations (Hg^{2+}, Ni^{2+} and Eu^{3+}), at low frequency, the increased ion concentration contributed to the diameter reduction in the Nyquist plot results. The bulk resistance R_m and charge transfer resistance R_{ct} also decreased

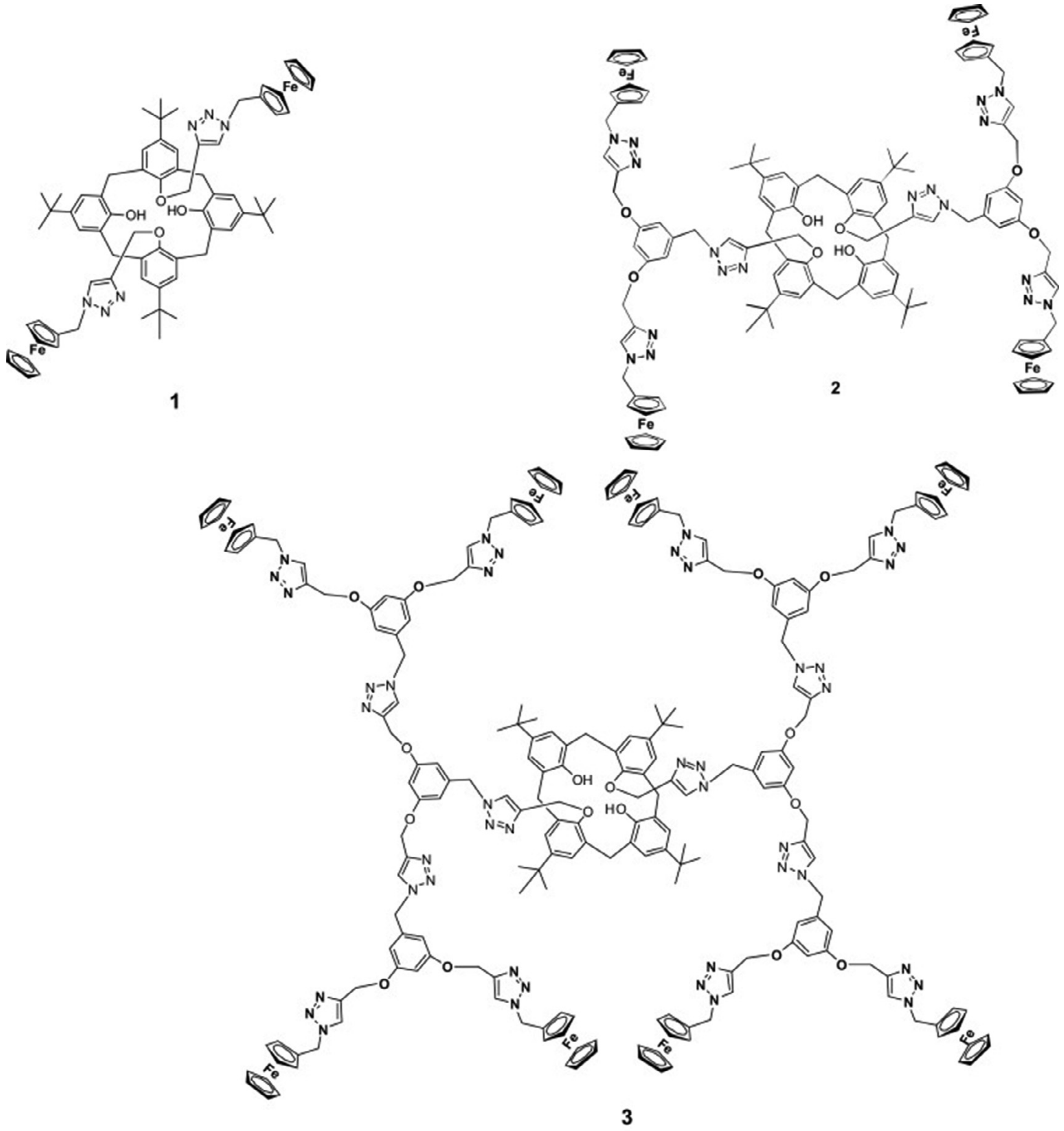

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Fig. 45 The structure of p-*tert*-butylcalix[4]arene cored triazolyl ferrocene conjugates 1 – 3 (Saravanan et al., 2017).

with the increased cation concentrations. Azo-calix[4]arene derivative thin film was found to be porous under the scanning electron microscope as shown in Fig. 43. Hence, a large amount of electrolyte solution was able to penetrate the pores and form a new liquid/metal interface because of the roughness and porosity of the sensing film (Ebdelli, 2011).

Table 6 lists a summary of various calixarene derivative electrochemical sensors associated with the electrical impedance spectroscopy of heavy metal ion detection.

4.7. Other technique

4.7.1. Cyclic voltammetry (CV) technique

Cyclic voltammetry (CV) is the most versatile electroanalytical method for studying electroactive species because it affords ease of measurement. Hence, it is widely used in the chemistry field, including in electrochemistry, organic chemistry, inorganic chemistry, and biochemistry (Kissinger and Heineman, 1983). It is employed to evaluate the oxidation and reduction

