

A Comprehensive Review Of Potentiometric Biosensors

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ABSTRACT

Potentiometry based on ion-selective electrodes (ISEs) has undergone a renaissance with improvements in the detection limits and selectivities of ISEs, the introduction of new materials, new sensing concepts (from conventional potentiometry to dynamic electrochemistry approaches), and deeper theoretical understanding and modelling of the potentiometric responses of ISEs. The most recent innovations support improvements in software for ion sensing and biosensing. Additionally, adaptable sensing techniques have been created for a wide range of various target molecules, including enzymes, antibodies, aptamers, and peptides, in response to the introduction of new receptors by using ISEs as powerful transducers. Current potentiometric biosensor trends are examined in this paper. Their applications in the biosensing of metal ions, small molecules, DNA, proteins, microorganisms, and poisons have been discussed. This review provides a forecast for potentiometric biosensing based on the integration of potentiometric ISEs with innovative materials and cutting-edge techniques.

Keywords

Ion-selective electrode, bioreceptor, potentiometric biosensing, and potentiometric biosensing.

1. INTRODUCTION

A scientific field known as analytical chemistry develops and uses techniques, tools, and approaches to learn more about the makeup and properties of matter over time and space. Analytical chemistry's main goal is to extract as much high-quality chemical information as possible from objects and systems while consuming the fewest amount of materials, time, and labour, as well as minimising costs and dangers. Because of our growing concerns about pollution, our health, and safety, there is an increasing need and desire for us to monitor every aspect of our environment in real-time. Additionally, there is a need to identify pollutants and analytes at ever-decreasing concentrations. In fact, one could argue that the entire goal of modern analytical chemistry is to reduce detection limits while enhancing accuracy and precision at those limits. Since chemical information needs arise in a number of economic and social sectors, such as industry, the environment, food science and technology, pharmaceutical analysis, and clinical analysis, analytical chemistry is directly involved with finding solutions to these analytical difficulties. In analytical chemistry, a qualitative analysis provides details about the atomic or molecular species or functional groups present in the material. While a quantitative analysis provides numbers to indicate how much of each of these components is present in relation to the others. Gravimetry and titrimetry, two conventional or classical methods of chemical analysis, are based on the quantitative execution of chemical reactions. Chromatographic techniques, spectrophotometric techniques, and electroanalysis were all developed in response to the requirement for trace-level analysis. Chromatography is primarily a technique for separation. Rare earths and transuranic ions are separated and concentrated using ion chromatography. Cations are also determined via gas chromatography, which separates a mixture into its components by passing a moving gas phase through a stationary sorbent. Utilising a spectrophotometer is precisely referred to as spectrophotometry. Beer's law, which connects absorbance to concentration, is used in quantitative applications of absorption/emission spectroscopy. Inductively coupled plasma atomic emission spectroscopy (ICP AES), which is extremely accurate, has developed from simple spectrophotometric methods using a spectrophotometer to flame emission spectroscopy (FES), atomic absorption spectroscopy (AAS), and atomic fluorescence spectroscopy (AFS). Another analytical method used for trace-level analysis is called electroanalysis, which is the use of electrochemistry to address analytical issues in the real world. A group of quantitative and qualitative analytical techniques based on the electrical characteristics of an analyte solution when it is incorporated into an electrochemical cell is referred to as electroanalytical chemistry. Low detection limits and a wealth of characterization data characterising electrochemically accessible systems can be produced by these techniques. Electroanalytical measures have a number of significant advantages, including. [1-5]

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1. High sensitivity and low detection limit
2. Miniaturized sensors for application in cases where other probes may not be usable
3. Portable sensors with dedicated instrumentation can be fabricated for use outside the laboratory
4. Results can be furnished in real-time or close to real-time
5. Selectivity and specificity
6. Selectivity results from the choice of electrode material

The primary need for an electroanalytical approach is that the species being analysed must directly react at, or be adsorbed onto, the electrode (or indirectly through coupled reaction). Only in conditions where the medium between the two electrodes constituting the electrical circuit is sufficiently conducting can electroanalytical measurements be performed. Consequently, electroanalysis is an additional method of analysis. When compared to other analytical techniques, electroanalytical methods have a few advantages, including the ability to determine the oxidation state of the element, the ability to provide quick answers without digestion, and the ability to conduct the experiment directly in the field. Electroanalysis offers a ready-made option when other analytical procedures cannot be used because they need expensive and complicated equipment. [5-10]

1.1. Types of Electroanalysis

There are essentially four types of electro-analytical measurements that can be performed

1. Amperometry, 2. Conductometry, 3. Potentiometry, 4. Voltammetry

1.1.1. Conductometry

In conductometry, species selection is not possible because the concentration of the species is determined by measuring the solution resistance. It is helpful for determining whether the total ion concentration is below a specific permitted maximum level or when used as an online detector following the ion chromatographic separation of a mixture of ions.

