Sensors International 3 (2022) 100189

Contents lists available at ScienceDirect

Sensors International

journal homepage: www.keaipublishing.com/en/journals/sensors-international

Recent advances in potentiometric analysis: Paper–based devices

Oguz Özbek [a,*], Caglar Berkel [b,**]

[a] Zonguldak Bülent Ecevit University, Science and Technology, Application and Research Center, 67600, Zonguldak, Turkey
[b] Tokat Gaziosmanpasa University, Faculty of Science and Arts, Department of Molecular Biology and Genetics, 60250, Tokat, Turkey

ARTICLE INFO

Keywords:
Potentiometry
Paper–based electrodes
Electroanalytical methods
Sensors
Analysis

ABSTRACT

Paper has been increasingly used in recent years as a substrate in the structure of sensors to determine diverse biological and pharmaceutical molecules and ions. Potentiometric sensors built with paper offer certain improvements since they are cost–effective, portable, biodegradable, eco–friendly, disposable and easy to manufacture. Paper is also an ideal substrate to be used, considering that it is flexible, lightweight, mechanically–resistant, a good medium for immobilization and trapping, and that it can be easily chemically and physically modified for customized applications, it can adsorb and transport liquid via capillary forces, can close the electrical circuit between electrodes when wet, it can be produced in diverse geometrical dimensions and porosities. Due to these characteristics, paper–based potentiometric sensors are more eco–friendly, suitable to be used in resource–limited areas, can be used in remote locations or on–site settings with low–cost analytical instrumentation. To our knowledge, the most recent advancements in the field have not been collectively reviewed, and this is of high importance considering the rapid developments made in paper–based potentiometric sensors lately. In these review, we covered paper–based potentiometric devices developed in the very recent years, detailed their structures, and compared their certain performance parameters including detection limit, linear concentration range, response time and applicability.

1. Introduction

Potentiometry, an electrochemical analysis technique, is based on the measurement of the potential against time of a system consisting of working and reference electrodes under conditions without a current flow [1]. Potentiometric sensors were first defined by Cremer in 1906, and since then, great progress has been made in the field of potentiometry with the developing technology [2–4]. The most important milestones of this field are given in Fig. 1. Potentiometric methods have become popular among researchers due to their particular advantages since the day they were first defined. These devices offer advantages such as wide linear concentration range, ease of preparation and use, low cost, short response time, low detection limit, long lifetime, high selectivity, good reproducibility and stability [5–10]. These advantages have allowed the use of potentiometry in diverse fields including environmental, industrial, agricultural, routine laboratory analysis, medicinal drug analysis and process control [11–16].

There is an urgent need to develop inexpensive portable sensing platforms for various applications from environmental monitoring to disease diagnostics [17]. Recently, paper has been used as a substrate to fabricate various micro–fluidic devices [17]. Paper–based analytical devices have started to be preferred by researchers since paper is low cost, flexible, easily disposable, lightweight, thin, compatible with a wide array of patterning methods, mechanically–resistant (Fig. 2) and it also allows electrical communication between electrodes when wet (closes the electrical circuit between electrodes), it is able to be manufactured in various geometrical dimensions and porosities [18]. Paper–based analytical devices and their applications from the detection of neurotransmitters to nucleic acids and nerve agents have been reviewed before, and some of these devices have been developed using other

* Corresponding author.
** Corresponding author.
E-mail addresses: oguz.ozbek@beun.edu.tr (O. Özbek), caglar.berkel@gop.edu.tr (C. Berkel).

Production and hosting by Elsevier

https://doi.org/10.1016/j.sintl.2022.100189
Received 27 May 2022; Received in revised form 8 June 2022; Accepted 9 June 2022
Available online 13 June 2022

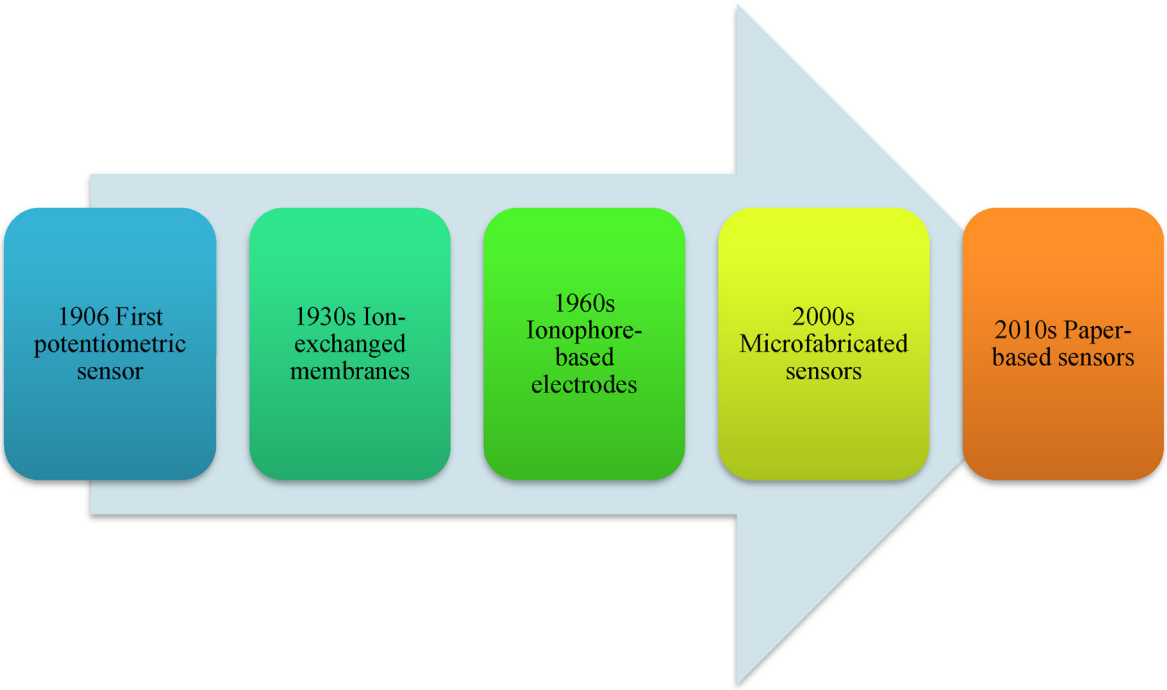

Fig. 1. Important milestones in the field of potentiometry.