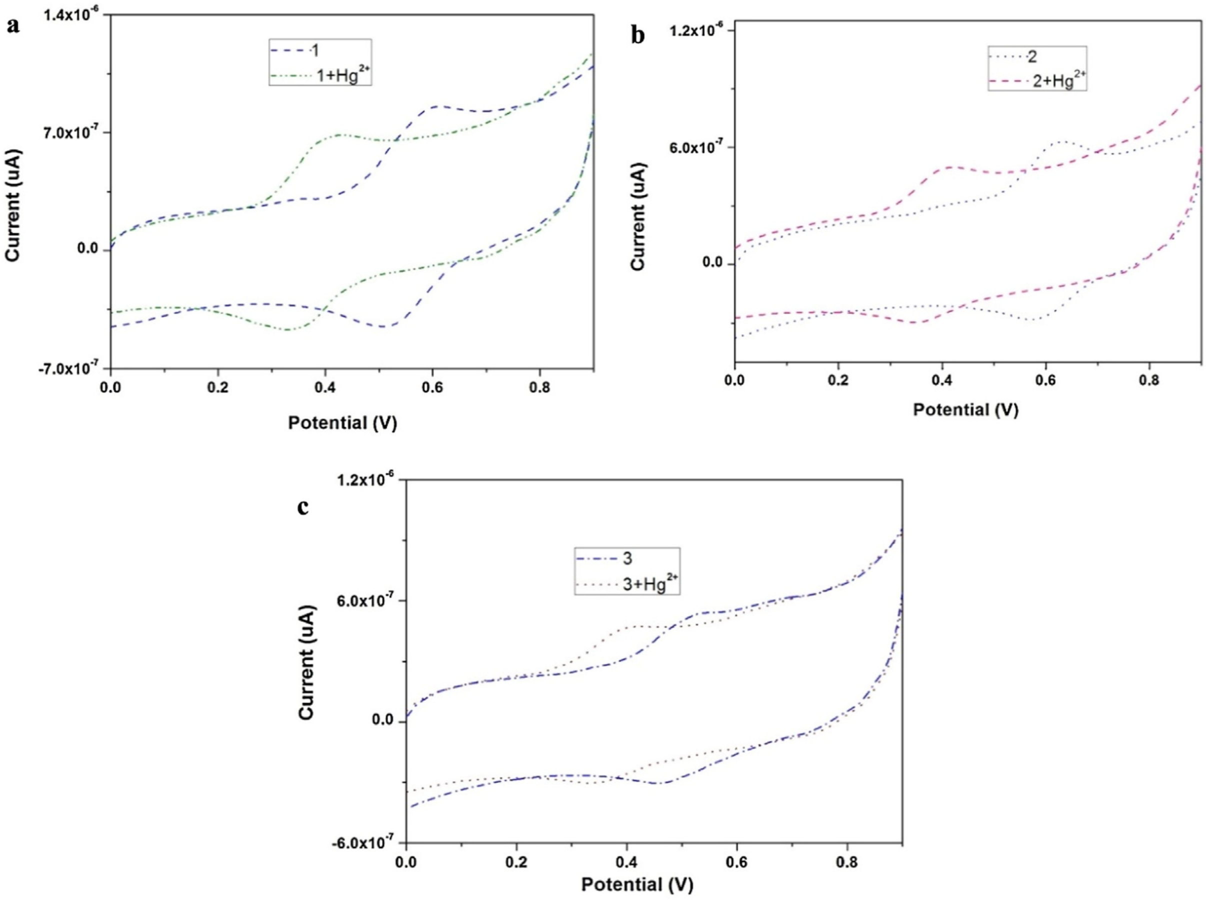

Fig. 46 Cyclic voltammetric redox sensing of Hg^{2+} on dendrimer 1, 2, and 3 (2 × 10^{-5} M): **(a)** dendrimer 1 with Hg^{2+} in CH_3CN (2 × 10^{-5}) **(b)** dendrimer 2 with Hg^{2+} in CH_3CN and **(c)** dendrimer 3 with Hg^{2+} in CH_3CN (Saravanan et al., 2017).

Table 7 Advantages and drawbacks of calixarene derivatives.

Material	Advantages	Drawbacks
Calixarene derivatives	• Low-cost • Excellent reproducibility and accuracy (Kumar et al., 2017; Cao, et al., 2010) • Can be selectively functionalized at upper rim (non polar)and lower rim (polar) (Bhat et al., 2004) • Remarkable ability to act as receptors • Low toxicity • Synthetic availability • Easy to modify (Español and Villamil, 2019)	• Some functional groups attached to calixarene has limited shelf-life stability (Blasi-Romero, 2021) • Cross sensitivity of other metal ions, not very selective to specific ions (Sliwa and Girek, 2010) • Calixarenes mostly insoluble in water and have only limited solubility in organic solvents. (Español and Villamil, 2019; Roundhill, 2003)

process of molecular species. The schematic representation of an electrochemical cell is shown in Fig. 44 a. The graph of cyclic voltammetry is presented in the form of "duck"-shaped voltammograms as shown in Fig. 44 b. The peak-to-peak separation between anodic and cathodic peaks is 57 mV at 25 °C when the reduction process is chemically and electrochemically reversible. Chemical reversibility is utilized to identify the stability of the analyte upon reduction, and whether or not it can subsequently be reoxidized. Electrochemical reversibility is related to the electron transfer kinetics between analyte and electrode (Elgrishi, 2018).

Cyclic voltammetry is almost always the first experiment conducted in an electrochemical study of an electrode surface, or a compound, or a biological material. The effectiveness of CV can be seen from its ability to rapidly observe the redox behavior over a broad potential range (Kissinger and Heineman, 1983). Cyclic voltammetry is different from differential pulse voltammetry as it is sensitive to residual currents;

Table 8 Advantages and drawback of different electrochemical techniques.

Electrochemical techniques	Advantages	Drawbacks
Potentiometric	• Simple instrumentation • Cost effective • Rapid response, simple procedure and preparation • Reasonable selectivity • Broad dynamic range (Lu, 2004; Demirel, 2006) • Real time diagnostic	• ISEs used in this method has low sensitivity, ions may act as ligands and poison the electrode (González and González, 2005) • Depend on change of temperature in surroundings • Depend on shift potential and ion activity (Bratovčić et al., 2009) • Obtaining solid contact ISEs with reproducible standard potentials is still a great challenge (Bobacka et al., 2008)
Amperometric	• Easier to implement experimentally • Give good sensitivity (Wen and Cassidy, 1996) • Low-cost • Miniaturization (Qiu et al., 2011; Luka, 2015)	• Sensitive to surrounding environment • Need redox species to enhance electrochemical response (Luka, 2015; Shi and Ma, 2011)
Diffrential Pulse Voltammetry (DPV)	• Rapid and sensitive method (Vilas-Boas, 2019; Aravindan and Sangaranarayanan, 2017) • Producing better define and less noisy signal as compared to LSV (Pérez-Ràfols, 2017) • Provide better detection limits than other electrochemical methods (Islam and Channon, 2020; Laborda, 2012)	• Longer analysis time than SWV (Ostapczuk et al., 1986; , 2565) • Less sensitive than SWV (Brahman, 2016)
Square Wave Voltammetry (SWV)	• Good selectivity • Good accuracy • Good precision • Good portability • Low-cost (Petovar et al., 2018) • More sensitive than DPV and CV (Brahman, 2016)	• Technique fairly complex • Volumetric data difficult to understand as compared to cyclic voltammetry (Laborda, 2012)
Anodic Stripping Voltammetry (ASV) Differential Pulse Anodic Stripping Voltammetry (DPASV) Square Wave Anodic Stripping Voltammetry (SWASV)	• Able to determine several elements simultaneously with concentration levels down to parts per billion range • Cost-effective (SWASV) • High sensitivity (SWASV) • High speed of the analytical measurement (SWASV) (Mirceski, 2019)	• DPASV is less sensitive than SWV in determine metal ions • DPASV has longer determination time than SWV (Ostapczuk et al., 1986)
Electrochemical Impedance Spectroscopy (EIS)	• Sensitive and robust technique to investigate the electrical resistance of a system • Sensitive to the changes of bulk properties and interfacial property at the electrode surface (Wu, 2017; Muñoz et al., 2017) • Simplicity • Possible to achieve real-time detection (Zamfir et al., 2020)	• Sensitive to surrounding environment • Required theoretical simulation for data analysis (Luka, 2015) • Need a Faraday cage to reduce noise (Zamfir et al., 2020) • The ability to differentiate different ions (Scott and Alseiha, 2017)
Cyclic Voltammetry (CV)	• Ease of measurement (Kissinger and Heineman, 1983) • Multiple point identification (Robinson, 2003)	• Low resolution with respect to structural information, and need to be addressed by coupling with structurally richer technique (Marken et al., 2010) • Less sensitive compared to other electrochemical technique such as SWV (Brahman, 2016) • Not sensitive enough to detect low concentration • Background noise control (Eddaif et al., 2019)

however, DPV is immune to residual currents (Vilas-Boas, 2019). The determination of metal ions including mercury ions (Hg^{2+}) was reported using the CV with calixarene derivatives as electrode modifiers.