1.1.2. Potentiometry

This method makes use of a high-impedance voltmeter to detect the equilibrium potential of the working electrode relative to a standard electrode while there is no current flowing. Selective species determination can be accomplished with little interference from other ions by carefully selecting the working electrode and ion-selective electrodes. Although changes in concentration as small as 10 picomolar can be observed, detection limits of the order of 100 nanomoles per liter of the total concentration of the ion present in a specific oxidation state are required.

1.1.3. Amperometry

In this method, the working electrode receives a set voltage that determines whether the species is being reduced or oxidised while also creating current. The size of the current is directly proportional to concentration if this potential is easily chosen. It is possible to attain the detection threshold in the micromolar range.

1.1.4. Voltammetry

Voltammetry uses a three-electrode setup to apply a changing voltage to the surface of an electrode and measure the current that results. This technique can show an analyte's electrochemical reactivity and reduction potential. Since only a very small amount of the analyte is consumed at the two-dimensional surface of the working and auxiliary electrodes, this approach in practical terms is non-destructive. Without the requirement for prior separation, several species that react at various applied potentials can be determined virtually simultaneously in the same experiment. Modern instrumentation and preconcentration of the analyte on the electrode surface enable very low detection limits down to the picomolar level. Analytical chemistry research shows that electrochemical sensors are the class of chemical sensors that is developing the fastest. For on-site monitoring of analyte in the sample matrix, electrochemical sensors and detectors are extremely appealing. They have built-in sensitivity to and selection against electroactive species, are quick and precise, small, transportable, and reasonably priced. These tools are among the most effective sensors now on the market, and they have a wide range of crucial uses in the sectors of clinical, industrial, environmental, and agricultural investigation.

2. CHEMICAL SENSOR

Chemical information, such as the concentration of a particular sample component or an analysis of the whole composition, can be converted into an analytically usable signal via a chemical sensor. The aforementioned chemical information may result from a physical characteristic of the system under investigation or a chemical reaction involving the analyte. A chemical sensor has two components: a zone where selective chemistry occurs, followed by a transducer. A signal is produced by a chemical reaction, such as a colour change, the emission of fluorescent light, a shift in the electrical potential at a surface, an electron flow, the generation of heat, or a shift in the crystal's oscillator frequency. The

transducer reacts to this signal and converts the signal's strength into a measurement of the analyte's amount. The following categories are used to classify chemical sensors based on the type of transducer they use.

2.1. Electrochemical Sensor

The result of the electrochemical interaction between the analyte and electrode is converted into a usable signal by electrochemical devices. Such interactions may occur naturally in the zero-current situation or may be electrically stimulated. These include solid electrolyte gas sensors, voltammetric sensors, and amperometric sensors such as potentiometric sensors (Ion selective electrode-ISE, Ion-selective field effective transistor-ISFETs).

2.2. Optical Sensors

A spectroscopic measurement is connected to the chemical reaction in optical sensors. Optodes are a common name for optical sensors, and optical fibres are frequently used in their construction. The various kinds of optical sensors use measurements of absorbance, reflectance, and luminescence.

2.3. Mass Sensitive Sensor

The surface acoustic wave sensor, which is particularly effective as a gas sensor, is one example of the piezoelectric effect-based sensor type. They rely on a shift in oscillation frequency caused by a change in mass on the surface of an oscillating crystal. The amount of material adsorbed on the surface is determined by how much the frequency shift has changed.

2.4. Heat Sensitive Sensors

These are frequently referred to as calorimetric sensors, which use a transducer like a thermistor or a platinum thermometer to measure the heat produced by a chemical process involving the analyte. Due to their exceptional detectability, ease of experimentation, and low cost, electrochemical sensors are particularly appealing when compared to optical, mass, and thermal sensors.

