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APPLICATIONS OF POTENTIOMETRY IN PHAMARACEUTICAL ANALYSIS – A REVIEW

[1]*Raj Kumar A., [2]Sarvesh Nikesh R., [2]Delphina T., [3]J. Rebekal, [1]Dinesh P., [4]Naveen Yadav J K and [5]Gnanasekar P.

[1]Department of Pharmaceutical Analysis, United College of Pharmacy Affiliated to Tamil Nadu Dr. M.G.R Medical University. G. Koundampalayam, Periyanaickanpalayam, Coimbatore-641020.
[2]Department of Pharmacology, United College of Pharmacy Affiliated to Tamil Nadu Dr. M.G.R Medical University. G.Koundampalayam, Periyanaickanpalayam, Coimbatore-641020.
[3]Department of Chemistry, JSS College of Pharmacy, Ooty, JSS Academy of Higher Education and Research, Mysore, OOTY-643001.
[4]Department of Pharmaceutics, United College of Pharmacy Affiliated to Tamil Nadu Dr. M.G.R Medical University. G.Koundampalayam, Periyanaickanpalayam, Coimbatore-641020.
[5]Department of Pharmacy, United College of Pharmacy Affiliated to Tamil Nadu Dr. M.G.R Medical University. G.Koundampalayam, Periyanaickanpalayam, Coimbatore-641020.

***Corresponding Author: Raj Kumar A.**
Department of Pharmaceutical Analysis, United College of pharmacy Affiliated to Tamil Nadu Dr. M.G.R Medical University. G. Koundampalayam, Periyanaickanpalayam, Coimbatore-641020.

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ABSTRACT
Potentiometry, the subject of this review, was extensively employed for the determination of numerous matrices, including plasma, serum, and urine. Potentiometry is appropriate for drug analysis in the pharmaceutical industry since their technology yields accurate results at a lower cost than more sophisticated methods. The review provided an overview of the state of the art in potentiometry at the time. Techniques for identifying drugs in this work, many biosensors and electrodes are utilized. The rapid reaction, simplicity, low cost, high sensitivity, quick static response, long-term stability, and application over a wide pH range of CPE, PVC, ISE, and GPE electrodes were demonstrated.

KEYWORDS: Potentiometry, Titration, CPE, PVC, ISE, GPE electrodes.

INTRODUCTION

This topic provides an overview of the potentiometry measurement technique. It's designed to be a major learning tool for Quantitative Analysis or Analytical Chemistry students, as well as a review resource for Instrumental Analysis students. It could also be a good place to start for new practitioners.[1]

Potentiometry is an electrochemical method in which the potential of an electrochemical cell is measured while little to no current is delivered through the sample. If you've ever used a pH meter, you've already done it. An indicator electrode responds to changes in the activity, or "effective concentration," of the analyte in a potentiometric measurement. A potential, or voltage, that develops at the electrode-analyte solution interface is measured in comparison to a reference electrode. The amount of analyte in the sample will determine this potential. The hydrogen ion or pH electrode is displayed in the upper right-hand corner of this page as an example of one type of indicator electrode.[2]

ISEs, or ion-selective electrodes, are the most common type of indicator electrode. ISEs have a high degree of selectivity, as the name suggests. In clinical laboratories, these electrodes are commonly used to determine ion concentrations (such as calcium) in blood samples. ISEs, on the other hand, do not have to be used in clinical settings. ISEs are also commonly employed in environmental analysis, such as measuring nitrate levels in a water treatment plant.[3]

Potentiometry is performed with simple equipment that includes an indication electrode, a reference electrode, and a potential measurement device. Potentiometry is a less expensive technology than atomic spectroscopy or ion chromatography because of its simplicity.[4] When doing a potentiometric measurement, the sample is usually just slightly altered. Furthermore, as said before, measurements at ISEs are unaffected by the color or turbidity of a sample, making them suitable for clinical and environmental applications.

Before we get into the specifics of potentiometry and ion-selective electrodes, we'll go over some basic electrochemical theory that's required to properly understand potentiometric measurements. Junction potentials, reference electrodes, and the Nernst equation are among the subjects covered. If you need a refresher on electrochemical cells and standard potentials.[5]

MATERIAL AND METHODS

Recent Articles from PubMed and google scholar were taken for references. All relevant papers were reviewed for application of potentiometry in pharmaceutical analysis and were cited for this paper. Some information's were taken from reliable online web sources for reviewing. Recent papers of past 8 to 10 years have been reviewed.

LITERATURE REVIEW

1. Hazem M. Abu-Shawish *et al.,* determined the potentiometric approach for pethidine in medicines and urine. The composition, useable pH range, response time, and temperature of a chemically modified carbon paste electrode (CMCPE) for pethidine hydrochloride (DBL) based on pethidine-phosphotungstate (PD-PT) as ion-pair complex were all completely described. The pethidine electrode demonstrated Nernstian responses in the concentration range of 2.1 $x10^{-6}$ - 1.0x 10^{-2} M, with a detection limit of 7.3x 10^{-7} and usability in the pH range of 3.5 to 6.6. This sensor had a quick response time (about 5 - 8 seconds) and good stability. The electrode's value (dE/dt) was determined to be 0.00071 V/C, indicating a good level of thermal stability. DBL had high selectivity for a large variety of inorganic cations, organic cations, sugars, and some popular pharmacological excipients, selectivity coefficients measured by Separating solution method (SSM) and matching potential method (MPM) (SSM). The sensor was found to be effective in estimating DBL in ampoules and spiked urine samples.

2. EmanY.Z.Frag and co-workers compared the performance of unmodified Membrane selective electrodes made of carbon paste (CPE; the paste contains no ions) and polyvinyl chloride (PVC). in the potentiometric measurement of ketotifen fumarate using sodium tetraphenylborate (NaTPB) as titrant. According to IUPAC standards, Over the concentration range of 10-7 to 10-2 molL-1, the performance characteristics of these sensors show a rapid, stable, and linear response for KTF. For CPE and PVC membrane electrodes at 30°C, the Nernstian slope values are 52.51±0.20 and 51.51±0.25mVdecade1, respectively. Over the pH range, the potential of CPE and PVC membrane electrodes is almost constant ranges of 3.0–6.0 and 2.0–7.0, respectively. The great selectivity of the produced electrodes is reflected in the Values of selectivity coefficients for inorganic cations, sugars, and amino acids. The responses of the electrodes at various temperatures were also studied, and CPE and PVC membrane electrodes were shown to have long operational lifetimes of 12 and 5 weeks, respectively. These are used to determine ketotifen fumarate in pure materials, pharmaceutical preparations (Zaditen tablets), and biological fluids utilizing potentiometric titration, calibration, and standard addition procedures (urine). For the CPE and PVC membrane selective electrodes, direct potentiometric determination of KTF yielded recoveries percent of 98.97 ±0.53 and 98.62± 0.74, respectively, with RSD 1.42 and 0.63 percent. The proposed sensors are suitable for use in quality control assessment of KTF, according to the method's validation.

3.Eman Y.Z. Frag*et al.,* developed a potentiometric measurement of chlorpromazine HCl, carbon paste electrode. The to create a carbon paste ion selective electrode for potentiometric titration with sodium tetraphenylborate to determine the medication under research. The performance of this sensor is compared to that of PVC membrane, coated wire, and coated graphite electrodes in the potentiometric detection of chlorpromazine HCl. The chlorpromazine HCl concentration in medicinal formulations was determined using this carbon paste electrode. The reproducibility and precision of measurements made during the investigation of these pharmaceutical matrices with a novel carbon paste sensor were assessed. The influence of electrode composition, electrode conditioning period, and test solution pH on electrode performance was examined. The drug electrode demonstrated in the concentration range of $1x10^{-7}$ to $1x10^{-2}$ mol L^{-1}, a Nernstian response with a slope of 58.06±0.34 mV $decade^{-1}$, Within the pH range of 2–6, it was shown to be quite exact and usable. This sensor had a low detection limit ($1x10^{-7}$ mol L^{-1}), a long lifetime (>2 months), and was very stable. With a relative standard deviation of≤ 0.28 percent, the percentage recovery gained is 97.72 percent.