Fig. 2. Certain advantages of paper–based analytical devices.

electrochemical techniques including amperometry and voltammetry or some other non–electrochemical methodologies; however, this review aims to focus on paper–based sensors developed using potentiometric methods in the very recent years [19–29].

Potentiometric sensors built with paper as a substrate are biodegradable; and thus, they are more eco–friendly compared to their alternatives. Besides, paper is a good medium for immobilization and trapping, and its hydrophilic structure containing large connected pores composed of cellulose fibres makes it possible to adsorb and transport liquid via capillary forces, and this ultimately results in a fast response. In addition, this porous structure allows nano– or micro–particles to remain immobilized in the paper, and paper can also be functionalized with the use of certain materials, it can be easily chemically and physically modified for customized applications; thus, paper can be used in a wide spectrum of analysis. Paper–based potentiometric devices are also highly portable, enabling their use in remote locations or on–site settings with low–cost analytical instrumentation. Since paper is also permeable to gasses, the formation of air bubbles is not experienced in the analyses performed using paper. Due to all these advantages of paper–based analytical devices, recent years have seen a growth in research on this subject [30]. Numerous analytical methods have been adapted as paper–based, including electrochemical, colorimetric, fluorescent and (electro)chemiluminescence methods [31]. In recent years, paper has also been successfully integrated with potentiometric electrodes. In these devices, a full potentiometric cell is embedded in the paper, making the device a quite useful tool.

In this article, we summarized paper–based potentiometric devices for the detection of various species and provide insights for possible future research directions.

2. Paper–based devices

2.1. Paper–based sensors for the determination of ionic species

Bouhoun et al. proposed a paper–based potentiometric sensor for the simple and fast monitoring of water hardness, which is defined as the amount of dissolved calcium and magnesium in the water [32]. In this study, firstly, potentiometric ion–selective electrodes for calcium and magnesium ions printed on a paper substrate were prepared by the authors. Subsequently, these ion–selective electrodes (ISEs) were used to determine the concentration of calcium and magnesium ions present in water samples. The authors reported that their proposed sensor for Mg^{2+} and Ca^{2+} works in the concentration range of $1.0 \times 10^{-6} – 1.0 \times 10^{-1}$ M. These sensors had detection limits of 3.6×10^{-7} M and 3.3×10^{-7} M for Mg^{2+} and Ca^{2+} paper–based ISEs, respectively. In addition, the authors stated that the developed method can be applied in various domestic and industrial settings as it is easy to use and cost–effective.

A simple, cost–effective, portable and disposable paper–based

solid–state ISEs for the determination of Cu(II) ions were developed by Kamel et al. [33]. In the study, newly synthesized macrocyclic pyrido–pentapeptide derivatives were used as ionophores. The all–solid–state paper–based Cu^{2+}–ISEs displayed a linear response over the concentration range from 5.0×10^{-7} to 1.0×10^{-3} M with a limit of detection of 8.0×10^{-8} M. The Cu^{2+} ion–selective electrode was found to have a short response time of < 10 s. The authors reported that they have successfully applied this paper–based analytical device for the detection of Cu^{2+} in serum and whole blood samples from different children with autism spectrum disorder.

In addition to Mg^{2+}, Ca^{2+} and Cu^{2+}, the concentration of many other ions in various samples can be determined using paper–based potentiometric sensors. This is of high importance since the consistent and reliable monitoring of ion concentrations is crucial to maintain environmental quality (e.g. heavy metals incl. Cd^{2+} and Pb^{2+}) and human health. Devices mostly used for ion analysis (such as ASS, IC and ICP MS) require cumbersome sample pre–treatment and a relatively costly/bulky equipment. Therefore, they are not suitable for quick analysis of samples in on–site applications or in resource–limited situations, unlike some portable, low cost and miniaturized analytical devices. For instance, a portable and inexpensive paper–based potentiometric determination of chlorine, potassium, sodium and calcium ions was performed by Lan et al. [34]. The composition of the prepared sensors in this study included poly (vinyl chloride) (PVC), *o*–nitrophenyl octyl ether (*o*–NPOE), potassium tetrakis(4-chlorophenyl)borate (KT*p*ClPB) and ionophore. Valinomicine, 4-tert-butylcalix [4]arenetetraacetic acid tetraethyl ester and *N*,*N*,*N*′,*N*′-tetracyclohexyl-3-oxapentanediamide (ETH 129) were used as ionophores in potassium, sodium and calcium selective sensors, respectively. The developed paper–based sensors had linear concentration ranges of $1.0 \times 10^{-4} - 1.0 \times 10^{-1}$, $1.0 \times 10^{-3} - 1.0$ and $1.0 \times 10^{-4} - 1.0 \times 10^{-1}$ M; and slope of 54.9 ± 0.6, 54.8 ± 1.4 and 22.9 ± 0.8 mV/decade for potassium, sodium and calcium ions, respectively.

Ding et al. reported a novel concept of solid reference electrode integrated with micro–fluidic paper–based sampling, and used it in potentiometric ion sensing [35]. This reference electrode consisting of an Ag/AgCl reference element was connected to a paper–based micro–fluidic device via a disposable paper substrate (DPS) containing solid KCl. Since sample solution dissolved the solid KCl present in the paper, and thus provided the electrolyte for the Ag/AgCl reference element, there was no need to use a KCl reference solution in the analysis step. Authors found that this reference electrode gives a relatively constant potential after <1 min of equilibration, and that the potential of developed the sensor was not affected by the presence of electrolytes commonly observed in real samples. They also showed that the reference electrodes equipped with substrates offering higher KCl levels generally have shorter equilibration time and higher potential reproducibility. Authors integrated this reference electrode with a paper–based micro–fluidic device and solid–contact ion–selective electrodes sensitive to K^+, Na^+ and Cl^-. These sensors displayed near–Nernstian sensitivities (59.1 ± 1.5, 57.5 ± 0.5 and -56.4 ± 0.6 mV dec^{-1}) and detection limits ($10^{-4.1\pm0.1}$, $10^{-3.3\pm0.1}$ and $1^{-\ 4.1\pm0.1}$ mol dm^{-3}) for the indicated ions, respectively. It was also reported in the study that these paper-based sensors could be used as semiquantitative analytical devices in the determination of ions in wastewater sludge and sweat samples, pointing to the applicability of these sensors in both environmental and clinical samples.