4.7.1.1. Cyclic voltammetry analysis of Hg^{2+}. This sensor **50** (as shown in Fig. 45) with calix[4]arene conjugated ferrocenyl dendrimers **1, 2,** and **3** is highly sensitive to Hg^{2+} with the lowest concentration 2×10^{-5} M (**1**, **2**), 1×10^{-5} M (**3**) using cyclic voltammetry. From the cyclic voltammograms, the redox sensing of Hg^{2+} shifted the CV curve to a less positive side (as shown in Fig. 46) which demonstrated the ion-pairing reaction between mercury ions and the –OH group attached at the lower rim of calixarene and one N atom of each triazoyl groups. The ferrocenyl dendrimers (as shown in Fig. 45) were able to detect Hg^{2+} ion selectively in river water and other water resources containing competitive ions such as Ag^{+}, Cu^{2+}, and Zn^{2+} (Saravanan et al., 2017).

All in all, the work focuses on the detection limit of the calixarene derivatives-based electrochemical sensor. For the sensing parameters, other than detection limit (LOD), parameters such as linear detection range, selectivity, sensitivity, stability and reproducibility also significant in analytes detection (Gu, 2020; Liu et al., 2020; Gu, 2020). These parameters were discussed further in the works of (Gu, 2020). In the work of Liu et al. (Liu et al., 2020) , the structure of MOF-based materials have impact on the sensitivity, selectivity, stability, and accuracy of sensor. Moreover, the size and morphology also affect the performance and applicability of MOFs (Gu, 2020). Hence, in this field, the design of calixarene is also crucial to yield an excellent reproducibility and long shelf life sensors for heavy metal determination.

4.8. Advantages and disadvantages

4.8.1. Calixarene derivatives

Calixarene derivatives-based are used in sensing platforms due to their advantages such as a well-defined chemistry structure and different sizes of cavities. However, every material has its own limitations. Table 7 summarizes the advantages and drawbacks of the construction of electrochemical sensor for heavy metal ions based on calixarene derivatives.

4.8.2. Electrochemical methods

Electrochemical methods have advantages of low-cost, simplicity, high stability, selectivity and sensitivity, allowing the construction of portable instruments (Mei et al., 2021; Ostojić, 2017; Mu and Wang, 2019; Arvas, 2021). Table 8 summaries the advantages and drawbacks of each electrochemical method. As compared to potentiometric methods, voltammetric analyses were found to have better sensitivity, and can detect multiple ions simultaneously (Chen, 2018). However, there are some limitations of voltammetric methods such as high over potential, electrode contamination, low sensitivity, and low reproducibility (Sebastian and Mathew, 2018).

According to the strengths and weaknesses of electrochemical methods, voltammetric methods (DPV, SWV, DPASV, and SWASV) work well in heavy metal ions determination. In this field, DPASV is most widely applied in detecting heavy metal ions, which it seems has the potential to solve the existing problem—simultaneously detection of several elements.

5. Conclusion

This review presents the various calix[n]arene (n = 4, 6) derivatives used to detect heavy metal ions by using different electrochemical techniques such as potentiometric, amperometric, voltammetric techniques, and electrochemical impedance spectroscopy. This review briefly discussed the general electrochemical measurement setup for heavy metal ions quantification and the optimal parameters of calixarene derivatives. Moreover, the host–guest interaction mechanism between calixarene derivatives and target metal ions was also highlighted.

Calixarene derivatives with different functional moiety groups displayed excellent sensing behavior towards heavy metal ions with good sensitivity, reproducibility, and repeatability, for real application analysis. Although calixarene derivatives showed great ability in electrochemically sensing cationic substrates, we look forward to explore other more novel structures of calixarene derivatives for heavy metal ion sensing, which can be translated into miniaturized electrochemical sensors for in-situ operations used in real samples and other environmental matrices. The strengths of electrochemical methods and materials allow the development of portable devices for on-site environmental monitoring. However, the translation of developed sensors into commercial purposes is hampered because the challenges of fabricating an ideal 'Lab-on-a-Chip and of intergrating multiples electrochemical techniques to detect multielement at a low cost. Further work to achieve wide commercialization of ideal and cheap electrochemical sensor for multiple analytes is required in order to monitor trace-level ion *in situ* heavy metal sensors.

Ethical Approval

Not applicable.

Author agreement

The authors have read the manuscript and approved the submission.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors gratefully acknowledge the financial support provided by Ministry of Higher Education Malaysia through FRGS/2/2014/ST01/UPM/02/3.

References

Toutianoush, A. et al, 2005. Selective Ion Transport and Complexation in Layer-by-Layer Assemblies of p-Sulfonato-calix [n] arenes and Cationic Polyelectrolytes. Advanced Functional Materials. 15 (4), 700–708. https://doi.org/10.1002/adfm.200400223.

Adhikari, B.B. et al, 2011. Multiple proton ionizable calixarene derivatives with different ring sizes and complexation ability as efficient ionophores for complexation and solvent extraction of trivalent indium. Analyst. 136 (21), 4570–4579. https://doi.org/10.1039/C1AN15398F.

Satheeshkumar, K. et al, 2004. Calix [8] arene-mediated self-assembly of tetrapeptide H-Leu-Leu-Ile-Leu-OMe. Journal of Molecular Recognition. 17 (1), 67–75. https://doi.org/10.1002/jmr.629.

Torma, F. et al, 2009. Calixarene/Nafion-Modified Bismuth-Film Electrodes for Adsorptive Stripping Voltammetric Determination of Lead, Electroanalysis: An International Journal Devoted to Fundamental and Practical Aspects of Electroanalysis. 21 (17–18), 1961–1969. https://doi.org/10.1002/elan.200904634.

Chen, L. et al, 2001. Silver ion-selective electrodes based on novel containing benzothiazolyl calix [4] arene. Analytica chimica acta. 437 (2), 191–197. https://doi.org/10.1016/S0003-2670(01)00994-1.

Bhat, V.S., Ijeri, V.S., Srivastava, A.K., 2004. Coated wire lead (II) selective potentiometric sensor based on 4-tert-butylcalix [6] arene. Sensors and Actuators B: Chemical. 99 (1), 98–105. https://doi.org/10.1016/j.snb.2003.11.001.

Kumar, P., 2012. All Solid State Nickel (II)-Selective Potentiometric Sensor Based on an Upper Rim Substituted Calixarene. Electroanalysis. 24 (10), 2005–2012. https://doi.org/10.1002/elan.201200228.

Gutsche, C.D., Bauer, L.J., 1985. Calixarenes. 13. The conformational properties of calix [4] arenes, calix [6] arenes, calix [8] arenes, and oxacalixarenes. Journal of the American Chemical Society. 107 (21), 6052–6059. https://doi.org/10.1021/ja00307a038.

Moran, J.K. et al, 1994. Synthesis and structural characterization of calix [4] arenes, calix [6] arenes, and calix [8] arenes with 3-hydroxypropoxy or 2-hydroxyethoxy functional groups appended onto the lower rim. The Journal of Organic Chemistry. 59 (20), 5990–5998. https://doi.org/10.1021/jo00099a032.