4. Hasnamandiland co-workers by measured the gatifloxacin (GTFX) and ciprofloxacin (CPFX) in pure drug and dose forms, potentiometric titration. The oxidation of GTFX and CPFX with cerium (lV) in acid medium was used to develop this approach (HCl & HNO3). The reactions were found to be quantifiable using stiochiometry 1:4 (GTFX: Ce4+ & CPFX: Ce4+) in 0.25M HNO3 medium at 25oC, and the procedures are applicable over the ranges of 0.0125-2.500 mm (0.0510 mN) and 0.0250-2.500 m (0.1010 m). The relative standard deviations were ±5.13 percent and± 4.2 percent, respectively. Potentiometric and differential Potentiometric titrations were used for GTFX and CPFX, respectively. As a result, the provided approaches can be utilized to determine GTFX and CPFX on a regular basis.

5.Khorshid A.F *et al.,* developed four modified carbon paste electrodes, for the determination of neostigmine (Ns) ion in bulk powder, multiple pharmaceutical dose forms, and biological fluids (plasma and urine). Sensor 1 is based on the ion-association Ns-TPB, sensor 2 on Ns-PT, sensor 3 on a combination of (Ns-PT + Ns-TPB),

and sensor 4 on (Ns-PT + -CD). Over the pH range of 3.8–10, the solvent mediator 2NPPE showed correct behavior, with Nernstian slopes ranging from 61.5±0.5 to 64.5±0.5 mV per decade for the four sensors. Ns showed linear responses in the concentration range of $1.0x10^{-7}$-$1.0x10^{-2}$ mol/L. With a detection limit of $6.3x10^{-8}$ M, the reaction times are relatively short (less than ≤10 s). Sensor 3 has a Nernstian slope value of 75.5±0.5mV per decade in the concentration range of $1x10^{-6}$-$1x10^{-2}$ mol/L and a detection limit of $7.5x10^{-7}$ mol/L, according to flow injection analysis (FIA). When compared to sensors 1 and 2, the use of mixtures or additions of -CD had a substantial impact on boosting the sensitivity of sensors 3 and 4. The sensors were used to measure the ion neostigmine (Ns) in bulk powder, various medicinal dosage forms, and biological fluids (plasma and urine). The results were satisfactory, with a high percentage recovery that was comparable to the official method for the assay, which was based on non-aqueous titration with perchloric acid as a titrant.

6. Sutida Jansod*et al.*, described an electrochemical procedure on perm-selective membranes that provides valuable information regarding the speciation of ionizable medicines. At zero current (potentiometry and with applied current containing various quantities tetra dodecyl ammonium chloride (TDDA) were read out (chronopotentiometry). The ionized form of phenytoin (pKa-8.2), which corresponds to a negatively mono charge Dion, can be measured using potentiometry. The membrane components were carefully optimized, resulting in a lower limit of detection (-1.6 M) than previously reported. When the pH (from 9 to 10) or albumin concentration (from 0 to 30 g.L-1) in the sample is changed, the potentiometric signal changes suddenly as the ionized concentration of phenytoin is reduced or increased. As a result, potentiometry is insufficient to get information about the concentration and speciation of the drug in the system on its own. As a result, the total and ionized concentrations of phenytoin were determined using a tandem arrangement with chrono potentiometry as an additional readout basis. The diffusion of ionized phenytoin appears to be the rate-limiting phase for the chronopotentiometry readout in samples with high albumin, followed by fairly quick deprotonation and decomplexation reactions. This methodology was used to determine the concentration of phenytoin in pharmaceutical tables (100 mg per tablet). This tandem technique could potentially be extended to more ionizable medicines and used in the future for pharmacological drug monitoring during the delivery procedure.

7. Moslem Ardeshiriaand co-workers modified a graphite paste electrode (GPE) with methadone phosphotungstic acid and multiwalled carbon nanotubes as the ion pair to produce a rapid and easy approach for methadone detection in biological fluids (MWCNTs). In terms of graphite powder, the electrode's composition has been optimized: paraffine oil: The ion pair for MWCNTs was 58:30:8:4 (w/w percent). In a wide linear range of $1.0x\ 10^{-8}$ – $4.6x\ 10^{-3}$ M, for methadone, the electrode had a near-Nernstian slope of 58.9± 0.3 mV / decade and a detection limit of $1.0\ x10^{-8}$ M. In the pH range 5–11, the electrode response was pH-independent at 25 ^{o}C, with a quick reaction time (4 s). The sensor demonstrated good selectivity and was effectively used to determine sub-micromolar methadone concentrations in human blood serum and urine samples, with recoveries ranging from 95 to 99.8%. Using the proposed approach, the average recovery of methadone from tablets (5 mg/tablet) was 98 percent. Because of the property of GPE, which allows it to be cut off and a new electrode surface to be available, the modified electrode had a life span of more than 5 months. Using phosphotungstic acid as a titrating agent, a titration method for methadone analysis was carried out, which revealed an accurate end point and 1:1 stoichiometry for the ion-pair produced (methadone: phosphotungstic acid). The suggested methadone sensor has several advantages, including a simple and quick procedure, as well as an outstanding detection limit and selectivity.

8. Eman S. Elzanfaly *et al.*, developed the most ecologically friendly approach of analysis is the ability to get analytical signals without sample pre-treatment or derivatization. Comparison of potentiometric approaches, classical spectrophotometric, and HPLC methods for assessing drug dissolution was established in this study. For example, using an in-line potentiometric measurement instrument and no sample pre-treatment, an electroanalytical approach was designed and validated for analyzing the dissolution of sustained release capsules containing verapamil hydrochloride (VER). Using a poly (vinyl chloride) (PVC) based membrane and tetraphenylborate (TPB) as a cation exchanger, a sensor for determining VER in its dissolving liquid was created. As a plasticizer, nitrophenyl octyl ether (NPOE) was utilized. The ion pair was formed in situ by soaking the PVC membranes in a VER solution containing $1x10^{-3}$ mol/L. The sensor was validated in accordance with IUPAC guidelines. VER concentrations ranged from 4x10-5 to 1x10-2 mol/L, and the proposed sensor showed quick, stable near Nernstian responses across a large VER concentration range ($4x10^{-5}$ to $1x10^{-2}$ mol/L). The dissolution method was designed in accordance with FDA standards, utilizing USP apparatus I, 75 rpm rotation speed, 37.0±0.5^{o} C, 1000 ml water, pH 3.0 (adjusted with 2.0 N HCl) as the dissolution medium and USP apparatus I, 75 rpm rotation speed, at 37.0±0.5^{o} C. Over the course of 24 hours, dissolution profiles were created and compared to those acquired using the official spectrophotometric method. The conversion of potential to percentage of dissolution was done using the transpose of a Nikolskii-Eisenman type function. The suggested sensor can be utilized as a bench-top real-time analyzer to track the concentration of VER in real time while monitoring its dissolving and in medicinal applications. The proposed method has been validated and is regarded as a green, environmentally friendly methodology that

does not require sample pre-treatment or the use of any solvents.

9. Salwa Fares Rassi *et al*., used two modified carbon paste electrodes, for the determination of atorvastatin calcium in pharmaceutical formulations. The ion-pair of atorvastatin with 5,6 diamino uracil hydrochloride (ATS-DAUH) in one electrode (sensor A) and atorvastatin with picric acid in the other (sensor B) (ATS-PC). Dioctyl phthalate (DOPH) was the only solvent mediator to show correct behavior, with Nernstian slopes of the calibration curve at 58.76±0.8 and 57.48±1mV per decade for sensors A and B, respectively. The response durations were 10 and 12 seconds, with detection limits of $1.3x10^{-6}$ and $2.2x10^{-6}$ M, respectively, and concentration ranges of $2.5x10^{-6}$-$7.9x10^{-2}$M and $3.0x10^{-6}$ to $7.9x10^{-2}$M. The current electrodes are capable of distinguishing atorvastatin calcium from a variety of inorganic, organic, and sugar ions, as well as certain common excipients. Using standard addition and calibration curve methods, the sensors were used to determine atorvastatin calcium in medicinal formulations. The results were satisfactory, with excellent percentage recovery that was comparable to, and sometimes better than, that achieved by other standard assay methods. Were Simple, accurate, automation-friendly, and applicable to turbid and colorful sample solutions. The advantages of the suggested potentiometric methods.