3. POTENTIOMETRIC SENSOR

By translating the recognition process into a potential signal that is proportional (in a logarithmic fashion) to the concentration (activity) of species generated or consumed in the recognition event, potentiometric sensors are able to gather analytical information. The essential element of all potentiometric ion sensors is an ion-selective membrane. It determines how the sensor responds to the analyte preferentially in the presence of different interfering ions from the sample. An electrochemical equilibrium will be reached, where distinct potentials in the two phases are established if ions can cross the boundary between the two phases. If just one kind of ion can be modified between the two phases, then the activities of this target ion in these phases are the only factors controlling the potential difference that results from the phases. The potential difference (E) across the membrane is given by the Nernst equation, which goes like this: $E = \text{constant} + RT / nF$ when the membrane divides two solutions with differing ionic activity (a_1 and a_2). In (a_2/a_1). The unknown activity in phase 2 ($a_2 = a_x$) is related to (E) by $E = \text{constant} + RT / nF$ if the target ion's activity in phase 1 is kept constant. In the equation (a_x / a_1) = const + $S \cdot \log(a_x)$, where n is the analyte's charge and $S = 59.16/n$ [mV] at 298 K. Between two identical reference electrodes positioned in the two phases, the potential difference can be measured. In actual practice, an ion-selective electrode and a reference electrode are placed in the sample solution, and the potential difference, or electromotive force, is measured between them. At 0 mA of current, the potential measurements are taken. The first potentiometric sensors were made of glass electrodes for pH measurements, and they have been around since the 1930s. Al_2O_3 , Na_2O , and SiO_2 are fused to create sodium silicate glass, which serves as the membrane in pH electrodes. The sensitivity to other monovalent cations increases as the glass' Al_2O_3 concentration rises. Kolthoff and Sanders created the initial silver halide disc electrodes in 1937.

Early in the 1960s, Pungorll published his first study on AgI-based electrodes and, with his colleagues, filed a patent on heterogeneous selective membranes, the foundation for the first industrial solid-state ISEs. Additionally, ideas from physiology and medicine influenced the development of ISEs. Neutral macrocyclic antibiotics promote ion permeation in mitochondria, which leads to the creation of neutral carrier electrodes, as noted by Cyril Moore and Berton C. Pressman in 1964. Toxic mushroom extracts containing the dipetide valinomycin were employed by Wilhelm Simon, a renowned chemical chemist at ETH Zurich (Switzerland). The extracts were dissolved in a liquid ion exchange membrane. Despite the delayed response, a K^+ electrode that could be used in the presence of a 5000-fold excess of Na^+ was shortly created and patented. He was able to create unique ISEs thanks to his research on the structure selectivity relationships of numerous synthetic ionophores, plasticizers, and additives. The first single-crystal electrode-based potentiometric fluoride sensor was published in 1966 by Frant and ROSS. A new generation of potentiometric chemical sensors emerged as a result of this groundbreaking work. Ion-selective electrodes were first developed by Ross and Frant, who also founded Orion Research Inc. The first liquid membrane sensor, which allowed for the direct measurement of calcium ions, was

shown in 1967. When the electroactive component was immobilised in poly (vinyl chloride), a polymer film with sensing characteristics was created, marking a significant advancement. In 1970, Ruzicka et al. introduced liquid-state electrodes made of carbon for the first time. Henry Freiser introduced the first coated wire electrode in 1971, and because it did away with the inner reference solution, it attracted a lot of interest. By adding finely distributed silver iodide to a silicone rubber monomer and then carrying out polymerization, Pungor and his colleagues created an iodide ion selective electrode. Additionally, an ISE enzyme for amygdalin has been suggested. Mesaric and Dahmen²⁹ documented the creation of sensors in 1973 utilising spectral-grade graphite powder, Pujol oil, and metal salts with poor solubility in a plastic body. The first application of a polymer film chemically modified carbon paste electrode (CMCPE) was disclosed by Heimen et al. in 1980. Potentiometric sensors' intrinsic specificity, breadth of application, dynamic behaviour, and simplicity make them useful for a variety of online monitoring systems. In high-speed automated flow analyzers like air-segmented and flow-injection systems, they are now frequently utilised as detectors. Additionally, potentiometric detection coupled with modern Ion chromatography has been employed with great effectiveness.