Dernane, C. et al, 2013. Cadmium-sensitive electrode based on tetracetone derivatives of p-tert-butylcalix [8] arene. Materials Science and Engineering: C. 33 (7), 3638–3643. https://doi.org/10.1016/j.msec.2013.04.049.

Bergougnant, R.D., Robin, A.Y., Fromm, K.M., 2007. From simple rings to one-dimensional channels with calix [8] arenes, water clusters, and alkali metal ions. Tetrahedron. 63 (44), 10751–10757. https://doi.org/10.1016/j.tet.2007.07.048.

Martin, S., Griswold, W., 2009. Human health effects of heavy metals. Environmental Science and Technology briefs for citizens. 15, 1–6 http://citeseerx.ist.psu.edu/viewdoc/download?doi = 10.1.1.399.9831&rep = rep1&type = pdf.

Duffus, J.H., 2002. " Heavy metals" a meaningless term?(IUPAC Technical Report). Pure and applied chemistry. 74 (5), 793–807. https://doi.org/10.1351/pac200274050793.

Nagajyoti, P.C., Lee, K.D., Sreekanth, T., 2010. Heavy metals, occurrence and toxicity for plants: a review. Environmental chemistry letters. 8 (3), 199–216. https://doi.org/10.1007/s10311-010-0297-8.

Jaishankar, M. et al, 2014. Toxicity, mechanism and health effects of some heavy metals. Interdisciplinary toxicology. 7 (2), 60–72. https://doi.org/10.2478/intox-2014-0009.

Barakat, M., 2011. New trends in removing heavy metals from industrial wastewater. Arabian journal of chemistry. 4 (4), 361–377. https://doi.org/10.1016/j.arabjc.2010.07.019.

Gupta, V.K. et al, 2014. Cadmium (II) ion sensing through p-tert-butyl calix [6] arene based potentiometric sensor. Journal of Molecular Liquids. 195, 65–68. https://doi.org/10.1016/j.molliq.2014.02.001.

Sayin, S., 2020. Fabrication of Efficient Calix [4] arene-Adorned Magnetic Nanoparticles for the Removal of Cr (VI)/As (V) anions from Aqueous Solutions. Polycyclic Aromatic Compounds, 1–12. https://doi.org/10.1080/10406638.2020.1764986.

Priastomo, Y. et al, 2020. Simultaneous Removal of Lead (II), Chromium (III), and Copper (II) Heavy Metal Ions Through an Adsorption Process using C-Phenylcalix [4] pyrogallolarene Material, Journal of Environmental. Chemical Engineering. https://doi.org/10.1016/j.jece.2020.103971 103971.

Sultan, S. et al, 2019. Simultaneous Ultrasensitive Detection of Toxic Heavy Metal Ions Using bis (imidazo [4, 5-f][1, 10] phenanthroline) Appended bis-triazolo Calix [4] Arene (8)/Glassy Carbon Electrode. Journal of The Electrochemical Society. 166 (16), B1719. https://doi.org/10.1149/2.0541916jes.

Xie, Y. et al, 2019. Emerging natural and tailored materials for uranium-contaminated water treatment and environmental remediation. Progress in Materials Science. 103, 180–234. https://doi.org/10.1016/j.pmatsci.2019.01.005.

Wang, X. et al, 2016. Application of graphene oxides and graphene oxide-based nanomaterials in radionuclide removal from aqueous solutions. Science bulletin. 61 (20), 1583–1593. https://doi.org/10.1007/s11434-016-1168-x.

Wu, Y. et al, 2019. Environmental remediation of heavy metal ions by novel-nanomaterials: a review. Environmental pollution. 246, 608–620. https://doi.org/10.1016/j.envpol.2018.12.076.

Wang, X. et al, 2016. Surface modification of graphene oxides by plasma techniques and their application for environmental pollution cleanup. The Chemical Record. 16 (1), 295–318. https://doi.org/10.1002/tcr.201500223.

Eddaif, L., Shaban, A., Telegdi, J., 2019. Sensitive detection of heavy metals ions based on the calixarene derivatives-modified piezoelectric resonators: a review. International Journal of Environmental Analytical Chemistry. 99 (9), 824–853. https://doi.org/10.1080/03067319.2019.1616708.

Al-Trawneh, S.A., 2015. Studies on adsorptive removal of some heavy metal ions by calix [4] resorcine. Jordan Journal of Earth and Environmental Sciences. 7 (1), 1–9 http://jjees.hu.edu.jo/files/Vol7N1/Vol7N1_HQ_P1-9.pdf.

Yarur, F., Macairan, J.-R., Naccache, R., 2019. Ratiometric detection of heavy metal ions using fluorescent carbon dots. Environmental Science: Nano. 6 (4), 1121–1130. https://doi.org/10.1039/C8EN01418C.

Massadeh, A.M., El-Rjoob, A.-W.O., Gharaibeh, S.A., 2020. Analysis of Selected Heavy Metals in Tap Water by Inductively Coupled Plasma-Optical Emission Spectrometry After Pre-Concentration Using Chelex-100 Ion Exchange Resin. WATER AIR AND SOIL POLLUTION. 231 (5). https://doi.org/10.1007/s11270-020-04555-5.

Kılıç Altun, S. et al, 2017. Analyses of mineral content and heavy metal of honey samples from south and east region of Turkey by using ICP-MS. International Journal of Analytical Chemistry. 2017. https://doi.org/10.1155/2017/6391454.

Zhong, W.-S., Ren, T., Zhao, L.-J., 2016. Determination of Pb (Lead), Cd (Cadmium), Cr (Chromium), Cu (Copper), and Ni (Nickel) in Chinese tea with high-resolution continuum source graphite furnace atomic absorption spectrometry. Journal of food and drug analysis. 24 (1), 46–55. https://doi.org/10.1016/j.jfda.2015.04.010.

Eddaif, L. et al, 2020. A piezogravimetric sensor platform for sensitive detection of lead (II) ions in water based on calix [4] resorcinarene macrocycles: Synthesis, characterization and detection. Arabian Journal of Chemistry. 13 (2), 4448–4461. https://doi.org/10.1016/j.arabjc.2019.09.002.

Stoytcheva, M. et al, 2019. Resolution of a mononitrophenol isomers mixture by differential alternative pulses voltammetry. Electroanalysis. 31 (4), 652–660. https://doi.org/10.1002/elan.201800762.

Xiao-bo, J. et al, 2004. Electrochemical determination of trace amounts of lead (II) and cadmium (II) at a calix [6] arene modified carbon paste electrode. Wuhan University Journal of Natural Sciences. 9 (6), 943–948. https://doi.org/10.1007/BF02850805.

Abdalla, N.S. et al, 2019. Tailor-made specific recognition of cyromazine pesticide integrated in a potentiometric strip cell for environmental and food analysis. Polymers. 11 (9), 1526. https://doi.org/10.3390/polym11091526.

Tymecki, Ł., Zwierkowska, E., Koncki, R., 2004. Screen-printed reference electrodes for potentiometric measurements. Analytica Chimica Acta. 526 (1), 3–11. https://doi.org/10.1016/j.aca.2004.08.056.

Hulanicki, A. and S. Głąb, 2005. TITRIMETRY| Potentiometric. https://doi.org/10.1016/B978-0-12-409547-2.00546-1.