10. Arezoo Zarezadeh and co-workers the glassy carbon electrode (GCE) and a carbon paste electrode (CPE) modified with a synthetic nano-structured molecularly imprinted polymer, electrochemical research and potentiometric assessment of captopril (CAP). A precipitation polymerization process was used to create a CAP-MIP sample with an average particle size of 95 nm. The electrochemical behavior of CAP was investigated in an aqueous solution at pH 3.0 using a MIP modified GCE. Electrochemical techniques were used to determine the electron transfer coefficient () for the CAP medication. Before its potentiometric determination, the prepared CAP-MIP was utilized as a modifier in a CPE to construct a selective CAP sensor. The improved CPE has a good electrochemical response, with a Nernstian slope of 59.15± 1.5 mV per decade over a wide linearity range of 3.0 $x10^{-9}$-1 .$0x10^{-1}$mol L^{-1}. For the 1H+/1e-process, the cyclic voltammetry results were in good agreement with the electrochemical studies. The developed electrode shows good selectivity for CAP over other pharmaceuticals such ibuprofen, paracetamol, acyclovir, pyrazinamide, dimenhydrinate, and naproxen, as well as good applicability in several pharmaceutical goods.

11. Amira M. El-Kosasy *et al*., developed a graphene with the advantages of ion selective potentiometric sensors in a single study. For the examination of Vilazodone hydrochloride in bulk, human plasma, and formula milk samples, they proposed two types of sensors: a graphene-based carbon paste and a poly vinyl chloride (PVC)-based membrane sensor. The electroactive agent is an ion-association complex made up of Vilazodone cationic cite and Molybdate anionic cite in a 1:1 ratio. Both sensors provide linear responses in the concentration ranges 10^{-7}-10^{-3} and 10^{-8}-10^{-3} M, with Nernstian slopes of 59.89 and 59.91 mV/decade for PVC membrane and Carbon paste sensors, respectively, according to IUPAC recommendation data. Both sensors performed well in the measurement of Vilazodone HCl in human plasma and formula milk samples, with high recovery percentages. Carbon paste sensor based on graphene has various advantages over traditional PVC membrane sensors, including lower detection limit, faster response time, longer life, and improved selectivity towards target ions.

12. Azar Dehnaviandco-workers., developed a new carbon paste electrode for the characterization of rifampicin (RIF). Composition, pH range, and temperature. In the carbon paste matrix, the sensor relies on 2hydroxypropylß-cyclodextrin as a good ionophore. Over a concentration range of $3.2x10^{-8}$ to $2.2x10^{-4}$ M, the modified electrode displayed with a limit of detection of $2.3x10^{-8}$ M and a Nernstian slope of 59.2 mV/decade. The electrode has a 4 s response time that is quick and consistent. Simple design, low cost, wide concentration range, great selectivity for rifampicin, use as an indicator electrode, and renewability were all features of the sensor. Rifampicin concentrations in tablet and blood serum samples were successfully determined with the sensor. In the temperature range studied, the temperature dependence of the sensor potential response. Rifampicin was effectively determined in tablet and blood serum samples using the sensor. In the temperature range of 15-55 °C, the temperature dependence of the sensor potential response was investigated. Within the measured temperature range, the sensor had a very low thermal coefficient.

13. Oguz ¨Ozbek*et al*., developed a potentiometric method for the determination of anti-epileptic drug valproic acid in human biological samples. A potentiometric poly (vinyl chloride) (PVC) membrane–based biosensor, was used with a Nernstian slope of 59.0± 3.6 mV/decade, this valproate-selective biosensor worked well over a broad concentration range of 1.0 $x10^{-6}$ to 1.0 $x10^{-1}$ mol L^{-1}. The lowest detection limit of the biosensor was 9.75 $x10^{-7}$ tens of mol L^{-1}. The developed valproate–selective biosensor showed high selectivity for antiepileptic drugs such carbamazepine, levetiracetam, and phenytoin, as well as ions present in human blood. The biosensor functioned in a pH range of 4.0–11.0 and had a reaction time of less than 10 seconds. It was also reusable and stable. The morphology of the fabricated PVC membrane biosensor was examined using SEM. Finally, valproic acid in human blood samples was determined using the conventional addition method., with very excellent recoveries.

14. Fatehy M. Abdel-Haleem and co-workers., developed a potentiometric measurement of IVB in pharmaceutical formulations. A highly sensitive carbon-paste electrode (CPEs) was developed. The ionophore t-butyl calixarene (t-BCX) was chosen because, as assessed by the sandwich membrane method (Log ILn= 8.62), it can mask IVB in the cavity via multiple H-bonding at the lower rim. Using Fe2O3@MWCNTs (multi walled carbon nanotubes covered with Fe2O3 nanoparticles) as a paste electrode addition increased the sensor's detection limit to 36 nM, with a Nernstian response of 58.9 mV decade-1 in the IVB linear dynamic range of 10^{-3}-10^{-7} M in aqueous solutions. Interfering species (e.g., Na^+, K^+, $NH4^+$, $Ca2^+$, Mg_2+, Ba_2+, Fe_3+, Co_2+, Cr_3+, Sr_2+, glucose, lactose, maltose, glycine, dopamine, and ascorbic acid) that may be present in physiological fluids or pharmaceutical formulations were detected with great selectivity by the built sensors. The sensors have been successfully used to measure IVB in the pharmaceutical formulations (Savapran).

15. Awad Ageel Al-Rashdi *et al.*, determined the Tenoxicam (TXM) by using potentiometric and conductometric methods with ten metal ions: Fe (III), Cr (III), La (II), Th (IV), Co (II), Mn (II), Pd(II), Ti(II), Sr(II), and Zr(II) (II). At 25± 0.1 °C in 0.05 M NaNO3 aqueous solution, the ionization constant of TXM as a ligand and the stability constants of the produced complexes were computed. The stoichiometry of the complexes was confirmed using conductometric techniques. Depending on the nature of the ligand-metal bonding, the metal/ligand ratio was 1:2 or 1:3. The potentiometric method, which was simple, precise, speedy, and economical, was used to determine TXM in pure form and three different dose forms (tablets, suppository, and injection). The well-known normal addition method was used to determine the amount of TXM. 4.50 mg L^{-1} was the average quantification limit. In the range of 0.09–4.66 mg L^{-1}, the suggested technique demonstrated excellent linearity. In the presence of other components found in the dosage forms, no interference was seen. TXM recovery from various tablet dosage formulations ranged from 96.66 to 101.21 %.

16. Khiena Brainina*etal.*, established a simple, rapid, and reliable sample preparation technique by potentiometric measurements of plant total antioxidant activity (AOA). The researchers looked at plant extracts and plant micro suspensions. The extraction parameters for plant extracts were chosen to have the maximum antioxidant activity at + 80 °C and a 20-minute extraction time. The AOA of extracts and micro suspensions increased as the degree of dispersion of the tested samples increased. The improved effect of micro suspension is due to the fact that antioxidants found in both liquid and solid fractions are involved in the signal-generating reaction zone. The study of plant micro suspensions shortens the time it takes to complete an AOA assessment. There was no difference between the antioxidant activity of black and green tea micro suspensions and the findings of an analysis of extracts generated using an approved method.

17. Jiansheng Liang andco-workers., developed a potentiometric titration for determination of active components in six distinct types of chemical disinfectants. The active components can help disinfectants be used more effectively. The active components in six distinct types of chemical disinfectants were systematically measured with high precision and accuracy. The coefficients of variance ranged from 0.04 % to 0.46 %. The sample recovery rates were all above 95%, with an extended uncertainty of 0.32g/L discussed. In the future, this approach could be used to analyze disinfectants more generally.

