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ORIGINAL PAPER

Improvement in performance of a hyoscine butylbromide potentiometric sensor using a new nanocomposite carbon paste: a comparison study with polymeric membrane sensor

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Abstract Multiwalled carbon nanotubes and TiO_2 nanoparticles were used for the improvement of a hyoscine butylbromide (HYBB) potentiometric carbon paste electrode response. The electrode was based on the ammonium reineckate-hyoscine ion association complex as an ion-exchange site dissolved in 2-nitrophenyloctyl ether as pasting liquid. The characteristics of the suggested potentiometric nanocomposite-modified HYBB carbon paste electrode in comparison with the PVC membrane sensor show better responses in terms of sensitivity, dynamic concentration range, detection limit, Nernstain slope, low potential drift, response time, lifetime, and mechanical stability. The electrode exhibits good selectivity for HYB ion with respect to a large number of cations. For investigation of the effects of carbon nanotubes and TiO_2 nanoparticles on the conductivity property of the electrode surface, electrochemical impedance spectroscopy measurements were done. The prepared electrode was successfully applied to the determination of hyoscine butylbromide in pharmaceutical formulations and biological samples.

Keywords Hyoscine butylbromide · Potentiometric sensor · TiO_2 nanoparticles · MWCNTs

Introduction

Over the past few years, pharmaceuticals are considered as an emerging environmental problem due to their continuous input and persistence to the aquatic ecosystem even at low concentrations [1]. The presence of residual pharmaceuticals in the environment and in the aquatic systems in particular constitutes a serious environmental problem as these compounds (a) are extremely resistant to biological degradation processes and usually escape intact from conventional treatment plants, (b) may impose serious toxic and other effects to humans and other living organisms, and (c) are present at minute concentrations, thus requiring more sophisticated and laborious analytical tools for their accurate determination. Consequently, the development of a rapid, simple, and accurate method with high sensitivity for the determination of these compounds at (ultra)trace levels in environmental and biological materials is of particular significance [2–7]. Hyoscine butylbromide (Scheme 1) is used as an antispasmodic in treating peptic ulcer, gastritis, and various disorders of the gastrointestinal tract which are characterized by spam. It has also found employment for the relief of spasmodic conditions of the bile duct and urinary tract and for the treatment of dysmenorrhea [8]. Various methods have been developed for the determination of hyoscine butylbromide, including spectrophotometry [9–12], comprising derivative techniques [9–11], GLC-MS [13], high-performance liquid chromatography [14], and capillary electrophoresis [15]. However, these instrumental techniques are too expensive that they are not available in most analytical laboratories or need time-consuming procedures. Thus, the development of convenient and direct methods for the assay of HYB in different samples is an urgent need. Potentiometric carbon paste electrodes can be considered good alternatives for their attractive characteristics [16, 17]. These sensors offer very attractive properties for the electrochemical investigation of inorganic and organic species over polymeric membrane electrodes. Also, these sensors are easy to prepare and use and possess the following characteristics: surface renewal, chemical inertness, robustness, stability of response, low ohmic resistance, no need of internal solution, and suitability for a variety of sensing and detection applications [18–29]. In recent years, to improve the sensitivity, selectivity, detection limit, and other features of potentiometric

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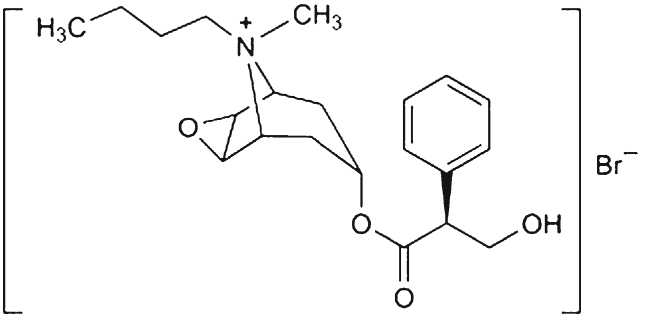