Bansod, B. et al, 2017. A review on various electrochemical techniques for heavy metal ions detection with different sensing platforms. Biosensors and Bioelectronics. 94, 443–455. https://doi.org/10.1016/j.bios.2017.03.031.

Lu, J.-Q. et al, 2004. A new solid-state silver ion-selective electrode based on a novel tweezer-type calixarene derivative. Journal of Electroanalytical Chemistry. 568, 37–43. https://doi.org/10.1016/j.jelechem.2004.01.017.

Demirel, A., et al., 2006. Silver (I)-Selective PVC Membrane Potentiometric Sensor Based on a Recently Synthesized Calix [4] arene, Electroanalysis: An International Journal Devoted to Fundamental and Practical Aspects of Electroanalysis. 18(10): p. 1019-1027. https://doi.org/10.1002/elan.200503494.

Gupta, V.K. et al, 2012. A novel copper (II) selective sensor based on dimethyl 4, 4′(o-phenylene) bis (3-thioallophanate) in PVC matrix. Journal of Molecular Liquids. 174, 11–16. https://doi.org/10.1016/j.molliq.2012.07.016.

Tyagi, S., Agarwal, H., Ikram, S., 2010. Potentiometric polymeric membrane electrodes for mercury detection using calixarene ionophores. Water Science and Technology. 61 (3), 693–704. https://doi.org/10.2166/wst.2010.860.

Alva, S. et al, 2019. The new lead (II) ion selective electrode based on free plasticizer film of pTHFA photopolymer. Journal of The Electrochemical Society. 166 (15), B1513. https://doi.org/10.1149/2.0601915jes.

Nielsen, S.S., 2017. Sodium Determination Using Ion-Selective Electrodes, Mohr Titration, and Test Strips. In: Food Analysis Laboratory Manual. Springer, pp. 161–170.

Brinić, S. et al, 2012. Solid-contact Cu (II) ion-selective electrode based on 1, 2-di-(o-salicylaldiminophenylthio) ethane. Journal of solid state electrochemistry. 16 (4), 1333–1341. https://doi.org/10.1007/s10008-011-1528-z.

Guinovart, T. et al, 2017. Characterization of a new ionophore-based ion-selective electrode for the potentiometric determination of creatinine in urine. Biosensors and bioelectronics. 87, 587–592. https://doi.org/10.1016/j.bios.2016.08.025.

Ma'mun, A., Abd El-Rahman, M.K., Abd El-Kawy, M., 2018. Real-time potentiometric sensor; an innovative tool for monitoring hydrolysis of chemo/bio-degradable drugs in pharmaceutical sciences. Journal of pharmaceutical and biomedical analysis. 154, 166–173. https://doi.org/10.1016/j.jpba.2018.02.007.

Duncan, D.M., Cockayne, J., 2001. Application of calixarene ionophores in PVC based ISEs for uranium detection. Sensors and Actuators B: Chemical. 73 (2–3), 228–235. https://doi.org/10.1016/S0925-4005(00)00693-6.

Mahajan, R.K. et al, 2004. Mercury (II) ion-selective electrodes based on p-tert-butyl calix [4] crowns with imine units. Analytical sciences. 20 (5), 811–814. https://doi.org/10.2116/analsci.20.811.

Lu, J., Tong, X., He, X., 2003. A mercury ion-selective electrode based on a calixarene derivative containing the thiazole azo group. Journal of Electroanalytical Chemistry. 540, 111–117. https://doi.org/10.1016/S0022-0728(02)01298-6.

Chen, L. et al, 2000. Calixarene derivative as the neutral carrier in silver ion-selective electrode and liquid membrane transport. Analytica chimica acta. 417 (1), 51–56. https://doi.org/10.1016/S0003-2670(00)00912-0.

Zeng, X. et al, 2000. Improved silver ion-selective electrodes using novel 1, 3-bis (2-benzothiazolyl) thioalkoxy-p-tert-butylcalix [4] arenes. Tetrahedron Letters. 41 (25), 4917–4921. https://doi.org/10.1016/S0040-4039(00)00746-2.

Chen, L., Zeng, X., He, X., 2000. Selective electrodes for silver based on polymeric membranes containing calix [4] arene derivatives. Fresenius' journal of analytical chemistry. 367 (6), 535–538. https://doi.org/10.1007/s002160000397.

Oh, H. et al, 2000. Poly (vinyl chloride) membrane cesium ion-selective electrodes based on lipophilic calix [6] arene tetraester derivatives. Talanta. 53 (3), 535–542. https://doi.org/10.1016/s0039-9140(00)00531-2.

Yaftian, M.R. et al, 2006. A coated wire-type lead (II) ion-selective electrode based on a phosphorylated calix [4] arene derivative. Analytical sciences. 22 (8), 1075–1078. https://doi.org/10.2116/analsci.22.1075.

Lu, J., Chen, R., He, X., 2002. A lead ion-selective electrode based on a calixarene carboxyphenyl azo derivative. Journal of Electroanalytical Chemistry. 528 (1–2), 33–38. https://doi.org/10.1016/S0022-0728(02)00840-9.

Cadogan, F. et al, 1999. Lead-selective electrodes based on calixarene phosphine oxide derivatives. Analytical Chemistry. 71 (24), 5544–5550. https://doi.org/10.1021/ac990303f.

Jain, A.K., Gupta, V.K., Raisoni, J.R., 2004. Strontium (II)-selective potentiometric sensor based on ester derivative of 4-tert-butylcalix (8) arene in PVC matrix. Sensors. 4 (8), 115–124. https://doi.org/10.3390/s40800115.

Vyas, G., Bhatt, S., Paul, P., 2019. Synthesis of calixarene-capped silver nanoparticles for colorimetric and amperometric detection of mercury (HgII, Hg0). ACS omega. 4 (2), 3860–3870. https://doi.org/10.1021/acsomega.8b03299.

Wilke, S. et al, 1996. Amperometric detection of heavy metal ions in ion pair chromatography at an array of water/nitrobenzene micro interfaces. Fresenius' journal of analytical chemistry. 356 (3–4), 233–236. https://doi.org/10.1007/s0021663560233.

Kappes, T., Hauser, P.C., 1999. Simplified amperometric detector for capillary electrophoresis. Analyst. 124 (7), 1035–1039. https://doi.org/10.1039/A901897B.

Wen, J., Cassidy, R.M., 1996. Anodic and cathodic pulse amperometric detection of metal ions separated by capillary electrophoresis. Analytical Chemistry. 68 (6), 1047–1053. https://doi.org/10.1021/ac9508715.

Kappes, T., Schnierle, P., Hauser, P.C., 1999. Field-portable capillary electrophoresis instrument with potentiometric and amperometric detection. Analytica chimica acta. 393 (1–3), 77–82. https://doi.org/10.1016/S0003-2670(99)00149-X.

Zhang, J. et al, 2014. electrical transducers: Electrochemical sensors and semiconductor molecular sensors. In: Molecular Sensors and Nanodevices. William Andrew Publishing, Oxford, pp. 169–232.

Maity, D. et al, 2014. Calix [4] arene functionalized gold nanoparticles: application in colorimetric and electrochemical sensing of cobalt ion in organic and aqueous medium. Sensors and Actuators B: Chemical. 191, 757–764. https://doi.org/10.1016/j.snb.2013.10.066.