18. IbrahimCavus *et al.*, to determine the maprotiline, tricyclic pharmaceutical drug substance using a potentiometric ion selective electrode (ISE). The Tetraphenylborate ion pair of Maprotiline was synthesized. Elemental analysis results showed that the Maprotiline Tetraphenylborate ion pair combinationratewas1:1. The synthesized ion pair was utilized as a sensing material in the electrode membrane's construction. Polyvinylchloride (PVC) membrane ion selective electrodes were fabricated indifferent compositions using the produced ion pair for membrane optimization, and the potentiometric performance properties of the electrodes were investigated. The optimum potentiometric performance properties were discovered in an electrode with a 3.0% Maprotiline-Tetraphenylborate ion pair, 65.0% Dibutyl phthalate, and 32.0 % Polyvinylchloride composition. The linear working range of this electrode was $1.0x10^{-5}$–$1.0x10^{-2}$ M, with a slope of 55.4mV in a 10-fold concentration shift; the detection limit was $5.0x10^{-6}$M, the pH working range was 3–5, and the response time was 5s. The electrode has shown a potentiometric response that is very reproducible. This electrode was used to assess the maprotiline content of two distinct pharmaceutical tablets used to treat depression. The resulting findings were compared to the GC method's results. The results acquired using the potentiometric technique are 95 % similar to results using the GC method.

19. Ana Luiza G. Mendes andco-workers., studies the fluoride concentration in medicinal plants was measured using potentiometry using an ion selective electrode (ISE). Using the microwave-induced combustion (MIC) method, Samples weighing between 0.1 and 1.0 g were compressed into pellets and burnt. After burning, fluoride was absorbed in diluted ammonia for further ISE analysis. Near-100 percent recovery was achieved with a low relative standard deviation (5%) with 20 bars of oxygen and 5 minutes of reflux. The MIC method produced solutions with a low carbon content (less than 25 mg L^{-1}) and so eliminated the need for additional dilution before analysis. Fluoride measurement at low levels was facilitated by the efficient digestion of up to

1.0 g of medicinal plant (limit of quantification was 2.5 µg g-1). There was no statistical difference between the results obtained using ISE after MIC digestion and the values of certified reference materials (CRMs) of aquatic plant (BCR 60) and olive leaves (t-test, 95 percent confidence level) (BCR 62). Furthermore, when compared to data obtained using the AOAC's approved Method 975.04, there was no statistical difference (Fluoride in plants). Using the adjusted MIC settings, in addition, a microwave-assisted extraction (MAE) method was investigated (1 g, 6 mL of 25 mmol L^{-1} ammonia solution and 5 min of reflux). digests of MAE, on the other hand, had the high carbon content in final solutions (about 5 g L^{-1}) interfered with fluoride detection using ISE. As a result, the MIC approach was able to efficiently digest up to 1.0 g of material, with the analyte absorbed in a suitable alkaline solution.

20. A.O.Santini *et al.,* discussed the properties, performance, and application of a Pt|Hg|Hg2(PABzt)2| graphite electrode. PABzt stands for *p*-aminobenzoate ion. At pH 6.5–8.0, this electrode responds to PABzt with a sensitivity of (58.1±1.0) mV per decade over the range 1.0 x 10^{-4} –1.0 x10^{-1} $moll^{-1}$ and a detection limit of 3.2 x 10^{-5} $moll^{-1}$. The electrode is simple to manufacture, has a quick reaction time (within 10–30 seconds), is inexpensive, and has excellent response stability (lifetime greater than 6 months, in continuous use). In the presence of many chemicals, particularly carboxylate and inorganic anions, the suggested sensor showed good selectivity for *p*-aminobenzoate. The standard additions method was used to determine *p*-aminobenzoate in pharmaceutical formulations. The results obtained with this electrode were extremely similar to those obtained with an HPLC method.

21. M N Abbas and co-workers et al., determined the mercuric lipoate ion-pair as a membrane carrier in a potentiometric lipoate-selective sensor. The electrode was made by covering the surface of the graphite electrode with a membrane solution containing PVC, plasticizer, and carrier. On the response qualities of the electrode, they examined membrane composition, pH, and potentially interfering anions. Over the concentration range of 1 x10^{-7} $molL^{-1}$ to 1 x10^{-2} $molL^{-1}$, the sensor demonstrates significantly increased responsiveness toward lipoate ions, with a lower detection limit of (LDL) of 9x10^{-8} $molL^{-1}$ and a slope of --29.4mV$decade^{-1}$, with a S.D. of the slope of 0.214mV. It has been shown to have a fast and stable reaction, good repeatability, long-term stability, and applicability throughout a pH range of 8.0–9.5. The sensor has a response time of ≤12 seconds and can be utilized for at least 6 weeks without significant variations in its potential response. Lipoate is well separated from a variety of inorganic and organic anions using the proposed electrode. The CGE was employed in flow injection potentiometry (FIP), which produced well-defined peaks for lipoate ions with a steady baseline, outstanding repeatability, and a tolerable sampling rate of 30 injections per hour. The suggested sensor has been used to determine LA in pharmaceutical preparations and urine using direct and FI potentiometric methods, as well as an indicator electrode in potentiometric titration.

22. Raluca-Ioana Stefan van Staden *et al.,* proposed a method of R-baclofen, based on two enantioselective, potentiometric membrane electrodes and cyclodextrins. The electrode slopes for - and -cyclodextrin-based electrodes were 59.50 and 51.00mV/pR-baclofen, respectively. The proposed electrodes had detection limits of 7x10^{-9} $moll^{-1}$ for the -cyclodextrin-based electrode and 1.44x10^{-10} $moll^{-1}$ for the -cyclodextrin-based electrode. Over S-baclofen, the enantioselectivity was determined. The proposed electrodes can be used to test R-baclofen raw materials and Norton-Baclofen® tablets, a pharmaceutical formulation of R-baclofen. The electrodes' surfaces are stable and easily renewable by polishing them with alumina paper.

23. Mojtabashamsipur *et al.,* developed the new potentiometric titration for the dissemination of diclofenac by using ion selective electrode in pharmaceutical analysis. By soaking the PVC membranes in a 1x10^{-2} M diclofenac solution, the diclofenac combination with hexadecyl pyridinium bromide is formed in situ. Dibutyl phthalate (DBP) showed proper performance among the four solvent mediators evaluated, including a Nernstian slope of the calibration curve, a fast response time, and good reproducibility of the emf readings. For diclofenac in the concentration range 1.0x10^{-5} to 1.0x10^{-2} M, the electrode has a Nernstian slope of - 59±1mVdecade-1 with a limit of detection of 4.0x10^{-6}M. In comparison to a number of typical inorganic and organic compounds, the electrode has a high selectivity for diclofenac. It works in the pH range of 6.0–9.0. The membrane sensor was used to determine the presence of diclofenac in tablets as well as to recover it from blood serum and urine samples.

24. A O Santini *et al.,* developed a novel and simple electrode, Pt|Hg|Hg2(MF1)2|Graphite for the determination of mefenamic acid. With a detection limit of 6.2x10^{-7} $molL^{-1}$ and a sensitivity of (58.9±0.7) decade spanning the range 1.0x10^{-6} to 1.0x10^{-2} $molL^{-1}$ at pH 6.0–9.0. The electrode is simple to make at a low cost, has a quick response time (within 10–25s), and can be utilized for up to four months without losing its performance characteristics. The sensor showed good selectivity for mefexamide, particularly for carboxylate and inorganic anions. Mefenamic acid was successfully determined in pharmaceuticals and human serum samples using the new developed potentiometric sensor.