The ability to use ISE as on-column detectors for capillary electrophoresis has been made possible by their miniaturisation. The use of coated graphite epoxy ion selective electrodes for the measurement of cations utilising an ion-pair foundation with tricapyrylmethylammonium cation in a PVC matrix has been demonstrated by Rodwedder et al. and Fatibello and coworkers. Rover et al. have documented the creation of a tubular ion-selective electrode useful for the measurement of saccharin using a similar method with the addition of saccharinate anion and toluidine. Alfaya et al. report a more accurate method for measuring saccharin by coating a graphite rod with a thin layer of silsesquioxane 3-n-propyl pyridinium chloride polymer. Stradiotto and colleagues have described the successful application of nickel(I) hexacyanoferrate-modified thin film electrodes for potassium determinations. Potentiometric sensors are easy to use, quickly automated, have little matrix interference, and may be used on small volumes. Potentiometric sensors are a great option for measurements in both clinical and industrial settings where accuracy, speed, and simplicity are crucial. As a result, research on potentiometric sensors attracted a lot of attention, and a number of sensors have been reported for metal ions like alkali, alkaline earth, transition, and lanthanides; for anions like perchlorate ion, Cl⁻; and for pharmaceutical compounds like acetylsalicylic acid, mebendazole, and diclofenac. Ion-selective electrodes (ISE), coated wire electrodes (CWES), and field effect transistors (FETS) are the three main categories of potentiometric devices [10-17].

3.1. Ion-Selective Electrodes

Ion-selective electrodes are a component of a class of electroanalytical instruments that are generally referred to as potentiometric chemical sensors because, at the electrode, selective chemistry occurs, resulting in an interfacial potential. With a potentiometric chemical sensor, species recognition is accomplished through a chemical equilibrium process at the sensor surface. Therefore, a component that will react chemically and irreversibly with the analyte must be present on the surface. Ion-selective electrodes enable the precise and quantitative analysis of an almost inconceivably wide range of chemicals, from basic inorganic ions to complex organic compounds and amino acids.

3.2. Coated-wire electrodes

In the middle of the 1970s, Freiser made the first appearance of coated-wire electrodes (CWEs). To create an electrode system that is sensitive to electrolyte concentrations, a conductor is directly covered with an appropriate ion-selective polymer membrane (often poly(vinyl chloride), poly(vinyl benzyl chloride), or poly(acrylic acid)). Regarding detectability and concentration range, the CWE response is comparable to that of conventional ISE. The design's major feature is that it does not require an internal reference electrode, which has advantages when miniaturisation, for example. This is especially helpful for "vitro and in vivo biological and clinical monitoring of various types of analytes.

3.3. Ion-selective field effect transistors (ISFET)

Extensions of CWE are ion-selective field effect transistors (ISFET). Ion-sensing membranes are integrated into ISFETs right on the gate of a field effect transistor (FET). The FET is a solid-state device that can monitor charge accumulation on the ion-sensing membrane since it has a high input impedance and a low output impedance. The construction is based on the methodology used to create microelectronic chips, and its major contribution is the ability to create compact multisensor systems with multiple gates, allowing them to simultaneously sense multiple ions while their small size enables in vivo analyte determination.

4. CLASSIFICATION

Potentiometric sensors are categorised into two groups according to the physical state of the material covering the electrode membrane:

4.1. Ion-selective electrodes with solid membranes

Solid membrane ion-selective electrodes it comes to the immobility of the anionic groups, the membrane can either be homogeneous (a single crystal, crystalline substance, or glass) or heterogeneous (where a crystalline substance is built within a matrix derived from a suitable polymer).

4.2. Ion-selective electrodes with liquid membranes

In this scenario, the electrode membrane is represented by a liquid that is immiscible with water and contains a dissolved material that can exchange the electrode's target ion. This substance is either an ion complex for which the electrode is selective or it is an association of this ion with an oppositely charged ion that is soluble in the membrane. Potentiometric sensors are once more divided into categories based on the sort of membrane utilised.

4.3. Glass membrane

They are selective for ions such as H^+ , Na^+ , and NH_4^+ . Since the 1930s, potentiometric sensors have been employed to measure pH; the first of these was a glass electrode constructed around glass membranes. The membrane in a pH electrode is a sodium silicate glass produced by the fusion of Al_2O_3 , Na_2O , and SiO_2 .