Sakata et al. showed the ability of paper–based metal electrodes for wearable biosensors as part of a wireless potentiometric measurement system, in particular for the detection of pH and sodium ions [36]. These electrodes were developed by coating a silicone–rubber–coated paper sheet with an Au (/Cr) thin film with sputtering, and then by modifying it with different functional membranes including an oxide membrane (Ta_2O_5) and a fluoropolysilicone (FPS)–based Na^+–sensitive membrane. These sensors were stable and sensitive over several weeks even when they were highly curved, due to their high flexibility. Authors were able to measure the Na^+ concentration in a sweat sample using this paper–based Au electrode with the FPS–based Na^+–sensitive membrane in a wireless and real–time manner while the electrode was bent.

Paper–based potentiometric devices can also be used in the food industry and food quality control. Nery and Kubota developed a paper–based electronic tongue with an integrated Ag/AgCl reference electrode for the analysis of beer and wine [37]. They reported the development of a potentiometric electronic tongue with integrated reference electrodes and electrodes based on paper, for the first time. Authors optimized the fabrication protocol by testing different methods: electroless plating, use of silver nanoparticles and commercial silver paints. The developed sensor required a minimum of 40 uL of sample, and it was composed of electrodes sensitive to sodium, calcium, ammonia and a cross–sensitive, anion–selective electrode. This sensor was applied in the analysis of 34 beer samples (12 types, 19 brands). This system was reported to be able to discriminate beers from different brands and types, to identify the presence of stabilizers, antioxidants, dyes, unmalted cereals and carbohydrates. They also minimized the sample volume required by using paper sample pads and by measuring in flow conditions. To test this improvement, a four electrode system with cross-sensitive (anion–selective, cation–selective, Ca^{2+}/Mg^{2+}, K^+/Na^+) electrodes was used in the analysis of 11 types of wine (4 types of grapes, red/white, 3 countries). The proposed matrix was able to group wines based on different varieties of grapes from which wines were produced.

Others reported that a gold–modified paper as a micro–fluidic substrate can be used for the potentiometric determination of Na^+, K^+, and Cl^- ions in various clinical samples [38]. Authors compared the measurements performed using paper substrates to other commonly used micro-fluidic substrates including sponge, polyester textile, and polyamide textile; and found that unmodified paper exhibits 1–2 orders of magnitude lower rate of fluid transport, compared to the sponge and textiles studied. Solid–contact ion–selective electrodes based on plasticized PVC membranes for Na^+, K^+, and Cl^- ions, and PEDOT(PSS) or PEDOT(Cl) as the ion–to–electron transducer were used in the design of sensors. Authors reported that the modification of the paper substrates with gold nanoparticles (AuNPs) slows down the transport of bovine serum albumin (BSA, a protein) through the paper by approximately 20–50%, in comparison to unmodified paper substrates and all the other alternative sampling matrices. The retention of BSA on paper substrates modified by AuNPs was found to significantly improve the accuracy of the potentiometric ion measurements in clinically relevant samples such as sweat, saliva, artificial tears and artificial serum. Devices with unmodified paper was found to show better precision but lower accuracy, whereas those with the gold–modified paper showed better accuracy but lower precision. Authors also validated the results obtained using these paper–based sensors with those obtained using inductively coupled plasma optical emission spectrometry (ICP–OES) and ion chromatography (IC).

2.2. *Paper–based potentiometric pH sensors*

Kawahara et al. described the development of a paper-based potentiometric pH sensor using carbon electrode drawn by pencil [39]. It has been reported that the pH sensitivity of the prepared electrodes varies between 16.5 and 26.9 mV/pH. The authors stated that the pH sensor developed is more robust compared to other techniques, and it is simple to fabricate and also easily disposable. Another paper–based potentiometric pH sensor was reported by Chow et al. [40]. They have integrated a potentiometric pH sensor with an electrochromic readout system, all on paper substrates. The most important advantage of this method is the versatility of the electrochromic readout system, and its ability to be integrated with the potentiometric sensor. The authors stated that this integrated system can be applied in the development of other potentiometric sensor types; therefore, it is not limited with the detection of hydrogen ions.

2.3. Paper–based sensors for the determination of drugs

Others utilized paper–based potentiometric sensors for the determination of drug salicylhydroxamic acid, which is usually used for the treatment of urinary tract infections, by integrating both the salicylhydroxamic acid sensor and the reference Ag/AgCl electrode on paper substrates [41]. The ion–sensing membrane of this sensor was based on the use of Sn^{IV}–tetraphenylporphyrin (Sn^{IV}TPP) as a charged carrier within a plasticized poly(vinyl chloride) matrix, and as an ion–to–electron transducer, multi–walled carbon nanotubes (MWCNTs) were used in the design of these sensors. This sensor showed a rapid and stable response with a Nernstian slope of -59.3 ± 0.7 mV/decade over the concentration range from 1.0×10^{-6} to 1.0×10^{-3} M, and it had a detection limit of 0.7 μM. Intra– and interday– precision were measured and found to be 1.7%. Authors also reported that the relative standard deviation (RSD%) is calculated as 2.43%, and the sensor shows a good selectivity pattern in the presence of different lipophilic anions. They also applied this sensor successfully for the assessment of salicylhydroxamic acid in various pharmaceutical samples with high reproducibility, and stated that this device can be mass produced with high speed in the future due to its high portability, rapidity, low cost, easy handling and disposability.

Yehia et al. developed a paper–based micro–fluidic device to be used in the on–site determination of ketamine hydrochloride, a cyclohexanone derivative used for the induction of anesthesia [42]. This sensor designed with wax–printing combines potentiometric, fluorimetric and colorimetric detection zones (thus, called a trimodal system); therefore, it possesses the merits of these three detection systems. The device used polyaniline nano–dispersion as conducting polymer in ion sensing paper electrodes which are designed to fit USB plug connector. Carbon dots–gold nanoparticles were used in fluorescence detection zones, whereas cobalt thiocyanate were used in color detection zones. On–site fluorimetric and color detection could be performed with this device by using a mobile phone. This sensor was highly specific to ketamine hydrochloride in the presence of several other interferences, and the combination of the three detection mechanisms in this device improved its specificity over a specified concentration range. Authors stated that the developed chip fulfills WHO criteria for point-of-care devices, pointing that this device can be used in on-site drug diagnostics and can also be modified to be utilized in the detection of other similar drugs.