25. Siminsabah and co-workers., synthesized the Valproate-doped polypyrole (PPy-val) was electrochemically in the presence of valproate ion in an aqueous solution and employed as a valproate ion selective sensor. A pulse galvanostatic approach was used to investigate polymerization. Also studied the

impact of polymerization conditions on the sensor's potential response properties. The time approach was used to optimize the concentration of pyrrole and valproate ions, electrode type, solvent effect, current, time, and number of pulses. In an aqueous solution, the solid-state PPy-val sensor, which was made by electropolymerizing pyrrole in the presence of valproate ions on a platinum rod, displayed quasi-Nernstian behavior over $4x10^{-5}$–$4x10^{-2}$MVal^{-} with a detection limit of $1x10^{-5}$ M. The electrode had a response time of about 20 seconds and could be utilized for at least 4 months without any dispersion. The electrode's potential response was repeatable in the pH range of 2–11 and was unaffected by pH between 4 and 7.5. The sensor's selectivity was tested against a variety of epileptic medicines (carbamazepine, phenobarbital, and phenytoin) as well as inorganic salts. Using titration potentiometry, the drug sensor was used to determine the presence of valproate ions in medicinal formulations.

26. Ahmadsoleymanpour*et al.,* investigated a new potentiometric carbon paste electrode based on the integration of the carvedilol-phosphotungstate ion-association complex. To carvedilol, the electrode showed a Nernstian slope of 58.7 mV/decade throughout a large concentration range of 3.0 $x10^{-7}$ to 1.0 $x10^{-3}$ M, with a low detection limit of 1.5x 10^{-7} M. Fast reaction, long life time, and, most significantly, strong selectivity for carvedilol over a wide range of common foreign inorganic cations, biological species, and other β-blockers were all advantages of the sensor. In potentiometric titration and potentiometric measurement of carvedilol in carvedilol tablet, blood serum, and urine samples, the sensor was successfully used as an indicator electrode. The suggested sensor was used to study the development of inclusion complexes between a- and b-cyclodextrin and carvedilol, and the formation constant of the inclusion complexes was computed.

27. Santhy A, Beena Saraswathyamma and co-workers., developed a potentiometric PVC membrane for clopidogrel sulphation measurement of clopidogrel from clopilet tablets. The effect of the PVC membrane matrix was investigated, and the optimal membrane composition, which resulted in a Nernstian slope of 58.83±0.340mV/decade, was determined to be PVC 32 percent, ion association 3%, NaTBP 2%, and DBP 63 percent. In the concentration range $1x10^{-2}$ -$1x10^{-6}$ M, the sensor demonstrated a rapid response time of 3s and a lower detection limit of 9.12x 10^{-7}M. The working pH range and response time, respectively, were found to be 2.0 - 4.5 and 5s. Comparative investigations on the many parameters that depend on the potential response of the current sensor were also included, are reported.

28.Gamal A.E Mostafa *et al.,* reported a Poly (vinyl chloride) membrane sensor for pioglitazone HCl (PG) in terms of their manufacture and electrochemical response properties. As electroactive materials, the sensing membranes contain pioglitazone cation and sodium tetraphenylborate (NaTPB) (sensor 1), phosphomolybdic acid (PMA) (sensor 2), or phosphotungstic acid (PTA) (sensor 3). Over a relatively wide pioglitazone concentration range ($1x10^{-2}$ to 10^{-6}) M, the sensors show a rapid, steady, and near-Nernstian response, with cationic slopes of 55.0±0.5, 58.0±0.5, and 53.0±0.5mV per concentration decade over a pH range of 1.0–5.0. The sensors are capable of distinguishing pioglitazone from a variety of inorganic and organic substances. At 100.0g/ml, the direct determination of 2.5–3900.0g/ml of pioglitazone shows an average recovery of 98.5, 99.0, and 98.4 percent, respectively, and a mean relative standard deviation of 1.6, 1.5, and 1.7 percent. The proposed sensors have been used to determine the presence of pioglitazone in a variety of medicinal formulations. The findings obtained using the suggested sensors for determining pioglitazone in tablets are equivalent to those obtained using the HPLC approach. The sensors were employed as indication electrodes for pioglitazone potentiometric titration.

29.Emilia M.G.Santosand co-workers., compared the potentiometric response properties of diclofenac selective electrodes based on Fe(III) tetraphenyl porphyrin-chloride (Fe(III)TPP-Cl) and Fe(III) tetrakis (pentafluoro phenyl)porphyrin-chloride (Fe(III)TPFPP-Cl). The kind of carrier substituent and the pH value of the sample solution have a major impact on the membrane sensor's sensitivity, working range, detection limit, response mechanism, and selectivity. The potentiometric mechanism of action of the employed metalloporphyrin was determined using studies with varied levels of cationic additive (tetra-n-octyl ammonium bromide (TOABr)) and anionic additive (sodium tetraphenylborate (NaTPB)) in the membranes. Fe (III)TPFPP-Cl (type G), produced in o-NPOE with 10mol percent TOABr, was employed for the examination of genuine samples. In a buffered solution of ammonia–ammonium sulphate with pH 9.9, this potentiometric unit displayed a linear response towards diclofenac concentrations between 10^{-5} and 10^{-2} moll^{-1} (I=0.1moll^{-1}) and slopes of roughly -59mVdec^{-1}, with a response time of 10s. Direct potentiometry was used to determine the potency of sodium diclofenac in pharmaceutical formulations, and the results were compared to those obtained by HPLC, with relative errors that were lower.

30.Emilia M.G.Santos*et al.,* developed ion selective electrodes sensitive to penicillin-G antibiotics for the analysis of pharmaceutical formulations. Using 5,10,15,20-tetraphenylporphyrinate (TPP)manganese (III) (Mn (III)TPP-CI) as an electroactive material, different types of polymeric membranes based on PVC (poly (vinyl chloride)) and EVA (ethyl-vinyl acetate) were created without an internal reference solution. Different additives, such as stetra-n-octylammoniumbromide (cationic additive) and sodium tetraphenylborate (anionic additive), were inserted into the membranes to see how they affected the performance

of the electrodes. The produced detectors were compared based on their general analytical properties, selectivity, and lifetime. Two selective membranes, 33.0 percent (w/w) of PVC, 66.0 percent (w/w) of o-NPOE, 1.0 percent (w/w) of Mn (III)TPP-Cl, and 10 percent mol (relative to the molar concentration of Mn (III)TPP-Cl) of sodium tetraphenylborate (type B) were used to analyze genuine samples. Type A electrode had a linear response for penicillin-G between $2x10^{-5}$ and 10^{-1} $moll^{-1}$, a5 slope of about 59mVdec, and a reproducibility of about ±1 0.5mVday^{-}, whereas type B had a linear response for penicillin-G between $5x\ 10^{-1}$ and 10^{-1} $moll^{-1}$, a slope of about- 61mVdec, and a reproducibility of about± 0.3mV day^{-1}. Direct potentiometry was used to determine the potency of penicillin-G in pharmaceutical products, and the results were compared to those obtained using the HPLC reference method. These membranes (types A and B) were utilized to make tubular electrodes that were connected to a sequential injection system (SIA) and had linear ranges of $2x\ 10^{-4}$ and $1\ x10^{-2}$ $moll^{-1}$, with slopes of - 59.3± 0.8 and -57.3± 1.2$mVdec^{-1}$, respectively. The potentiometric measurement of penicillin-G in pharmaceutical formulations was carried out using a tubular electrode made of type B membrane (type TB). The proposed technique resulted in relative errors ranging from 0.1 to 1.2 percent (n = 4) and a sampling rate of approximately 25 samples per hour.

31.**FahimehJalaliand co-workers.,** developed the new gabapentin ion-selective electrode in pharmaceutical analysis. By soaking the PVC membrane in a $1.0x10^{-3}$ M gabapentin solution, the gabapentin combination with phosphomolybdic acid (MO) was created in situ. Dioctyl phthalate (DOP) was the only one of three solvent mediators examined to show correct behavior, with a Nernstian slope of 59.8±2$mVdecade^{-1}$ for gabapentin in the concentration range of $1.0x10^{-5}$ to $5.0x10^{-2}$ M and a limit of detection of $1.0x10^{-5}$ M. In comparison to a number of medications that may be taken with gabapentin at the same time, the electrode shows good selectivity for gabapentin. In the pH range of 1.8–3.2, the sensor can be used. The membrane sensor was used to determine gabapentin levels in tablets as well as recover gabapentin from blood serum samples.