4.4. Sparingly soluble inorganic salt membranes

This category includes single crystal sections of inorganic salts like LaF_3 , pressed powder discs of inorganic salts, and salt combinations like $Ag_2S/AgCl$. Such membranes are ions like F^- , S^{2-} , and Cl^- ion-selective.

4.5. Liquid membrane sensor

In these, a polymeric matrix like poly(vinyl chloride) immobilises an ion-selective complexing agent or ion exchanger.

4.6. Gel -Gel-immobilised and chemically bonded enzyme membranes

These membranes make use of the enzyme-catalyzed, extremely selective processes. The enzyme is bound to a solid substrate surface or integrated into a matrix. These are the earliest instances of biosensors since they involve biological mechanisms.

5. ION RECOGNITION ELEMENTS

The ionophore or On carrier, which lets the sensor respond to a specific ion preferentially in the presence of other ions, is the most important aspect of the sensor. The ionophores can be neutral macrocyclic compounds with molecule-sized dimensions that contain cavities or semi-cavities, Schiff bases, crown others, etc., or they can be ion exchangers.

6. PERFORMANCE FACTORS

1. Working concentration range and detection limit

The calibration curve portion through which a linear regression would show that the data points do not vary from linearity by more than 2 mV is known as the electrode's linear range. The cross-section of the two extrapolated linear sections of the calibration curve is used, per the IUPAC recommendation, to determine an ISE's detection limit.

2. Effect of PH

The potentiometric sensors' response is significantly influenced by pH. It can affect the equilibrium between protonated and unprotonated forms of the same material, encourage redox reactions at the electrode, or under some circumstances make the electrode pH selective.

3. Response time

A sensor's dynamic reaction time is a crucial metric. When measuring the potential of each ion repeatedly with a ten-fold variation in concentration, the response time of an electrode is assessed by calculating the average time needed to reach a potential that is within 1 mV of the final steady-state potential.

4. Selectivity

The most significant attribute of the sensors is selectivity. In the presence of other ions, it characterises the sensor's ion-specificity towards the target ion.

5. Lifetime

The stability of the selected material determines the sensor's lifetime, which is the time frame during which it can be utilised to determine the analyte. After that, the sensor's slope and detection limit will change in opposite directions. The loss of plasticizer, carrier, or ionic site from the polymeric film as a result of leaching into the sample may be the cause of the carrier-based sensors' short lifespan.

6.1. Application

It is also important that the sensors can be used for both online and offline activities in the industry as well as for continuous real-time monitoring of specific environmental analytes. In addition to applications for reducing pollution, sensors are required for environmental monitoring in farming, gardening, veterinary care, and mining.

7. A BRIEF REVIEW OF IMPORTANT POTENTIOMETRIC SENSORS FOR LANTHANIDES

Potentiometric sensors have been created for the following lanthanides as part of the investigations: La^{3+} , Sm^{3+} , Pr^{3+} , Nd^{3+} and Gd^{3+} .

Below is a brief overview of these metal ion potentiometric sensors.