Yadav, P.K. and R.M. Sharma, 2019. The Role of Voltammetric Methods in Determination of Metals in Alcoholic Beverages: A Critical Review. https://doi.org/10.26735/16586794.2019.010.

Vilas-Boas, Â. et al, 2019. Evaluation of total polyphenol content of wines by means of voltammetric techniques: Cyclic voltammetry vs differential pulse voltammetry. Food chemistry. 276, 719–725. https://doi.org/10.1016/j.foodchem.2018.10.078.

Aravindan, N., Sangaranarayanan, M., 2017. Differential pulse voltammetry as an alternate technique for over oxidation of polymers: Application of electrochemically synthesized over oxidized poly (Alizarin Red S) modified disposable pencil graphite electrodes for simultaneous detection of hydroquinone and catechol. Journal of Electroanalytical Chemistry. 789, 148–159. https://doi.org/10.1016/j.jelechem.2017.02.037.

Harris, M. et al, 2012. Affibodies as an alternative to antibodies in biosensors for cancer markers. In: Biosensors for Medical Applications. Elsevier, pp. 217–232.

Islam, M.N., Channon, R.B., 2020. Electrochemical sensors. In: Bioengineering Innovative Solutions for Cancer. Elsevier, pp. 47–71.

Scott, K., 2016. Electrochemical principles and characterization of bioelectrochemical systems. In: Microbial Electrochemical and Fuel Cells. Elsevier, pp. 29–66.

Pérez-Ràfols, C. et al, 2017. A Voltammetric Electronic Tongue Based on Commercial Screen-printed Electrodes for the Analysis of Aminothiols by Differential Pulse Voltammetry. Electroanalysis. 29 (6), 1559–1565. https://doi.org/10.1002/elan.201700053.

Laborda, E. et al, 2012. Electrode modification using porous layers Maximising the analytical response by choosing the most suitable voltammetry: Differential Pulse vs Square Wave vs Linear sweep voltammetry. Electrochimica Acta. 73, 3–9. https://doi.org/10.1016/j.electacta.2011.07.107.

Nur Abdul Aziz, S.F., Zawawi, R., Alang Ahmad, S.A., 2018. An Electrochemical sensing platform for the detection of lead ions based on dicarboxyl-Calix [4] arene. Electroanalysis. 30 (3), 533–542. https://doi.org/10.1002/elan.201700736.

Bingol, H. et al, 2010. A novel benzothiazole based azocalix [4] arene as a highly selective chromogenic chemosensor for Hg2+ ion: a rapid test application in aqueous environment. Talanta. 82 (4), 1538–1542. https://doi.org/10.1016/j.talanta.2010.07.047.

Mei, C.J., Yusof, N.A., Alang Ahmad, S.A., 2021. Electrochemical Determination of Lead & Copper Ions Using Thiolated Calix[4] arene-Modified Screen-Printed Carbon Electrode. Chemosensors. 9 (7), 157. https://doi.org/10.3390/chemosensors9070157.

Bingol, H. et al, 2011. Spectrophotometric and electrochemical behavior of a novel azocalix [4] arene derivative as a highly selective chromogenic chemosensor for Cr+ 3. Electrochimica acta. 56 (5), 2057–2061. https://doi.org/10.1016/j.electacta.2010.11.081.

Ruslan, N. et al, 2017. Ultrasensitive electrochemical detection of metal ions using dicarboethoxycalixarene-based sensor. Journal of Electroanalytical Chemistry. 799, 497–504. https://doi.org/10.1016/j.jelechem.2017.06.038.

Mirceski, V. et al, 2019. Differential square-wave voltammetry. Analytical Chemistry. 91 (23), 14904–14910. https://doi.org/10.1021/acs.analchem.9b03035.

Petovar, B., Xhanari, K., Finšgar, M., 2018. A detailed electrochemical impedance spectroscopy study of a bismuth-film glassy carbon electrode for trace metal analysis. Analytica Chimica Acta. 1004, 10–21. https://doi.org/10.1016/j.aca.2017.12.020.

Dauphin-Ducharme, P. et al, 2017. Simulation-based approach to determining electron transfer rates using square-wave voltammetry. Langmuir. 33 (18), 4407–4413. https://doi.org/10.1021/acs.langmuir.7b00359.

Göde, C. et al, 2017. A novel electrochemical sensor based on calixarene functionalized reduced graphene oxide: application to simultaneous determination of Fe (III), Cd (II) and Pb (II) ions. Journal of colloid and interface science. 508, 525–531. https://doi.org/10.1016/j.jcis.2017.08.086.

Finšgar, M., Xhanari, K., Petovar, B., 2019. Copper-film electrodes for Pb (II) trace analysis and a detailed electrochemical impedance spectroscopy study. Microchemical Journal. 147, 863–871. https://doi.org/10.1016/j.microc.2019.04.007.

Copeland, T., Skogerboe, R., 1974. Anodic stripping voltammetry. Analytical Chemistry. 46 (14), 1257A–1268A. https://doi.org/10.1021/ac60350a021.

Wang, J. et al, 2000. Bismuth-coated carbon electrodes for anodic stripping voltammetry. Analytical chemistry. 72 (14), 3218–3222. https://doi.org/10.1021/ac000108x.

March, G., Nguyen, T.D., Piro, B., 2015. Modified electrodes used for electrochemical detection of metal ions in environmental analysis. Biosensors. 5 (2), 241–275. https://doi.org/10.3390/bios5020241.

Zhu, X. et al, 2017. The polypyrrole/multiwalled carbon nanotube modified au microelectrode for sensitive electrochemical detection of trace levels of Pb2+. Micromachines. 8 (3), 86. https://doi.org/10.3390/mi8030086.

Wang, F. et al, 2009. Langmuir-Blodgett film of p-tert-butylthiacalix [4] arene modified glassy carbon electrode as voltammetric sensor for the determination of Ag+. Journal of Electroanalytical Chemistry. 1 (630), 49–54. https://doi.org/10.1016/j.jelechem.2009.02.014.

Prashanth, S., Pandurangappa, M., 2016. Amino-calix [4] arene modified graphite as an electrochemical interface for mercury (II) quantification. Materials Letters. 185, 476–479. https://doi.org/10.1016/j.matlet.2016.09.010.

Adarakatti, P.S., Siddaramanna, A., Malingappa, P., 2019. Fabrication of a new calix [4] arene-functionalized Mn 3 O 4 nanoparticle-based modified glassy carbon electrode as a fast responding sensor towards Pb 2+ and Cd 2+ ions. Analytical Methods. 11 (6), 813–820. https://doi.org/10.1039/C8AY02648C.

Honeychurch, K.C. et al, 2002. Voltammetric Behavior and Trace Determination of Cadmium at a Calixarene Modified Screen-Printed Carbon Electrode. Electroanalysis. 14 (3), 177–185. https://doi.org/10.1002/1521-4109(200202)14:3<177::AID-ELAN177>3.0.CO;2-V.