32. Yousry M. Issa *et al*., described the Poly (vinyl chloride) (PVC) membrane selective electrodes for the measurement of distigmine (Ds) in terms of their fabrication and electrochemical response characteristics. The sensing membrane was made up of an ion-pair made up of distigmine phosphomolybdate (Ds-PM), distigminephosphotungstate (Ds-PT), distigminesilicomolybdate (Ds-SM), distigminesilicotungstate (Ds-ST), distigmine tetraphenylborate (Ds-TPB), and distigmineereineckate (Ds-Rein) in a plasticized PVC (DOP). The effect of membrane composition on the responsiveness of the electrodes was investigated. Over a large distigmine concentration range of $5.0x10^{-7}$–$1x10^{-2}$ mol L^{-1}, the electrodes displayed a rapid, steady, and Nernstian response with a slope of -30.5± 1.0 mV dec^{-1}. Within the pH range of 3.8–10.5, the reaction is unaffected by the pH of the test solution. The electrodes have a life duration of at least 2 months with no significant potential divergence and a response time of <15 seconds. In batch and FIA systems, the electrodes showed good selectivity towards distigmine when compared to large quantities of ions. Distigmine has been measured in pure solution, pharmaceutical compounds, and human urine using the electrodes. A 2010 Cairo University study looked at the dissolving profile of Ubretid tablets (5 mg/tablet).

33.MajidArvendand co-worker., developed the AlMCM-41 as a neutral carrier in a poly (vinyl chloride) (PVC) matrix to create a potentiometric aluminum sensor. Over the concentration range of $1.0x10^{-7}$ to $1.0x10^{-1}$ M, the sensor demonstrates dramatically enhanced selectivity toward Al3+ ions, with a detection limit of $8.6x10^{-8}$ M and a Nernstian slope of 19.5±0.4mV/decade of activity. Membrane compositions of 30% poly (vinyl chloride), 67 percent acetophenone, 3 percent ionophore, and 2mL tetrahydrofuran yielded the greatest results. It is quick and stable reaction, high repeatability, and long-term stability. The sensor has a reaction time of 10 seconds, and the membrane could be utilized for three months without significant potential divergence. The matched potential approach was used to calculate selectivity coefficients (MPM). The AlMCM-41-based sensor can be used in pH 3–6 aqueous solutions. The isothermal coefficient of the electrode was calculated using standard electrode potentials measured at various temperatures. It was used to determine the presence of Al3+ in medications and food.

34.B. Visser*et al.*, compared new coated wire potentiometric sensors based on composite coatings with traditional potentiometric sensors. The ionically conducting components of the composite sensors were clay montmorillonite (MM) and zeolite NaY, which were embedded in PVC-based rubber phase membranes. On 9 potentiometric sensors of various compositions, the behavior of 20 basic medical medicines and 5 biogenic amines was examined. The behavior of three composite sensors, as well as six more traditional PVC-based sensors (either "inner solution" or "coated wire"), was investigated. The analytes were chosen to span a large log P range, such as -1.54 (noradrenaline) to +5.55 (epinephrine) (promethazine). A high-throughput FIA-based approach was used to evaluate all sensors. Statistical data analysis was used to interpret the findings. All electrode responses were highly correlated with the log P of the analytes. This was also true for ion-pair electrodes with a specific cationic medication acting as the counterion. The least sensitive were traditional ion-pair based sensors using tetrakis (p-chlorophenyl) borate (TCPB) and a counterion with a high log P value (e.g. promazine). Sensors made of composite materials were the most sensitive. Coated wire electrodes were statistically proven to behave similarly to inner solution

electrodes in terms of selectivity and sensitivity. A physio-chemical model is used to explain the findings. In HPLC detection of pharmaceutical pharmaceuticals and biogenic amines, practical uses of the most performant (composite) sensors are illustrated. Lipophilic medicines (log P>2) have detection limits in the 10^{-7} M regio (injected concentrations).

35.Zholt Kormosh*et al.*, developed a Membrane sensor based on ion-pair Brilliant Green mefenamate. The sensitivity of the sensor to the mefenamate ion is (86.0 2.0) mV/pC over the range of 9 $x10^{-5}$–1x 10^{-2} mol/L, with a detection limit of 4.5 $x10^{-5}$ mol/L at pH 8.5–12. The sensor is simple to put together and has a quick response time (5–10 seconds). In the presence of various substances, the proposed sensor showed good selectivity for the mefenamate ion. It was used to find out how much mefenamic acid present in several medications.

36.Xiao-Xia Guo and co-workers., investigated the interaction of calf thymus dsDNA with TAM (tamoxifen) using zero current potentiometry, a novel electrochemical method. The dsDNA (dsDNA/CP) was immobilized on the surface of carbon paste. When dsDNA/CP was connected in series between the clips of a potentiostat's working and counter electrodes and a reference electrode in an aqueous solution containing TAM, the interaction of dsDNA with TAM resulted in a change in interfacial potential at the dsDNA/CP/solution interface. Interfacial potential offset the applied potential somewhat when linear sweep potential was applied to the dsDNA/CP and the associated I–E curve was recorded, causing the I–E curve to displace along the potential axis. To check the displacement of the I–E curve, a zero current potential was measured where circuit current, I was equal to zero. The thermodynamic constants of the interaction between dsDNA and TAM were calculated using the displacement. The apparent binding constant of dsDNA with TAM was determined to be $(6.85\pm0.20)10^{6}$ M^{-1} and the binding ratio of dsDNA with TAM was found to be 1:1. The interaction was examined in their natural forms without damage since zero current potentiometry was independent of changes in redox potential or current of both dsDNA and TAM. Furthermore, TAM can be calculated. The detection threshold was set at $1.1x10^{-7}$ M.

37.Hazem M. Abu-Shawish *et al.,* developed two modified carbon paste electrodes, for the determination of tramadol hydrochloride in urine, milk, and pharmaceutical preparations was devised. The ion-association of tramadol hydrochloride with phosphotungstic acid (TD-PT) is used in one electrode (sensor A), while a mixture of phosphotungstic acid (TD-PT) and silicomolybdic acid is used in the other electrode (sensor B) (TD-SM). 2-nitrophenyl octyl ether (NPOE) displayed Nernstian slopes of the calibration curve at 57.8±0.4 and 56.5±0.8mV per decade for sensors a and b, respectively, among seven different solvent mediators investigated. The response times were 8 and 5 seconds, respectively, with detection limits of $6.2x10^{-6}$ and $1.8x10^{-6}$ meters. $9.2x10^{-6}$ to $1.0x10^{-1}$ and $5.5x10^{-6}$ to $1.0x10^{-1}$ M concentration range in that order. The current electrodes are capable of distinguishing tramadol hydrochloride from a variety of inorganic organic ions, carbohydrates, and common medicinal excipients. The sensor was used to determine tramadol hydrochloride in urine, milk, and preparation using potentiometric determination, standard addition, and calibration curve methods. The results were satisfactory, with excellent percentage recovery comparable to, and sometimes better than, those obtained by other routine methods for the determination of tramadol hydrochloride in urine, milk, and preparation.

38. Saad S.M Hassan *et al.*, developed a miniaturized nitrate sensor for flow injection analysis (FIA) of nitrates in diverse samples. In a plasticized PVC membrane, the sensor uses silver bis(bathophenanthroline) nitrate $[Ag(bath)_2NO_3]$ as an electroactive material. The sensing membrane (3mm x 5mm) is mounted on a wafer polyimide microchip (13.5mm x 3.5mm) to provide a planar miniaturized design that may be employed in a single channel wall-jet flow injection system. The sensor exhibits fast response, high sensitivity, long-term stability, and good selectivity for NO_3- in the presence of several common associated anions when operating in hydrodynamic mode (FIA) Over the concentration range of $1.0x10^{-1}$ to $1.0x10^{-6}$ $molL^{-1}$, the calibration slope is $55.1\pm0.1mVdecade^{-1}$, the lower detection limit is 0.05 μgmL^{-1}, the working pH is 2–9, and the output is 70–90samples h^{-1}. The assay method was validated and shown to have good performance characteristics, indicating that it could be used for routine NO3 measurement in industrial wastewaters, fertilizers, and medicines. The results are in good agreement with data collected using traditional spectrophotometric methods.