7.1. Lanthanum

Sensors for lanthanum have been built using a variety of potential ion carriers. Ito and Goto evaluated how the 1-phenyl-3-methyl-4-octadecanoyl-5-pyrazolone-impregnated lanthanum sensor responded. Shamsipur et al. created a lanthanum-specific selector using the electroactive material 13, 5-trithiacyclohexane. Khalil used the ion carrier 5, 14-N, N'-hydroxyphenyl-4, 15-dioxo-1,5, 14, 18-tetra aza hexadecane to transport La^{3+} . Gupta et al. reported a liquid membrane sensor using monoazo-12-crown-4. The operational pH range was just 3-7, however, the sensor responded to lanthanum in the concentration range of 3.16×10^{-5} to 1.0×10^{-1} . Mittal et al. investigated the usage of the 18-crown ethers' cyclohexanol derivative as a lanthanum ionophore. A PVC membrane sensor and coated graphite electrode for La^{3+} based on bis(2-mercaptan) diacetyl were reported by Ganjali et al. in publication 74. The sensors responded linearly to lanthanum, however, they are sensitive to Na^{+} and Cr^{3+} interference. 2,2'-Dithiopyridine was proposed by Akhond et al. as a potential electroactive component in the construction of a La^{3+} selective sensor. Singh et al. investigated the hexaaza macrocycle-based membrane sensors' response properties. The membrane carrier 8,16-dimethyl-6,14-diphenyl-2,3,4,10,11,12-bipyridine-1,3,5,9, 11,13-hexaazacyclohexadeca-3,5,8,11,13,16-hexaene has a good working pH range and responds linearly to lanthanum in the range of 1.0×10^{-1} to 7.94×10^{-7} M. Suyanta et al. investigated the use of 1, 10-diaza-4,7, 13, 16-tetraoxacyclooctadecanoic, N'-diacetic acid as an ion carrier in the development of PVC membrane sensor. Even though the sensor was selective to lanthanum, other rare earth ions were found to be interfering with its working. PVC membrane sensors incorporating glyclazide, bis (thiophenol) phenylene-1,3-diamine, bis(2-methyl benzaldehyde)butane-2,3-dehydration, 4-methyl-2-hydrazinobenzo thiazole,3-hydroxy-N'-(pyridine-2-ylmethylene)-2-naphthol hydrazide, N-(2-pyridyl)-N'-(2-methoxyphenyl)-thiourea, edentates Schiff's base, and (1-[9 {2-[2-2-hydroxy-1-naphthyl]-3-(2- [(E)-I-(2-hydroxy-1 naphthyl)methylidene]amino Jethyl)-I-imidazolidyl} imino)methyl]-2-naphtho]) as ionophores were fabricated by Ganjali et. al. Among them sensor-based (1-[9 {2-[2-2-hydroxy-1-naphthyl]-3-(2- Qep~ {[(E)-I-(2-hydroxy-1-naphthyl)methylidene) amino} ethyl)-I-imidazolidyl} imino) methyl]-2-naphthol) exhibited a good detection limit of 4.5×10^{-10} M, but the analytical application sensor was not reported.

7.2. Samarium

Chowdhury et. al. reported the first samarium selective sensor impregnated with bis(thiaalkylxanthato)alkanes, but the sensor showed interferences in the presence of Cu^{2+} and Fe^{2+} . A liquid PVC membrane sensor was reported by Ganjali et. al. where the glypizide was used as the ionophore to detect Sm^{3+} . Shamsipur et al. fabricated a PVC membrane and coated graphite sensor for samarium based on 4,5,6,7- tetrathiocino [1,2-b:3,4-b]diimidazolyl-1,3,8, 10-tetraethyl-2,9-dithione. The coated graphite sensor was found to have a better concentration range and detection limit compared to the PVC membrane sensor, but the working pH range was only 4 - 6.5. Mittal et al. fabricated a samarium selective sensor incorporated with Tin (IV) organophosphate but the sensor gave a super Nernstian slope. Mittal and Sharma 90 studied the response characteristics of a sensor fabricated with Zirconium(IV)boratophosphate as an ionophore which had a good lifetime of 6 months. The use of Spiro[oxirane-pyrazolidinedione] derivative as an ionophore for samarium was reported by Saleh et. al. the sensor was applied in the determination of acetylsalicylate and carbonate in some drugs. Zamani et al investigated the response characteristics of membrane sensor impregnated with 3- {[2-oxo-1 (2H)-acenaphthyliden] amino} -2- thioxo-1,3-thiazolidin-4-one to Sm^{3+} ions. The first asymmetric potentiometric Sm^{3+} micro-sensor was reported by Ganjali et al. 193. 2- «(2-thioxothiazolidin-4- one) methyl) phenol was employed as an ionophore and the sensor showed a linear response in the range of 1.0×10^{-9} to 1.0×10^{-4} M with a slope of 18.27.