A robust, reliable and cost–effective paper–based potentiometric device for the detection of pholcodine, an opioid cough suppressant (antitussive agent), was prepared and characterized by Abd-Rabboh et al. [43]. An all–solid–state ISEs for pholcodine ion together with a reference Ag/AgCl electrode was designed on a common filter–paper. The sensory material used in the device was the ion association complex between pholcodinium ion and 5–nitrobarbaturate which was dispersed in a PVC membrane plasticized with *o*–NPOE. Chemically reduced graphene oxide (CRGO) was used as a solid-contact transducer in the structure of the sensor. The sensor had a potentiometric slope of 28.7 ± 0.3 mV dec^{-1} ($R^2 = 0.9998$) over a linear concentration range of $2.0 \times 10^{-7} - 1.0 \times 10^{-2}$ M, and a detection limit of 0.04 mg mL^{-1}. These sensors exhibited good repeatability, reproducibility and stability, and displayed a good recovery range (i.e. 94 – 104%) of pholcodine from artificial serum samples. Moreover, authors reported that the sensor could be successfully applied for the rapid quantification of pholcodine in syrup and suspension pharmaceutical samples.

2.4. Paper–based sensors in clinical analysis

The concentrations of various compounds of high clinical importance can also be determined potentiometrically using sensors based on paper. A paper–based potentiometric sensor was proposed by Bell et al. to perform the determination of serum bilirubin, which is predominantly formed as a result of the breakdown of hemoglobin in the liver [44]. Linear concentration, response time and pH range for the sensor was reported to be 1.0 mM – 0.10 μM, < 2 min and 7.0 – 9.0, respectively. The authors reported that this sensor can successfully detect free bilirubin in human blood serum samples with the requirement of only 15 μL of serum sample, showing that a very small volume of blood will be needed to detect bilirubin levels in blood. This is of importance since many of the clinical samples may have limited volumes; therefore, there is a need for analytical devices and measurement protocols which ensures reliable analysis in small sample volumes, such as the one developed in this paper.

Dolai and Tabib–Azar reported the development of a paper–based sensor using aptamers in order to detect the whole Zika virus, with a min sensitivity of 0.26 nV/Zika and a min detectable signal (MDS) of 2.4×10^7 Zika virus [45]. This was the first paper–based potentiometric device to be used in the detection of Zika virus. This paper sensor consisted of small regions of paper with conducting silver paint contact patches on both ends with slightly different ionic contents, ionic species and concentrations, in order to produce a potential difference between these two ends. This paper should be dipped in a buffer solution containing aptamers which have the ability to bind to capsid proteins present on the surface of Zika viruses. This binding creates a concentration gradient following the immobilization of the virus in the pores of paper and the formation of bonds between viral capsid proteins and aptamers. Upon binding of Zika viruses, potential between the two silver paints contacts is measured as more negative. Authors also showed that liquid crystalline display (LCD) powered by the sensor can be used to read the output from sensor. They stated that these sensors can be generalized to detect other viruses or pathogens in general just by incorporating aptamers specifically designed for those pathogens and also cautioned that cross–sensitivity of aptamers and thus of sensors should be verified to make sure that the developed sensor only detects the pathogen of interest, not other related pathogenic organisms.

Bouri et al. prepared a paper–based potentiometric galactose (a monosaccharide) biosensor based on platinum as a transducer by immobilizing galactose oxidase (GALOx) between two polymeric layers [46]. The biosensor exhibited a linear potentiometric response in the concentration range of 0.3 – 31.6 mM, and had a sensitivity of 62.8 ± 9.4 mV/decade. In addition, authors reported that the developed paper–based biosensor have a response time of 3 min. The developed biosensor successfully determined the presence of galactose in blood samples. Borràs-Brull et al. described the characterization and validation of a paper–based potentiometric sensor for the determination of another monosaccharide, glucose, in human saliva [47]. This sensor worked in the concentration range of 4.0–10 mM, and had a detection limit of 180 μM. The authors stated based on their data that their sensor is a simple and low-cost device to be used in the determination of glucose in human saliva. Another paper-based glucose sensor was developed by Yamaoka *et al* [48]. They proposed a low cost potentiometric sensor using paper-based fluidic channel and CMOS chip for the detection of glucose. In this study, fluidic channel consisted of chromatography paper and silicone resin. This paper-based channel had two areas: one for filtering a sample (filter layer) and one for reacting enzyme (enzyme layer). Following the incorporation of CMOS chip to this channel, glucose concentrations in the range from 0.5 to 10 mM, a relatively wider range compared to previous sensor, could be measured with this electrochemical sensor.

2.5. Other paper–based potentiometric devices

The paper–based potentiometric sensors were designed and characterized by Amr et al. for nicotine tracking in sweat samples and cigarette smoke [49]. The prepared sensors were based on ion association complexes of nicotinium cation (Nic) with tetraphenylborate (TPB) or 5–nitrobarbiturate (NB) anions as sensing materials for nicotine recognition. The authors showed that the novel sensors exhibit fast and stable Nernstian behaviour of 55.2 ± 0.3 and 51.2 ± 0.6 mV/decade, over the linear concentration range of $1.0 \times 10^{-5} - 1.0 \times 10^{-2}$ M, and detection

Table 1
Potentiometric performance characteristics of the reported sensor based on paper in literature.