39.Amr L.Saberandco-workers., proposed a new potentiometric method for measuring flucloxacillin . The method entails creating a flucloxacillin sensor with an electroactive membrane made of Aliquat 336S-flucloxacillin in a poly vinyl chloride matrix membrane plasticized with orthonitrophenyl-octylether or dioctyl phthalate. For o-nitrophenyloctylether (o-NPOE) and dioctyl phthalate (DOP) plasticized based membrane sensors, the sensor shows a fast, stable, and repeatable response over the concentration range of $1.0x10^{-5}$–$1.0x10^{-2}$Mflucloxacillin with anionic slopes of 60.7±0.3 and 61.2±0.2 and pH ranges of 6–11 and 7–11, respectively. The sensor's response time is consistent and quick (7 s). In the presence of amoxicillin, ampicillin, dicloxacillin, penicillin, numerous anions, and medication excipients and diluents, the sensor has a strong selectivity for flucloxacillin. Evaluation of the procedure according to quality assurance standards demonstrates that the proposed sensors are suitable for use in drug quality control assessment. For o-NPOE and DOP plasticized based membrane sensors, respectively, average recoveries of 99.6% and 99.7% and mean

standard deviations of 1.2 percent and 1.5 percent were achieved, which compare fairly well with data acquired using the British Pharmacopoeia technique.

40.TawficA.Saleh*et al.,* developed and validated promethazine by cerium in an acidic media, a simple and fast-automated of promethazine hydrochloride in pharmaceutical formulations. A portable device was built, consisting of a programmable syringe pump and a potentiometer. During promethazine oxidation, the generated change in potential was observed. The associated ideal working conditions were optimized, including supporting electrolyte concentration, cerium (IV) concentration, and flow rate. The proposed method has been effectively used to both pharmaceutical and synthetic materials. The results were acquired using the official British pharmacopoeia (BP) approach, which yielded comparable results. The resulting t-value suggests that there are no significant differences between the proposed and BP methods results, with the proposed method's advantages being simplicity, sensitivity, and cost effectiveness.

41.Saad S.M Hassan *et al*., developed new low-cost potentiometric membrane sensors with a cylindrical configuration that respond to ephedrine. The sensors are based on the usage of triacetyl-β-cyclodextrin [(triacetyl-β-CD)] as a neutral ionophore embedded in a plasticized poly (vinyl chloride) (PVC) matrix (sensor I) and carboxylated poly(vinylchloride)[(PVC–COOH)] as a simultaneous plastic matrix and ion exchanger (sensor II) (sensor II). Both sensors demonstrated a significant increase in response to the ephedrinium cation (EPD+) spanning a concentration range of 3.0 $x10^{-5}$–8.0 $x10^{-3}$ mol L^{-1}at pH 4–9 and 3–8, respectively, with low detection limits of 5.7 $x10^{-6}$ and 6.2 $x10^{-6}$ mol L^{-1}. For EPD^{+}, the sensors showed a near-Nernstian cationic slope of 57.0 and 55.6 mV $decade^{-1}$, respectively, and the impacts of lipophilic salts and other foreign common ions were investigated. The sensors were also successful as tubular detectors in a two-channel flow injection system. The inherent features of the detectors in a low dispersion manifold operating in hydrodynamic mode were determined and compared to data collected in batch mode. Long life span, good selectivity for EPD+ over a broad variety of other organic compounds, long term stability, high reproducibility, fast response, low detection limit, wide measurement range, acceptable accuracy and precision were all discovered during method validation. The sensors were used to determine EPD+ in pharmaceutical formulations and spiked biological fluid samples, and the results were compared to traditional procedures.

42. FahimehJalaliandco-workers., determined the Atorvastatin (ATR) by potentiometric method. As an ionophore, the ion-pair of ATR and acetyl trimethyl ammonium bromide (CTAB) was employed. Multiwalled carbon nanotubes (MWCNTs) and an ionic liquid, 1-butyl-3-mtehyl-imidazolium hexafluoro phosphate, were added to a graphite paste electrode (BMIMPF6). The proportions of electrode materials (graphite powder: paraffin oil: ATR-CTAB: MWCNTs: BMIMPF6) were optimized (58:26:5: 8:3w/w percent). Surface characterization was done by using scanning electron microscopy. The potential measurements were recorded at optimized Ph by using acetate buffer solution ($0.1mol^{-1}$, pH5.5). The calibration curve (E vs. log [ATR]) was linear (R2= 0.9977) in the concentration range of 1.0x 10^{-9}–1.0 $x10^{-3}molL^{-1}$(0.0012–1209mgL^{-1}) of ATR with a Nernstian slope of 58.14±0.2mV$decade^{-1}$, and detection limit of 1.0$X10^{-9}molL^{-1}$(0.0013mgL^{-1}After each injection of ATR to the buffer solution, the potential was stabilized in avery short time (averageresponsetime~6s) at 25°C. The improved graphite paste electrode lasted for a long time (N 4 months). The fidelity of electrode response to ATR was demonstrated by the recovery of the spiked substance to blood serum samples (95.3–98.2%). The proposed approach was used to evaluate blood serum samples from customers, and the findings were comparable to those obtained using the HPLC standard method. The potentiometric analysis of ATR tablets by the proposed electrode resulted in relative errors of 0.8 percent and 1.5 percent, respectively, for 20 and 40 mg per tablet. Finally, the electrode was employed in the potentiometric titration of ATR (1.0x 10^{-3}mol L^{-1}) by CTAB (1.0x 10^{-3}mol L^{-1}). The volume of the titrant at the end point provided excellent accuracy (100 percent).

43.Julia Atta-Politou*et al.,* conducted invitro study to determine the adsorption rate constant as well as the adsorption features of fluoxetine (F) to activated charcoal and its commercial formulation Carbomix powder. The method employed was ion-selective electrode (ISE) potentiometry, which was based on the selective, direct, and continuous monitoring of F with an F-ISE built in our lab. The kinetic studies were carried out by rapidly adding a slurry containing charcoal to the drug solution while swirling it and continuously monitoring the F-ISE potential until equilibrium was reached. The recorded adsorption curve was used to compute the free ionized drug concentration at appropriate time intervals, and the apparent adsorption rate constant was estimated using pseudo first order kinetics. The estimations' R.S.D. within run ranged from 0.24 to 11.5 percent, while the R.S.D. between runs (n=3–4) ranged from 0.90 to 13.8 percent. The apparent adsorption rate constants were found to be linearly related to the amount of charcoal employed, with slopes (±S.D.) of 1.14(±0.21) and 0.146(±0.009) s^{-1} g^{-1} for activated charcoal and Carbomix, respectively. The F-ISE potential was measured at equilibrium after successive additions of microvolumes of F solution to a charcoal slurry. The highest adsorption capacity (±S.D.) of activated charcoal and Carbomix was 254.8±1.8 and 405±41 mg/g, respectively, while the affinity constant (±S.D.) was 45.6±2.2 and 55.5±2.9 l/g. The adsorption of F to charcoals was rapid, with 95 percent of F adsorbed in the first 5 minutes for amounts of charcoal 10 times greater

than the amount of drug. Both types of charcoals examined adsorbed efficiently F at stomach pH, compared to hazardous and deadly dosages in cases of F intoxication. In cases of F poisoning, Carbomix might be considered an acceptable charcoal formulation for medical treatment.

44.MojtabaShamsipurandco-workers., determined the manufacture, characterization, and application of a new cimetidine ion-selective electrode in pharmaceutical analysis. PVC membrane containing cimetidine–phospohotungstate ion pair combination is used in the electrode. For cimetidine, the electrode exhibits a Nernstian response with a slope of 58±1 mV per decade in the concentration range $1.0x10^{-5}$–$1.0x10^{-2}$ M. The detection limit is $5.0x10^{-6}$ M. In comparison to a variety of typical foreign inorganic and organic species, the electrode has a high selectivity for cimetidine. It works best when the pH is between 3.0 and 5.5. Cimetidine was successfully determined in its tablets as well as recovered from a urine sample using the membrane sensor.