7.3. Neodymium

There are only a limited number of reports on the design of highly selective electrodes for neodymium based on different non-cyclic and macrocyclic ionophores. Shamsipur et al 94 reported the construction of a neodymium sensor based on 5-Pyridino-2,8-dithia[9](2, 9)-1,10-phenanthroline phane. The sensor exhibited linear response in the concentration range 1.0×10^{-6} to 1.0×10^{-2} with a fast response time and was applied to the recovery of Nd³⁺ ion from tap water samples. The working pH range of the sensor was found to be very low. P. Norouzi et al 95 developed a membrane sensor based on N-(2-Furylmethylene) pyridine-2,6-diamine which showed Venetian response to neodymium ions in the concentration range 1.0×10^{-5} to 1.0×10^{-2} M. The sensor was applied to direct monitoring of Nd³⁺ in various binary mixtures. 2-[[6-aminopyridin-2-yl]imino]methyl}-phenol-based sensor was developed by Ganjali et al 96 which showed Nernstian response to Nd³⁺. Behmadi et al. demonstrated the use of benzyl bis (thiosemicarbazone) in the determination of Nd³⁺ over the concentration range 1.0×10^{-2} and 1×10^{-6} M. The sensor was employed for the monitoring of Nd³⁺ from soil and sediment samples. Sensors based on two neutral ionophores, N, N'-bis ((1-H-pyrrol-2-yl) methylene) cyclohexane-1, 2-diamine and 3, 3'(cyclohexane-1, 2-diylbis (azan-1-yl-1-ylidene) bis (methan-1-yl-1-ylidene) bis (5hydroxymethyl) pyridine-2-01) are described for quantification of neodymium (III) by Gupta et al 97. Sensor based on 3, 3'-(cyclohexane-1, 2-diylbis(azan-1-yl-1-ylidene) bis(methan-1-yl-1-ylidene) bis(5-hydroxymethyl) pyridine-2-01) showed enhanced selectivity for Nd³⁺.

7.4. Praseodymium

Only four reports have been published in the literature for praseodymium. Ganjali et al produced a novel PVC membrane sensor for-praseodymium based on hydrazide derivative, 9. Zamania and coworkers [Oo.] reported the use of N, N'-bis(a-methylsalicylidene)diethylenetriamine and NI, N₂bis-(2-oxo-1, 2-diphenyl ethylidene) ethanedihydrazide as electroactive components for the determination of Pr³⁺ ions. Both the sensors showed a linear response in the concentration range of 1.0×10^{-6} to 1.0×10^{-2} M. The sensor based on N, N'-bis (a-methyl salicylidene)diethylenetriamine was applied for the determination of Pr³⁺ from soil and sediments while with NI, N₂bis-(2-oxo-1, 2- diphenyl ethylidene) ethanedihydrazide based sensor used for the recovery of praseodymium from different water samples and the determination of fluoride ions in mouthwash samples. Gupta et al 102 developed two PVC membrane sensors by incorporating 1,3- diphenyl propane-1,3-diylidenebis(azan-1-ylidene) diphenol and N,N'₂bis(pyridoxylideneiminato)ethylene as ion recognition element. Sensor-based on N, N'-bis (pyridoxylideneiminato)ethylene exhibited enhanced selectivity for praseodymium.

7.5. Gadolinium

Ganjali and Coworkers reported three sensors for the determination of gadolinium-based on different ionophores such as omeprazole, (2-[[3-[(2-sulfanylphenyl) imino]-1-methylbutylidene] amino] phenyl hydrosulfide and bis(thiophenol)pyridine-2,6-diamine. Among them sensor based on bis(thiophenol)pyridine-2,6-diamine showed an enhanced response in the concentration range 1.0×10^{-6} to 1.0×10^{-1} M. Zamania et al 106 fabricated membrane sensor based on 6-methyl-4-[[1-(2-Thienyl)methyl indene]amino] 3-thioxo-3,4-dihydro-1,2,4-triazin-5-(2H)-one and was applied to the determination of concentration of Gd (III) ions in soil and sediment samples. Faridbod et al 107 developed a PVC membrane, sensor based on N-(2-pyridyl)-N'-(4-nitrophenyl) thiourea. The sensor showed a linear response in the concentration range 1.0×10^{-5} to 1.0×10^{-3} M, but with sub Nernstian slopes. Shanna et al 108 studied the response characteristics of a sensor fabricated with Zirconium (IV)tungstophosphate (inorganic ion exchanger) as the ionophore which had a good working pH range of 4 - 10, but the slope was found to be super Nernstian of 30 mv/decade.