Analyte	Concentration range	Limit of detection	pH working range	Response time (s)	Slope (mV/decade)	Ref
water hardness (Mg^{2+})	1.0×10^{-6} – 1.0×10^{-1} M	3.0×10^{-7} M			29.8 ± 0.1	[32]
water hardness (Ca^{2+})	1.0×10^{-6} – 1.0×10^{-1} M	3.3×10^{-7} M			29.8 ± 0.1	[32]
Cu(II)	5.0×10^{-7} – 1.0×10^{-3} M	8.0×10^{-8} M	3.0 – 9.0	<10	28.6 ± 0.5	[33]
Cu(II)	4.0×10^{-7} – 1.0×10^{-3} M	6.5×10^{-8} M	1.0 – 13.0	<10	25.6 ± 0.8	[33]
potassium	1.0×10^{-4} – 1.0×10^{-1} M	1.0×10^{-6} M			54.9 ± 0.6	[34]
sodium	1.0×10^{-3} – 1.0 M	2.0×10^{-6} M			54.8 ± 1.4	[34]
calcium	1.0×10^{-4} – 1.0×10^{-1} M	7.0×10^{-6} M			22.9 ± 0.8	[34]
potassium	1.0×10^{-4} – $1.0 \times 10^{-1.1}$ M	$1.0 \times 10^{-4.1}$ M			59.1 ± 1.5	[35]
sodium	1.0×10^{-3} – $1.0 \times 10^{-1.1}$ M	$1.0 \times 10^{-3.3}$ M			57.5 ± 0.5	[35]
chloride	1.0×10^{-4} – $1.0 \times 10^{-1.1}$ M	$1.0 \times 10^{-4.1}$ M			-56.4 ± 0.6	[35]
salicylhydroxamic acid	1.0×10^{-6} – 1.0×10^{-3} M	0.7 μM	7.2	<5	−59.3 ± 0.7	[41]
Pholcodine	2.0×10^{-7} – 1.0×10^{-2} M	0.04 mg mL^{-1}	4.2 – 6.0		28.7 ± 0.3	[43]
serum bilirubin	1.0 mM – 0.10 μM		7.0 – 9.0	<60	−26.5 mV	[44]
Galactose	0.3–31.6 mM	0.25 mM		180	62.8 ± 9.4	[46]
Glucose	4.0–10 mM	180 μM			93.2 ± 1.8	[47]
Nicotine [Nic/TPB]	1.0×10^{-5} – 1.0×10^{-2} M	6.0 μM	3.5 – 6.5		55.2 ± 0.3	[49]
Nicotine [Nic/NB]	1.0×10^{-5} – 1.0×10^{-2} M	8.0 μM	3.5 – 6.5		51.2 ± 0.6	[49]
bisphenol A	0.5 to 13 μM	0.15 μM				[50]

limits of 6.0 and 8.0 μM for [Nic/TPB] and [Nic/NB], respectively. The authors also reported that the sensors they developed are portable, inexpensive and disposable to measure trace levels of nicotine in human sweat of heavy smokers, showing the potential applicability of these devices to detect low levels of nicotine in certain body fluids of smokers.

Kamel et al. developed a paper–based potentiometric sensing platform based on molecularly imprinted nano–beads for the determination of neutral bisphenol A (BPA), an endocrine disruptor with estrogenic activity, released from real plastic samples [50]. Uniform–sized nano-beads were used as recognition receptors to obtain a higher affinity against bisphenol A, since they have higher binding capability and can be well dispersed in the polymeric membrane potentiometric sensor. Chromatography paper was used as the electrode substrate in the development of this sensor. The sensor worked in the concentration range from 0.5 to 13 μM with a limit of detection of 0.15 μM. The authors said that the sensor they developed is simple and independent of sample volume, and also fast, easy and inexpensive to fabricate. Besides these features, they reported that it has advantages such as a good selectivity over other phenols and an excellent accuracy. Since the current electrode substrates of solid–contact potentiometric sensors for bisphenol A are mostly expensive materials such as glassy carbon, gold or platinum; this method offers a low cost alternative, enabling its use in diverse settings with limited resources. Authors also stated that this paper–based sensor has a similar performance with the classical glassy carbon–based sensor in terms of analysis of bisphenol A; thus, it may represent a more economical alternative which is more suitable for mass deployment in resource–limited areas.

Paper–based potentiometric sensors can also be utilized in the construction sector. Colozza et al. developed a filter paper–based screen–printed Ag/AgCl electrode to evaluate the extent of corrosion in reinforced concrete samples [51]. This is of high importance since the monitoring of corrosion extent in constructions is a public safety concern, and it should be checked on a regular basis. They reported that the developed potentiometric sensor needs only 70 μL of electrolyte solution (0.1 M KCl), and can be used for the on–site and real–time evaluation of the probability of corrosion in reinforced concrete artefacts. This sensor was reported to display a good resistance and working stability. As authors indicated, this sensor could be mass-produced with low cost and easily disposed in addition to its certain advantages including its small size and easiness of handling; thus, these sensors may represent a cost-effective and versatile alternatives to be used in the early diagnosis of the corrosion probability of metallic components present in the structures made from concrete.

Others showed that paper–based potentiometric ion sensors could be prepared by ink–jet printing, reproducibly [52]. Sjöberg et al. printed ion–selective and reference electrodes on a recyclable low–cost paper by using a stable suspension of gold nanoparticles (AuNP) as the ink, and printed electrodes were made conductive by sintering. Then, a poly(3, 4–ethylenedioxythiophene) (PEDOT) layer, with poly(styrene sulfonate) (PSS) ions as counterions was deposited on these electrodes by several methodologies: electropolymerization, drop–casting or ink–jet printing. The reference electrode was developed by coating the PEDOT (PSS) layer with a PVC membrane which contains alipophilic salt, tetrabutylammonium tetrabutylborate (TBA–TBB), in order to prepare a solid–contact reference electrode (SCRE). The working electrode was coated with the PEDOT(PSS) layer with a K^+–selective membrane, resulting in a solid–contact K^+–ISE. Electropolymerized PEDOT (PSS) films were found to be much thicker and rougher than the printed PEDOT (PSS) layers. Authors stated that a planar electrode platform with good electrochemical characteristics could be prepared by ink–jet printing which enables faster, easier mass manufacturing of paper–based sensors, and that this electrode offers a user–friendly and ecological alternative to existing ones.

Paper–based potentiometric ion–sensing platforms mentioned so far were mostly planar (1D) devices. Ding et al. reported the development of a 3D origami paper–based potentiometric device for the first time [53]. This potentiometric biosensor had a solid–contact ion–selective electrode integrated with an all–solid–state reference electrode, and it had the advantages of solid–contact ISEs for rapid sensing and of micro–fluidic paper–based analytical devices for simple use and multifunctionality. The paper was impregnated with appropriate bio–receptors and reporting reagents on different zones. Authors stated that *in situ* measurement can be performed easily with a USB–controlled miniaturized electrochemical detector. They used butyrylcholinesterase as a model enzyme for the detection of enzyme activities and organophosphate pesticides involved in the enzymatic system as inhibitors. As shown in the study, the device could be fabricated in a manner that is fast, easy, flexible and inexpensive. Furthermore, all production steps could be easily automated. Authors stated that the 3D structure of the device makes it possible to control the timing and has the potential for multiplex analyses, which is relatively difficult to achieve with other paper-based devices. Others also used 3D origami paper in the design of paper–based potentiometric devices in recent years [54].