Canpolat, E.Ç. et al, 2007. Determination of trace amounts of copper in tap water samples with a calix [4] arene modified carbon paste electrode by differential pulse anodic stripping voltammetry. Electroanalysis: An International Journal Devoted to Fundamental and Practical Aspects of Electroanalysis 19 (10), 1109–1115. https://doi.org/10.1002/elan.200603829.

Adarakatti, P.S., Banks, C.E., Malingappa, P., 2017. Amino-thiacalix [4] arene modified screen-printed electrodes as a novel electrochemical interface for Hg (ii) quantification at a pico-molar level. Analytical Methods. 9 (48), 6747–6753. https://doi.org/10.1039/C7AY02468A.

D.M.Roundhill, 2003. 1.22 - Calixarenes. Comprehensive Coordination Chemistry 1, 485–491. https://doi.org/10.1016/B0-08-043748-6/01054-9.

Dong, H. et al, 2006. Electrode modified with Langmuir-Blodgett (LB) film of calixarenes for preconcentration and stripping analysis of Hg (II). Electroanalysis: An International Journal Devoted to Fundamental and Practical Aspects of Electroanalysis 18 (12), 1202–1207. https://doi.org/10.1002/elan.200603520.

Kocer, M.B. et al, 2019. A Calix [4] arene-tren modified electrode for determination of Lead ions in aqueous solution. Organic Communications. 12 (3), 168. https://doi.org/10.25135/acg.oc.65.19.07.1330.

Wang, L. et al, 2012. Thiacalixarene covalently functionalized multiwalled carbon nanotubes as chemically modified electrode material for detection of ultratrace Pb2+ ions. Analytical chemistry. 84 (24), 10560–10567. https://doi.org/10.1021/ac302747f.

Adarakatti, P.S., Malingappa, P., 2016. Amino-calixarene-modified graphitic carbon as a novel electrochemical interface for simultaneous measurement of lead and cadmium ions at picomolar level. Journal of Solid State Electrochemistry. 20 (12), 3349–3358. https://doi.org/10.1007/s10008-016-3306-4.

Zheng, H. et al, 2007. Simultaneous determination of lead and cadmium at a glassy carbon electrode modified with Langmuir-Blodgett film of p-tert-butylthiacalix [4] arene. Sensors and Actuators B: Chemical. 120 (2), 603–609. https://doi.org/10.1016/j.snb.2006.03.032.

Dong, H. et al, 2006. Determination of thallium and cadmium on a chemically modified electrode with Langmuir-Blodgett film of p-allylcalix [4] arene. Sensors and Actuators B: Chemical. 115 (1), 303–308. https://doi.org/10.1016/j.snb.2005.09.017.

Liu, L., Zhang, K., Wei, Y., 2019. A simple strategy for the detection of Cu (ii), Cd (ii) and Pb (ii) in water by a voltammetric sensor on a TC4A modified electrode. New Journal of Chemistry. 43 (3), 1544–1550. https://doi.org/10.1039/C8NJ05089A.

Adarakatti, P.S. et al, 2017. Calixarene bulk modified screen-printed electrodes (SPCCEs) as a one-shot disposable sensor for the simultaneous detection of lead (II), copper (II) and mercury (II) ions: Application to environmental samples. Sensors and Actuators A: Physical. 267, 517–525. https://doi.org/10.1016/j.sna.2017.10.059.

Pizarro, J. et al, 2019. Synthesis and characterization of the first cyrhetrenyl-appended calix [4] arene macrocycle and its application as an electrochemical sensor for the determination of Cu (II) in bivalve mollusks using square wave anodic stripping voltammetry. Sensors and Actuators B: Chemical. 281, 115–122. https://doi.org/10.1016/j.snb.2018.09.099.

Li, X. et al, 2016. A novel design of engineered multi-walled carbon nanotubes material and its improved performance in simultaneous detection of Cd (II) and Pb (II) by square wave anodic stripping voltammetry. Sensors and Actuators B: Chemical. 236, 144–152. https://doi.org/10.1016/j.snb.2016.05.149.

Zou, L. et al, 2012. Langmuir-Blodgett film of tetraoxocalix [2] arene [2] triazine modified electrode for voltammetric determination of copper ion. Journal of Solid State Electrochemistry. 16 (2), 505–511. https://doi.org/10.1007/s10008-011-1359-y.

Zou, L. et al, 2009. Simultaneous Determination of Thallium and Lead on a Chemically Modified Electrode with Langmuir-Blodgett Film of ap-tert-Butylcalix [4] arene Derivative. Electroanalysis: An International Journal Devoted to Fundamental and Practical Aspects of Electroanalysis. 21 (23), 2563–2568. https://doi.org/10.1002/elan.200900300.

Alcañiz, M. et al, 2012. Design of an electronic system and its application to electronic tongues using variable amplitude pulse voltammetry and impedance spectroscopy. Journal of Food Engineering. 111 (1), 122–128. https://doi.org/10.1016/j.jfoodeng.2012.01.014.

Wu, J. et al, 2017. A DNAzyme-based electrochemical impedance biosensor for highly sensitive detection of Cu2+ ions in aqueous solution. Int. J. Electrochem. Sci. 12, 11666–11676. https://doi.org/10.20964/2017.12.46.

Muñoz, J., Montes, R., Baeza, M., 2017. Trends in electrochemical impedance spectroscopy involving nanocomposite transducers: Characterization, architecture surface and bio-sensing. TrAC Trends in Analytical Chemistry. 97, 201–215. https://doi.org/10.1016/j.trac.2017.08.012.

Yang, P. et al, 2012. A Highly Sensitive Electrochemical Impedance Spectroscopy Immunosensor for Determination of 1-Pyrenebutyric Acid Based on the Bifunctionality of Nafion/Gold Nanoparticles Composite Electrode. Chinese Journal of Chemistry. 30 (5), 1155–1162. https://doi.org/10.1002/cjoc.201100485.

Hammond, J.L. et al, 2016. Electrochemical biosensors and nanobiosensors. Essays in biochemistry. 60 (1), 69–80. https://doi.org/10.1042/EBC20150008.

Sakly, N. et al, 2002. Platinum electrode functionalized with calix [4] arene thin films for impedimetric detection of sodium ions. Materials Science and Engineering: C. 21 (1–2), 47–53. https://doi.org/10.1016/S0928-4931(02)00057-7.

Ebdelli, R. et al, 2011. Electrochemical impedance detection of Hg2+, Ni2+ and Eu3+ ions by a new azo-calix [4] arene membrane. Journal of electroanalytical chemistry. 661 (1), 31–38. https://doi.org/10.1016/j.jelechem.2011.07.007.

Echabaane, M. et al, 2017. Impedimetric sensing proprieties of ITO electrodes functionalized with PEDOT: PSS/Azo-calix [4] arene for the detection of Al 3+ ions under light excitation. Journal of Electronic Materials. 46 (1), 418–424. https://doi.org/10.1007/s11664-016-4838-1.

Ali, M.B. et al, 2006. Comparison study of evaporated thiacalix [4] arene thin films on gold substrates as copper ion sensing. Thin Solid Films. 495 (1–2), 368–371. https://doi.org/10.1016/j.tsf.2005.08.238.

Kissinger, P.T., Heineman, W.R., 1983. Cyclic voltammetry. Journal of Chemical Education. 60 (9), 702. https://doi.org/10.1021/ed060p702.