Scheme 1 Chemical structure of hyoscine butylbromide (HYBB)

sensors, several methods have been used. For example, the electrode structures of various materials such new synthesized Schiff bases, ion exchangers, ionic liquids or various nanomaterials such carbon nanotubes, semiconductor nanoparticles, functionalized nanoparticles, etc have been used as modifiers [22–34]. There is currently an intense interest in the use of these nanomaterials for the fabrication of modified electrodes and a wide range of bioscience applications [22–29]. The fabrication of electrodes modified with nanoparticles has been the focus of recent attention owing to enhancement of the response signal, increased sensitivity, decreased detection limit, and better reproducibility. TiO_2 nanoparticles have a wide range of technological applications due to their excellent physical and chemical properties "non-toxicity, excellent chemical and photochemical stability, large surface area, good biocompatible, high mechanical strength and fast electron transfer ability" [35–38]. It was concluded that TiO_2 nanoparticles have high specific surface area and relatively good electrical conductivity compared to their bulk form. These properties can improve the detection limit of the target analyte. Also, they provide more active sites at the electrode surface and improve the stability of the electrode. Due to these properties, we decided to use TiO_2 for the modification of the electrode.

The modification of a HYBB carbon paste electrode based on the ammonium reineckate-hyoscine ion association complex as ion-exchange site dissolved in 2-nitrophenyloctyl ether (2-NPOE) as pasting liquid by multiwalled carbon nanotubes (MWCNTs) and TiO_2 nanoparticles is studied and compared with polymeric membrane electrode [39]. The results obtained in this study show a wide concentration range, low detection limit, an excellent Nernstain slope, high mechanical stability, fast response time, long lifetime, and high selectivity over a wide variety of other compounds.

Experimental

Instruments

The suggested HYBB selective carbon paste electrode, as the working electrode, and a single junction saturated Ag/AgCl reference electrode (Azar electrode, Iran), as the reference electrode, were placed in a glass cell and used for the potentiometric measurements. Both the electrodes were connected to a digital milli-voltmeter (HIOKI 3256.50, Japan). Electrochemical impedance spectroscopy was performed in an analytical system, with the potentiostat/galvanostat (Autolab PGSTAT 302 N, Netherlands) connected to a three-electrode cell and linked to a computer (Pentium IV, 1,200 MHz). The system was run on a PC using Nova 1.7 software. A Metrohm pH meter (CRISON GLP 22, Swiss) with a combined glass electrode was used for pH adjustment, and a Heidolph type of stirrer (MR 2,000, Germany) was used for stirring the solutions. The size, morphology, and structure of the nanoparticle electrode surface were characterized by scanning electron microscopy (SEM-EDX, XL30, Philips, Netherlands).

Reagents and materials

All chemicals were of analytical reagent grade. Distilled deionized water was used throughout to prepare all solutions and in all the experiments. Graphite powder with a <50-μm particle size, 2.2 g cm^{-3} density, about 200–300 g L^{-1} bulk density, 0.35 cm^3 g^{-1} V_{total}, 4.5 m^2 g^{-1} S_{BET} (Merck, Darmstadt); 2-nitrophenyl octyl ether (2-NPOE); dioctyl phthalate (DOP); dibutyl phthalate (DBP); tris(2-ethylhexyl)phosphate (DOPh); and dioctyl sebacate (DOS) as well as metal salts were purchased from Sigma-Aldrich (CH-9471 Buchs-Germany) and used as received. The multiwalled carbon nanotubes (MWCNTs) with outer diameter of 5–20 nm, inner diameter of 2–6 nm, length of 1–10 μm, apparent density of 150–350 g/cm^3, and with 95 % purity were purchased from Plasmachem GmbH (Germany, www.plasmachem.com/). The titanium oxide (TiO_2) nanoparticles, chloride, and nitrate salts of the cations were purchased from the Merck Company (Germany) and used without any further treatment. Reagent grade HYBB was obtained from Tehran Shimi Pharmaceutical Company, Tehran, Iran. The HYBB tablets (one tablet≡10 mg HYBB) and suppository (one suppository≡10 mg HYBB) were obtained from local sources. Ammonium reineckate was obtained from Sigma-Aldrich Company.

Preparation of ion-pair

The ion association complex as ion-exchange site was prepared according to literature [39]. Ten milliliters of 10^{-2} mol L^{-1} HYBB aqueous solution was mixed with 10 mL of a saturated aqueous solution of ammonium reineckate. The obtained precipitate was filtered, washed with cold water, allowed to dry at room temperature, and ground to a fine powder.