The potentiometric properties of some paper–based sensors mentioned so far are given in Table 1.

Paper–based potentiometric sensors is not limited with the papers mentioned in the current study. Many more studies in recent years have reported the novel strategies to develop paper–based sensors based on potentiometry [55–60].

3. Conclusion

Sensor technology is an area where significant developments are reported almost every day. Sensors prepared by the potentiometric methods have been an important research area due to the particular advantages that these devices offer. New potentiometric sensors with better performance characteristics have been produced with various modifications in parallel to the advancing technology and the search for innovation. Paper–based potentiometric sensing tools have been the focus of research for the last 10 years, especially based on their low cost, flexibility, lightweight and high portability [61,62]. Researchers working on potentiometry have also turned to paper–based sensors and obtained considerable results. In the last few years, highly successful paper–based potentiometric devices have been reported in the literature. In this review, we investigated paper-based devices, which is a relatively new topic in the field of potentiometry, and thus aimed to offer a new perspective to researchers working in the field of potentiometry.

Declaration of competing interest

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

References

[1] Ö. Isildak, O. Özbek, Application of potentiometric sensors in real samples, Crit. Rev. Anal. Chem. 51 (2021) 218–231, https://doi.org/10.1080/10408347.2019.1711013.

[2] M.Z. Cremer, Origin of electromotor properties of tissues, and instructional contribution for polyphasic electrolyte chain, Z. Für. Biol. 47 (1906) 562.

[3] M.S. Frant, Progress in ISE development has occurred rapidly in the past 35 years, with promising innovations still on the horizon, Analyst 119 (1994) 2294–2301, https://doi.org/10.1039/AN9941902293.

[4] R.P. Buck, E. Lindner, Peer Reviewed: tracing the history of selective ion sensors, Anal. Chem. 73 (2001) 88–97, https://doi.org/10.1021/ac012390t.

[5] H.M. Abu Shawish, S.M. Saadeh, S.T. Al-kahlout, PVC membrane, coated-wire, and carbon-paste electrodes for potentiometric determination of vardenafil hydrochloride in tablet formulations and urine samples, Sensors International 3 (2022), 100175, https://doi.org/10.1016/j.sintl.2022.100175.

[6] S.M. Saadeh, H.M. Abu Shawish, M.Y. Abu Foul, Lowering detection limits of copper(II)-selective carbon paste electrodes using an SNO- and an SNNS- Schiff base ligands, Sensors International 3 (2022), 100151, https://doi.org/10.1016/j.sintl.2021.100151.

[7] O. Özbek, Potentiometric PVC membrane ion–selective electrode for the determination of Sr(II) isons, Sensors International 3 (2022), 100185, https://doi.org/10.1016/j.sintl.2022.100185.

[8] Ö. Isildak, O. Özbek, K.M. Yigit, Zinc(II)-selective PVC membrane potentiometric sensor for analysis of Zn^{2+} in drug sample and different environmental samples, Int. J. Environ. Anal. Chem. 101 (2021) 2035–2045, https://doi.org/10.1080/03067319.2019.1691542.

[9] O. Özbek, Ö. Isildak, I. Isildak, A potentiometric biosensor for the determination of valproic acid: human blood–based study of an anti–epileptic drug, Biochem. Eng. J. 176 (2021), 108181, https://doi.org/10.1016/j.bej.2021.108181.

[10] O. Özbek, Ö. Isildak, M.B. Gürdere, A. Cetin, The use of crown ethers as sensor material in potentiometry technique, Org. Commun. 14 (2021) 228–239, https://doi.org/10.25135/acg.oc.110.2106.2114.

[11] O. Özbek, C. Berkel, Ö. Isildak, Applications of potentiometric sensors for the determination of drug molecules in biological samples, Crit. Rev. Anal. Chem. 52 (2022) 768–779, https://doi.org/10.1080/10408347.2020.1825065.

[12] O. Özbek, C. Berkel, Ö. Isildak, I. Isildak, Potentiometric urea biosensors, Clin. Chim. Acta 524 (2022) 154–163, https://doi.org/10.1016/j.cca.2021.11.011.

[13] O. Özbek, A. Çetin, E. Koç, Ö. Isildak, Synthesis and sensor properties of a phenol derivative molecule: potentiometric determination of silver(I) ions, Electrocatalysis 13 (2022) 486–493, https://doi.org/10.1007/s12678-022-00738-2.

[14] O. Özbek, Ö. Isildak, Potentiometric PVC membrane sensor for the determination of anti-epileptic drug levetiracetam in pharmaceutical formulations, ChemistrySelect 7 (2022), e202103988, https://doi.org/10.1002/slct.202103988.

[15] Ö. Isildak, O. Özbek, Silver (I)-selective PVC membrane potentiometric sensor based on 5, 10, 15, 20-tetra (4-pyridyl)-21H,23H-porphine and potentiometric applications, J. Chem. Sci. 132 (2020) 29, https://doi.org/10.1007/s12039-019-1734-2.

[16] O. Özbek, Ö. Isildak, C. Berkel, The use of porphyrins in potentiometric sensors as ionophores, J. Inclusion Phenom. Macrocycl. Chem. 98 (2020) 1–9, https://doi.org/10.1007/s10847-020-01004-y.

[17] M. Sher, R. Zhuang, U. Demirci, W. Asghar, Paper-based analytical devices for clinical diagnosis: recent advances in the fabrication techniques and sensing mechanisms, Expert Rev. Mol. Diagn. 17 (2017) 351–366, https://doi.org/10.1080/14737159.2017.1285228.

[18] D.M. Cate, J.A. Adkins, J. Mettakoonpitak, C.S. Henry, Recent developments in paper-based microfluidic devices, Anal. Chem. 87 (2015) 19–41, https://doi.org/10.1021/ac503968p.

[19] F. Arduini, S. Cinti, V. Scognamiglio, D. Moscone, Comprehensive Analytical Chemistry, vol. 77, Elsevier, 2017, pp. 385–413.

[20] Y. Li, R. He, Y. Niu, Y.F. Li, Paper-based electrochemical biosensors for point-of-care testing of neurotransmitters, J. Anal. Test. 3 (2019) 19–36, https://doi.org/10.1007/s41664-019-00085-0.