8. SCOPE OF THE PRESENT WORK

Understanding elemental distributions and chemical speciation is crucial in many disciplines, including earth science, biology, the environment, and electronics. The assessment of metal levels, particularly dangerous ones, in the atmosphere and biological materials, is becoming more and more important to civilization. Electroanalytical techniques, particularly electrochemical sensors, hold a leading position among the various methods available for the trace level determination of metal ions as they have reached the commercial stage and found a wide range of significant applications in the fields of clinical, industrial, environmental, and agricultural analyses. The current effort concentrated on the manufacture of potentiometric sensors for the determination of lanthanides such as La³⁺, Pr³⁺, Nd³⁺, Sm³⁺, and Gd³⁺ as a continuation of our work in the area of low-level monitoring of metal ions. In this regard, it is important to keep in mind that very few sensors have been created thus far for the detection of lanthanide ions. The significance of the current work is increased by this fact. Ten sensors in total, including PVC membrane and CMCPE-type sensors, have been created for these metal ions. All of the sensors' response parameters, including working concentration range, slope, detection limit, pH range, and selectivity, were investigated. The created sensors have been used to determine the presence of metal ions in actual samples as well as to serve as an indicator electrode in potentiometric titrations. It is hoped that all 10 of the created sensors will be able to be utilised to accurately and precisely determine each metal ion.

9. CONCLUSION

Future biotechnological process control, medical, agricultural, and other industries will use biosensors extensively. A key tool in the clinical diagnosis of a variety of illnesses is cholesterol biosensor technology. Then, software that is efficient

for monitoring cholesterol levels must be developed. Real-time cholesterol monitoring is not possible or supported by current technology. They cannot be used by patients at home. Building inexpensive, minuscule cholesterol biosensors is crucial in light of these drawbacks. Future research on cholesterol biosensors will concentrate on totally autonomous devices that patients at home may easily use. There are now a number of technologies for the electrochemical detection of blood cholesterol as a result of this extensive research, but the miniaturisation of these biosensors is still under consideration, so there is still a long way to go before the general public can access these biosensors. Cholesterol biosensors' level of sophistication, cost-effectiveness, dependability, and mobility will soon decide their desirability. Future healthcare professionals will be able to better detect medical disorders through a non-invasive method and tailor treatment to the individual patient's needs thanks to wearable and wire-free smart mobile technology. This type of autonomous machinery has various benefits, A few advantages are rapid response, less sample input, and cost-effectiveness.

REFERENCES

1. Hrdlicka, J. Havei, C. Moreno and M. Valiente, *Alia! Sci.*, 7, 925 (1991).
2. Hulanicki, S. Geah and F. Longman, *Pure Appl. Chem.*, 63, 1247 (1991).
3. J. Bard and L. R. Faulkner, *Electrochemical Methods, Fundamentals and Applications*, Wiley, New York (1980).
4. K. Lain, V. K. Gupta and J. R. Raison, *Sensors*, 4, 115 (2004).
5. K. Singh, P. Saxena, S. Mehtab and B. Gupta, *Anal. Sci.*, 22, 1339 (2006).
6. K. Singh, R. Singh and P. Saxena, *Sensors*, 4, 187 (2004). [37. T. Rosatzin, E. Bakker, Y. Suzuki and W. Simon, *Anal. Chem. Acta*, 280, 197 (1993).
7. Masuda, N. Nakamura and T. Tanaka, *Geochim. Cosmochim. Acta*, 37, 239 (1973).
8. Mazzucotelli, F. Depaz, E. Magi and B. Frache, *Anal. Sci.*, 8, 189 (1992).
9. Nann, I. Silvestri and W. Simon, *Anal. Chem.*, 65, 1662 (1993).
10. R. Fakhari, M. R. Ganjali and M. Shamsipur, *Anal. Chem.*, 69, 3693 (1997).
11. S. M. MontchenTfo, A. N. Araujo and C. M. C. M. Couto, *J. Auram. Meth. Managem. Chem.*, 24, 105 (2002).
12. Bing Li, Yali Sun and Ming Yin, *J. Anal. Al. Spectrom.*, 14, 1843 (1999).
13. M. A. Brett and A. M. Oliveira Brett, *Electroanalysis*, Oxford University Press, Oxford (1998).
14. M. A. Brett, *Pure Appl. Chem.*, 73, 1969 (2001). <http://www.wikipedia.com>
15. Macca, *Anal. Chim. Acta*, 512, 183 (2004).
16. Chowdhury, T. Ogata, S. Kamata and K. Ohashi, *Anal. Chem.*, 68, 366 (1996).
17. Skoog, D. M. West and F. J. Holler, *Fundamentals of Analytical Chemistry*, Saunders College Publishing, USA (1996).