Elgrishi, N. et al, 2018. A practical beginner's guide to cyclic voltammetry. Journal of Chemical Education. 95 (2), 197–206. https://doi.org/10.1021/acs.jchemed.7b00361.

Saravanan, V., Kannan, A., Rajakumar, P., 2017. p-tert-Butylcalix [4] arene core based ferrocenyl dendrimers: Novel sensor for toxic Hg2 + ion even in presence of Zn2+, Cu2+ and Ag+ ions. Sensors and Actuators B: Chemical. 242, 904–911. https://doi.org/10.1016/j.snb.2016.09.165.

Gu, C. et al, 2020. Controllable synthesis of copper ion guided MIL-96 octadecahedron: highly sensitive aptasensor toward alpha-fetoprotein. Applied Materials Today. 20,. https://doi.org/10.1016/j.apmt.2020.100745 100745.

Liu, C.-S., Li, J., Pang, H., 2020. Metal-organic framework-based materials as an emerging platform for advanced electrochemical sensing. Coordination Chemistry Reviews. 410,. https://doi.org/10.1016/j.ccr.2020.213222 213222.

Gu, C. et al, 2020. Morphology and size controlled synthesis of Co-doped MIL-96 by different alkaline modulators for sensitively detecting alpha-fetoprotein. Chinese Chemical Letters. 31 (9), 2263–2267. https://doi.org/10.1016/j.cclet.2020.02.044.

Kumar, S., Chawla, S., Zou, M.C., 2017. Calixarenes based materials for gas sensing applications: a review. Journal of Inclusion Phenomena and Macrocyclic Chemistry. 88 (3), 129–158. https://doi.org/10.1007/s10847-017-0728-2.

Cao, Z., et al. Fabrication of Piezoelectric Thickness-Shear-Mode Acoustic Wave Sensing Device and its Application. in Advanced Materials Research. 2010. Trans Tech Publ https://doi.org/10.4028/www.scientific.net/AMR.97-101.4261.

Español, E.S., Villamil, M.M., 2019. Calixarenes: Generalities and their role in improving the solubility, biocompatibility, stability, bioavailability, detection, and transport of biomolecules. Biomolecules. 9 (3), 90. https://doi.org/10.3390/biom9030090.

Blasi-Romero, A. et al, 2021. In Vitro Investigation of Thiol-Functionalized Cellulose Nanofibrils as a Chronic Wound Environment Modulator. Polymers. 13 (2), 249. https://doi.org/10.3390/polym13020249.

Sliwa, W., Girek, T., 2010. Calixarene complexes with metal ions. Journal of Inclusion Phenomena and Macrocyclic Chemistry. 66 (1–2), 15–41. https://doi.org/10.1007/s10847-009-9678-7.

Ostojić, J. et al, 2017. Advantages of an electrochemical method compared to the spectrophotometric kinetic study of peroxidase inhibition by boroxine derivative. Molecules. 22 (7), 1120. https://doi.org/10.3390/molecules22071120.

Mu, B., Wang, A., 2019. Fabrication and Applications of Carbon/Clay Mineral Nanocomposites. In: Nanomaterials from Clay Minerals. Elsevier, pp. 537–587.

Arvas, M.B. et al, 2021. Differential Pulse Voltammetric (DPV) Determination of Phosphomolybdenum Complexes by a Poly (Vinyl Chloride) Coated Molybdenum Blue Modified Pencil Graphite Electrode (PVC-MB-PGE). Analytical Letters. 54 (3), 492–511. https://doi.org/10.1080/00032719.2020.1772806.

Chen, X. et al, 2018. Rapid detection of nutrients with electronic sensors: a review. Environmental Science: Nano. 5 (4), 837–862. https://doi.org/10.1039/C7EN01160A.

Sebastian, M., Mathew, B., 2018. Ion imprinting approach for the fabrication of an electrochemical sensor and sorbent for lead ions in real samples using modified multiwalled carbon nanotubes. Journal of materials science. 53 (5), 3557–3572. https://doi.org/10.1007/s10853-017-1787-x.

Bratovčić, A., Odobašić, A., Ćatić, S., 2009. The advantages of the use of ion-selective potentiometry in relation to UV/VIS spectroscopy. Agriculturae Conspectus Scientificus. 74 (3), 139–142 https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.906.5199&rep=rep1&type=pdf.

Bobacka, J., Ivaska, A., Lewenstam, A., 2008. Potentiometric ion sensors. Chemical reviews. 108 (2), 329–351. https://doi.org/10.1021/cr068100w.

Qiu, J.-D., Huang, H., Liang, R.-P., 2011. Biocompatible and label-free amperometric immunosensor for hepatitis B surface antigen using a sensing film composed of poly (allylamine)-branched ferrocene and gold nanoparticles. Microchimica Acta. 174 (1), 97–105. https://doi.org/10.1007/s00604-011-0585-4.

Luka, G. et al, 2015. Microfluidics integrated biosensors: A leading technology towards lab-on-a-chip and sensing applications. Sensors. 15 (12), 30011–30031. https://doi.org/10.3390/s151229783.

Shi, W., Ma, Z., 2011. A novel label-free amperometric immunosensor for carcinoembryonic antigen based on redox membrane. Biosensors and Bioelectronics. 26 (6), 3068–3071. https://doi.org/10.1016/j.bios.2010.11.048.

Ostapczuk, P., Valenta, P., Nürnberg, H., 1986. Square wave voltammetry-a rapid and reliable determination method of Zn. Cd, Pb, Cu, Ni and Co in biological and environmental samples, Journal of electroanalytical chemistry and interfacial electrochemistry. 214 (1–2), 51–64. https://doi.org/10.1016/j.jpba.2007.07.010.

Instruments, E., Princeton Applied Research, PO Box. 2565.

Brahman, P.K. et al, 2016. Highly sensitive stripping voltammetric determination of a biomolecule, pyruvic acid in solubilized system and biological fluids. Arabian Journal of Chemistry. 9, S1897–S1904. https://doi.org/10.1016/j.arabjc.2014.02.003.

Zamfir, L.-G., Puiu, M., Bala, C., 2020. Advances in Electrochemical Impedance Spectroscopy Detection of Endocrine Disruptors. Sensors. 20 (22), 6443. https://doi.org/10.3390/s20226443.

Scott, D.W., Alseiha, Y., 2017. Determining detection limits of aqueous anions using electrochemical impedance spectroscopy. Journal of Analytical Science and Technology. 8 (1), 1–5. https://doi.org/10.1186/s40543-017-0126-9.

Robinson, D.L. et al, 2003. Detecting subsecond dopamine release with fast-scan cyclic voltammetry in vivo. Clinical chemistry. 49 (10), 1763–1773. https://doi.org/10.1373/49.10.1763.

Marken, F., Neudeck, A., Bond, A.M., 2010. Cyclic voltammetry. In: Electroanalytical methods. Springer, pp. 57–106.

M. González, V. González, 2005. Food and nutritional analysis | Water and Minerals, Encyclopedia of Analytical Science (Second Edition). pp. 241-250. https://doi.org/10.1016/B0-12-369397-7/00180-1.