[21] A.W. Martinez, S.T. Phillips, G.M. Whitesides, E. Carrilho, Diagnostics for the developing world: microfluidic paper-based analytical devices, Anal. Chem. 82 (2010) 3–10, https://doi.org/10.1021/ac9013989.

[22] C. Parolo, A. Merkoçi, Paper-based nanobiosensors for diagnostics, Chem. Soc. Rev. 21 (2013) 450–457, https://doi.org/10.1039/C2CS35255A.

[23] Y. Yang, E. Noviana, M.P. Nguyen, B.J. Geiss, D.S. Dandy, C.S. Henry, Paper-based microfluidic devices: emerging themes and applications, Anal. Chem. 89 (2017) 71–91, https://doi.org/10.1021/acs.analchem.6b04581.

[24] M. Novell, M. Parrilla, G.A. Crespo, F.X. Rius, F.J. Andrade, Paper-Based ion-selective potentiometric sensors, Anal. Chem. 84 (2012) 4695–4702, https://doi.org/10.1021/ac202979j.

[25] S. Cinti, D. Moscone, F. Arduini, Preparation of paper-based devices for reagentless electrochemical (bio)sensor strips, Nat. Protoc. 14 (2019) 2437–2451, https://doi.org/10.1038/s41596-019-0186-y.

[26] S. Cinti, D. Talarico, G. Palleschi, D. Moscone, F. Arduini, Novel reagentless paper-based screen-printed electrochemical sensor to detect phosphate, Anal. Chim. Acta 919 (2016) 78–84, https://doi.org/10.1016/j.aca.2016.03.011.

[27] G.O. da Silva, W.R. de Araujo, T.R.L.C. Paixão, Portable and low-cost colorimetric office paper-based device for phenacetin detection in seized cocaine samples, Talanta 176 (2018) 674–678, https://doi.org/10.1016/j.talanta.2017.08.082.

[28] A.A. Dias, T.M.G. Cardoso, C.L.S. Chagas, V.X.G. Oliveira, R.A.A. Munoz, C.S. Henry, M.H.P. Santana, T.R.L.C. Paixão, W.K.T. Coltro, Detection of analgesics and sedation drugs in whiskey using electrochemical paper-based analytical devices, Electroanalysis 30 (2018) 2250, https://doi.org/10.1002/elan.201800308.

[29] J. Noiphung, T. Songjaroen, W. Dungchai, C.S. Henry, O. Chailapakul, W. Laiwattanapaisal, Electrochemical detection of glucose from whole blood using paper-based microfluidic devices, Anal. Chim. Acta 788 (2013) 39–45, https://doi.org/10.1016/j.aca.2013.06.021.

[30] K. Yamada, H. Shibata, K. Suzuki, D. Citterio, Toward practical application of paper-based microfluidics for medical diagnostics: state-of-the-art and challenges, Lab Chip 17 (2017) 1206–1249, https://doi.org/10.1039/C6LC01577H.

[31] Y. Lin, D. Gritsenko, S. Feng, Y.C. Teh, X. Lu, J. Xu, A mini-review on functional nucleic acids-based heavy metal ion detection, Biosens. Bioelectron. 83 (2016) 256–266, https://doi.org/10.1016/j.bios.2016.06.075.

[32] M.L. Bouhoun, P. Blondeau, Y. Louafi, F.J. Andrade, A paper-based potentiometric platform for determination of water hardness, Chemosensors 9 (2021) 96, https://doi.org/10.3390/chemosensors9050096.

[33] A.H. Kamel, A.E.-G.E. Amr, A.A. Almehizia, E.A. Elsayed, G.O. Moustafa, Low-cost potentiometric paper-based analytical device based on newly synthesized macrocyclicpyrido-pentapeptide derivatives as novel ionophores for point-of-care copper(II) determination, RSC Adv. 11 (2021), 27174, https://doi.org/10.1039/d1ra04712d.

[34] W.-J. Lan, X.U. Zou, M.M. Hamedi, J. Hu, C. Parolo, E.J. Maxwell, P. Bühlmann, G.M. Whitesides, Paper-based potentiometric ion sensing, Anal. Chem. 86 (2014) 9548–9553, https://doi.org/10.1021/ac5018088.

[35] R. Ding, M. Fiedoruk-Pogrebniak, M. Pokrzywnicka, R. Koncki, J. Bobacka, G. Lisak, Solid reference electrode integrated with paper-based microfluidics for potentiometric ion sensing, Sensor. Actuator. B Chem. 323 (2020), 128680, https://doi.org/10.1016/j.snb.2020.128680.

[36] T. Sakata, M. Hagio, A. Saito, Y. Moria, M. Nakao, K. Nishib, Biocompatible and flexible paper-based metal electrode for potentiometric wearable wireless biosensing, Sci. Technol. Adv. Mater. 21 (2020) 380–387, https://doi.org/10.1080/14686996.2020.1777463.

[37] E.W. Nery, L.T. Kubota, Integrated, paper-based potentiometric electronic tongue for the analysis of beer and wine, Anal. Chim. Acta 918 (2016) 60–68, https://doi.org/10.1016/j.aca.2016.03.004.

[38] R. Ding, N.K. Joon, A. Ahamed, A. Shafaat, M. Guzinski, M. Wagner, T. Ruzgas, J. Bobacka, G. Lisak, Gold-modified paper as microfluidic substrates with reduced biofouling in potentiometric ion sensing, Sensor. Actuator. B Chem. 344 (2021), 130200, https://doi.org/10.1016/j.snb.2021.130200.

[39] R. Kawahara, P. Sahatiya, S. Badhulika, S. Uno, Paper-based potentiometric pH sensor using carbon electrode drawn by pencil, Jpn. J. Appl. Phys. 57 (2018), 04FM08, https://doi.org/10.7567/JJAP.57.04FM08.

[40] E. Chow, D.D. Liana, B. Raguse, J.J. Gooding, A potentiometric sensor for pH monitoring with an integrated electrochromic readout on paper, Aust. J. Chem. 70 (2017) 979–984, https://doi.org/10.1071/CH17191.

[41] H.S.M. Abd-Rabboh, A.El-G.E. Amr, A.A. Almehizia, A.H. Kamel, Paper-based potentiometric device for rapid and selective determination of salicylhydroxamate as a urinary struvite stone inhibitor, ACS Omega 6 (2021) 27755–27762, https://doi.org/10.1021/acsomega.1c03135.