45. G. Altiokka*et al.*, described a flow injection analysis (FIA) for levofloxacin (LVF) employing UV detection, potentiometry, and conductometry. The optimal solvent system was discovered to be 0.2 M acetate buffer at pH 3 with 10% MeOH. The active substance was detected at 288 nm with a flow rate of 1 ml min1. For FIA, the detection limit (LOD) and limit of quantification (LOQ) were determined to be $3x10^{-7}$ M (S/N=3) and $1x10^{-7}$ M (S/N=10), respectively. The RSD ++-values for FIA, potentiometric, and conductometric techniques, respectively, were 0.83, 0.98, and 0.99 in the analysis of tablets.

46.M. Arvandandco-workers., determined the integration of a triamterene/tetraphenylborate ion-pair in a poly (vinyl chloride) coating membrane resulted in the creation of a coated wire triamterene-selective electrode. Membrane composition, temperature, pH of the test solution, and foreign ions all had an impact on electrode performance. The electrode had a Nernstian response at 25^oC over a triamterene concentration range of $1.0x10^{-6}$ to $3.5x10^{-2}$ M, and was found to be exceedingly selective, precise, and usable within the pH range 4.5/7.5. The isothermal temperature coefficient (dE^o/dt) of the electrode was calculated using the standard electrode potentials, E^o, at 15, 20, 25, 30, 35, 40, and 45^oC. Temperatures above 45°C have a significant impact on the electrode performance. The electrode was effectively used to determine triamterene hydrochloride potentiometrically in both pure solutions and pharmaceutical formulations.

47.A.M. Othman *et al.*, developed the fabrication and performance features of one-selective membrane electrodes for sildenafil citrate (SC). In a poly vinyl chloride membrane, complex ion interacts of SC with sodium tetraphenylborate (SC–TPB) and phosphomolybdic acid (SC–PMA) are formed as ionophores (PVC). Over a wide range of concentrations 10^{-2} to 10^{-5} M sildenafil, both electrodes SC–PMA and SC–TPB demonstrated a linear and stable potential response with near-Nernstian slopes of 55.5 ± 0.35 and 53.5± 0.3 mV per decade, respectively, with good repeatability. The electrodes had a quick response time of 30 to 40 seconds and could be used throughout a pH range of 3 to 6. The selectivity coefficients showed that SC medication has good selectivity over a wide range of nitrogenous compounds as well as several inorganic cations. The proposed sensors have been put to the test in terms of analyzing SC in its purest form, medicinal formulations, and blood serum. The average recovery was 98.9–99.5±0.6 percent, with a correlation of 0.998 to known approaches.

48.Saad S.M. Hassan *et al.*, approached the ranitidine, the potentiometric technique uses innovative PVC matrix membrane sensors with ranitidine-reineckate, tungstophosphate, and tungstosilicate ion association complexes as electroactive chemicals and 2-nitrophenyl phenyl ether as a plasticizing solvent mediator to measure the drug cation directly. These sensors have rapid near-Nemstain stable responses for $1O^{-2}$-$1O^{-6}$ M ranitidine over the pH range 4-8, and they're employed in a flow-through sandwich cell to determine drug flow injection. The spectrophotometric approach involves forming a yellow di(N-nitroso) ranitidine chromophore by combining ranitidine with excess nitrite in an acetate buffer with a pH of 4.8 and a catalyst of Cu_2+/Br^- or micelles. At 450 nm, Beer's law is observed in the range of 0.3-12 mg ml^{-1}. The suggested potentiometric and spectrophotometric methods for determining ranitidine in a range of pharmaceutical dosage forms demonstrate an average recovery of 98.4 percent of the nominal values and a mean standard deviation of 0.5 percent. Drug excipients and diluents do not cause any interference. The results are comparable to those obtained using the US Pharmacopoeia's liquid chromatographic approach.

49.E.E. Sideris and co-worker., established a home-made diflunisal ion-selective electrode, the interaction of diflunisal ion (DF) with β-cyclodextrin (bCD), β-cyclodextrin (gCD), and hydroxypropyl-β-cyclodextrin (HPbCD) in phosphate buffer, pH 7.4, at $5–37^0C$ and varied CD concentrations. HPbCD was used to create typical direct binding plots and Scatcherd plots. The Scatcherd model was used to estimate binding parameters for the DF/HPbCD interaction for one class of binding sites. The n (number of binding sites per CD molecule) values were all extremely near to one, confirming 1:1 complexation. The estimations of the association constant (K) fall as the temperature rises. With varied βCD or ɣCD concentrations, sigmoidal direct binding plots and concave-downwards Scatcherd plots were obtained. For the DF/βCD and DF/ɣCD interactions, the Hill model was employed to estimate the binding parameters. The CD concentration had a significant impact on both the Hill coefficients and the binding

constants. The cooperative nature of DF/βCD and DF/γCD interactions is revealed by these findings. The Van't Hoff equation was used to calculate the free energy change, ΔG, as well as the thermodynamic parameters, ΔH and ΔS, for each of the interactions evaluated.

50.Cristina M.C.M. Couto &co-workers., developed a potentiometric method for the estimation of tetracycline (TCH), oxytetracycline (OTCH), and chlortetracycline (CTCH) by flow injection potentiometry is described in this study. TC samples are put in a carrier solution and converged with a Cu (II) solution of known concentration in the flow system described; the Cu (II) drop due to its complexation with tetracyclines (TC) was observed. A homogeneous crystalline CuS/Ag2S double membrane tubular electrode with improved sensitivity was used as the detector. Tetracyclines may be determined within a range of $48.1–4.8x10^{3}$ ppm for TCH, $49.1\text{-}4.9x10^{3}$ ppm for OTCH, and $51.5–5.1x10^{3}$ppm for CTCH, with a precision of less than 0.4 percent for all three TC species. With a Cu (II) consumption of about 13 mg determination^{-1}, this technique may complete 150–200 samples per hour^{-1}.

CONCLUSION

In conclusion, a broad range of techniques are available for the analysis drug in biological samples and pharmaceutical formulations. The analysis of the published data revealed that the potentiometry was extensively used for the determination of various matrices like plasma, serum, and urine. For analysis of drug in pharmaceutical, potentiometry is applicable because this method provides accurate results and low cost compared to more advanced detection techniques. This review carried out an overview of the current state of art of potentiometry methods for the determination of drug. Various biosensor and electrodes are used in this study. CPE and PVC and GPE electrodes proved the rapid, simple, low cost, good sensitivity, fast static response, long term stability, low detection limit and applicability over a wide pH range. The CPE represents excellent selectivity stability, Nernstian behavior and analytical application without any preliminary process.

The electro analytical methods are the greenest methods as regards to sample extraction and pretreatment and no solvent consumption. Graphene based sensors offers several advantages over the proposed PVC membrane-based sensor in terms of faster response allowing analysis of large number of samples in a short time, longer life time, lower limit of detection, wider linear dynamic range and higher selectivity towards the target ion. The sensor is comparable with different reported techniques. Such as chromatography, spectroscopy, and voltammetry. Which are more complex and costly than potentiometric sensors. The developed potentiometric biosensors might be an ideal method for the determined and follow up of human blood samples of patients due to its advantages over than analytical methods. The electrode can be successfully used in quality control laboratories for the routine analysis in pharmaceutical preparation without any pretreatment or separation steps as alternative to more sophisticated, expensive and five consuming analytical methods.

The CGE electrode is determination of pharmaceutical preparation is characterized by high degree of precision and accuracy when compared to validated HPLC method. However, the low cost of analysis and the precision of results compared with the results provided by HPLC method justify the use of potentiometry as an alternative analytical technique for the analysis of their type of products. It is suitable for satisfying the increasing demand for control and routine analysis in many fields of analytical chemistry and quality control analysis. The potentiometry is an advantages technique for the direct adsorption studies of ionic drugs provided that a successful electrode can be constructed.

CONFLICT OF INTREST

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