[42] A.M. Yehia, M.A. Farag, M.A. Tantawy, A novel trimodal system on a paper-based microfluidic device for onsite detection of the date rape drug “ketamine”, Anal. Chim. Acta 1104 (2020) 95–104, https://doi.org/10.1016/j.aca.2020.01.002.

[43] H.S.M. Abd-Rabboh, A.E.-G.E. Amr, E.A. Elsayed, A.Y.A. Sayed, A.H. Kamel, Paper-based potentiometric sensing devices modified with chemically reduced graphene

oxide (CRGO) for trace level determination of pholcodine (opiate derivative drug), RSC Adv. 11 (2021), 12227, https://doi.org/10.1039/d1ra00581b.
[44] J.G. Bella, M.P.S. Mousavia, M.K. Abd El-Rahmana, E.K.W. Tana, S. Homer-Vanniasinkamd, G.M. Whitesides, Paper-based potentiometric sensing of free bilirubin in blood serum, Biosens. Bioelectron. 126 (2019) 115–121, https://doi.org/10.1016/j.bios.2018.10.055.
[45] S. Dolai, M. Tabib-Azar, Whole virus detection using aptamers and paper-based sensor potentiometry, Med Devices Sens 3 (2020), e10112, https://doi.org/10.1002/mds3.10112.
[46] M. Bouri, J.C. Zuaznabar-Gardona, M. Novel, P. Blondeau, F.J. Andrade, Paper-based potentiometric biosensor for monitoring galactose in whole blood, Electroanalysis 33 (2021) 81–89, https://doi.org/10.1002/elan.202060285.
[47] M. Borràs-Brull, P. Blondeau, J. Riu, Characterization and validation of a platinum paper-based potentiometric sensor for glucose detection in saliva, Electroanalysis 33 (2021) 181–187, https://doi.org/10.1002/elan.202060221.
[48] K. Yamaoka, J. Eguchi, S. Uno, Potentiometric glucose detection by paper-based electrochemical sensor on CMOS chip, Telkomnika 15 (2017) 836–841, https://doi.org/10.12928/TELKOMNIKA.v15i2.6129.
[49] A.E.-G.E. Amr, A.H. Kamel, A.A. Almehizia, A.Y.A. Sayed, E.A. Elsayed, H.S.M. Abd-Rabboh, Paper-based potentiometric sensors for nicotine determination in smokers' sweat, ACS Omega 6 (2021) 11340–11347, https://doi.org/10.1021/acsomega.1c00301.
[50] A.H. Kamel, X. Jianga, P. Lia, R. Liang, A paper-based potentiometric sensing platform based on molecularly imprinted nanobeads for determination of bisphenol A, Anal. Methods 10 (2018) 3890–3895, https://doi.org/10.1039/C8AY01229F.
[51] N. Colozza, A. Sassolini, L. Agosta, A. Bonfanti, K. Hermansson, F. Arduini, A paper-based potentiometric sensor for solid samples: corrosion evaluation of reinforcements embedded in concrete structures as a case study, Chemelectrochem 7 (2020) 2274–2282, https://doi.org/10.1002/celc.202000330.
[52] P. Sjöberg, A. Määttänen, U. Vanamo, M. Novell, P. Ihalainen, F.J. Andrade, J. Bobacka, J. Peltonen, Paper-based potentiometric ion sensors constructed on ink-jetprinted gold electrodes, Sensor. Actuator. B Chem. 224 (2016) 325–332, https://doi.org/10.1016/j.snb.2015.10.051.
[53] J. Ding, B. Li, L. Chen, W. Qin, Athree-dimensional origami paper-based device for potentiometric biosensing, Angew. Chem. Int. Ed. 55 (2016) 13033–13037, https://doi.org/10.1002/ange.201606268.
[54] S. Pesaran, E. Rafatmah, B. Hemmateenejad, An all-in-one solid state thin-layer potentiometric sensor and biosensor based on three-dimensional origami paper microfluidics, Biosensors 11 (2021) 44, https://doi.org/10.3390/bios11020044.
[55] M.A.R. Khan, C.A. C Vieira, J. Riu, M.G.F. Sales, Fabrication and modification of homemade paper-based electrode systems, Talanta 224 (2021), 121861, https://doi.org/10.1016/j.talanta.2020.121861.
[56] N. Colozza, S. Tazzioli, A. Sassolini, L. Agosta, M.G. di Monte, K. Hermansson, F. Arduini, Vertical-flow paper sensor for on-site and prompt evaluation of chloride contamination in concrete structures, Anal. Chem. 93 (2021) 14369–14374, https://doi.org/10.1021/acs.analchem.1c03363.
[57] N. Ruecha, O. Chailapakul, K. Suzuki, D. Citterio, Fully inkjet-printed paper-based potentiometric ,on-sensing devices, Anal. Chem. 89 (2017) 10608–10616, https://doi.org/10.1021/acs.analchem.7b03177.
[58] J. Hu, A. Stein, P. Bühlmann, A disposable planar paper-based potentiometric ion-sensing platform, Angew. Chem., Int. Ed. Engl. 55 (2016) 7544–7547, https://doi.org/10.1002/anie.201603017.
[59] R. Cánovas, M. Parrilla, P. Blondeau, F.J. Andrade, A novel wireless paper-based potentiometric platform for monitoring glucose in blood, Lab Chip 17 (2017) 2500–2507, https://doi.org/10.1039/C7LC00339K.
[60] N.F.D. Silva, C.M.R. Almeida, J.M.C.S. Magalhães, M.P. Gonçalves, C. Freire, C. Delerue-Matos, Development of a disposable paper-based potentiometric immunosensor for real-time detection of a foodborne pathogen, Biosens. Bioelectron. 141 (2019), 111317, https://doi.org/10.1016/j.bios.2019.111317.
[61] V. Krikstolaityte, R. Ding, E.C.H. Xia, G. Lisak, Paper as sampling substrates and all-integrating platforms in potentiometric ion determination, Trends Anal. Chem. 133 (2020), 116070, https://doi.org/10.1016/j.trac.2020.116070.
[62] R. Ding, H. Cheong, A. Ahamed, G. Lisak, Heavy metals detection with paper-based electrochemical sensors, Anal. Chem. 93 (2021) 1880–1888, https://doi.org/10.1021/acs.analchem.0c04247.