Pretreatment of multiwalled carbon nanotubes

Due to the elimination of graphitic nanoparticles, amorphous carbon, and metallic impurities and finally for the improvement of the electron transfer properties of carbon nanotubes, it is necessary that carbon nanotubes should be activated before using them [40]. For pretreatment of MWCNTs, they were exposed to an acidic solution (such sulfuric, nitric, or hydrochloric acid, or a mixture of these) at room temperature and then refluxed or sonicated for several times [40, 41]. One of the procedures to purification was as follows: certain amounts of MWCNTs (500 mg) were heated at 400 °C using an air flow of 12 mL min^{-1}, for 1 h. To eliminate metal oxide catalysts, the heated amount of MWCNTs was dispersed in 60 mL of 6.0 mol L^{-1} HCl for 4 h under sonication and then filtered on a Whatman no. 42 filter paper and washed until the solution pH was neutral and was finally dried.

Electrode preparation

The general procedure to prepare the carbon paste electrode was as follows: different amounts of the ion-pair along with appropriate amounts of graphite powder, plasticizer, MWCNTs, and TiO_2 nanoparticles were thoroughly mixed. The resulting mixture was transferred into an insulin syringe with an internal diameter of 2.5 mm and a height of 3 cm as an electrode body. After the homogenization of the mixture, the prepared paste was carefully packed into the tube tip to avoid possible air gaps, which often enhance the electrode resistance. A copper wire was inserted into the opposite end of the carbon paste electrode (CPE) to establish an electrical contact. The external surface of the carbon paste was smoothed with soft paper. A new surface was produced by scraping out the old surface and replacing it with the new carbon paste. The resultant composite has remarkable advantages, such as compactness, high mechanical stability, and low electrical resistance and has renewal characteristics by simple polishing. Finally, the electrode was conditioned for 24 h by soaking it in a 1.00×10^{-3} mol L^{-1} drug solution.

Results and discussion

Many parameters affect the performance of the present potentiometric carbon paste electrode and must be taken into consideration when studying the performance of the electrode toward its respective ion. Some of these parameters are as follows: electrode composition and modification and the effect of operational conditions such as response time, presence of interferents, lifetime of the electrode, pH, etc.

Electrode composition and modification

It is well known that the sensitivity, linear dynamic range, and selectivity obtained for a given electrode depend significantly on the composition of the electrode [16–34]. Thus, several electrodes with different compositions were fabricated and investigated in this study. The unmodified CPE was prepared by mixing 49 % of graphite powder with 51 % of 2-NPOE (as pasting liquid) with a mortar and pestle. Modified pastes were prepared in a similar fashion, except that the graphite powder was mixed with a desired weight of the ion association complex as an ionophore and nanomaterials (MWCNTs and TiO_2 nanoparticles) to get different compositions as given in Table 1. According to this table, the electrode composed of 51 % 2-NPOE, 1.5 % ion association, 30.5 % graphite powder, 10 % MWCNTs, and 7.0 % TiO_2 nanoparticles (no. 10) was found to be optimal for the HYB sensing.

The ion association complex used in ion selective electrodes (ISEs) should have rapid exchange kinetics and adequate formation constants in the paste. In addition, they should have good solubility in the paste matrix and sufficient lipophilicity to prevent leaching from the paste into the sample solution [42]. Preliminary experiments showed that sensors of the same composition as the sensor (no. 1) but without ion-exchanger are hardly responsive to HYBB. But the response of the sensor to HYB was improved by adding of the ammonium reineckate-hyoscine ion association complex as ion-exchange site into the paste composition of the present electrodes. For this purpose, different percentages of the ion-exchanger were prepared, namely 0.5, 1.0, 1.5, and 2.0 % (*w*/*w*). The results obtained indicate that the best sensitivity and linear range were obtained for 1.5 wt% of the ion-exchanger.

Using MWCNTs in the carbon paste improves the conductivity and, therefore, the conversion of the chemical signal to an electrical one. Carbon nanotubes have many properties that make them ideal as components in electrical circuits, including their unique dimensions and their unusual current conduction mechanism [43–46]. By increasing the conductivity, the dynamic working range and response time of the sensor improve [23]. If the transduction property of the sensor increases, the potential response of the sensor improves to Nernstian values [23]. As can be seen in Table 1, the addition of 10 % MWCNTs to the unmodified sensor (no. 10) caused an increase in its Nernstian slope from 41.87 to 59.55 mV/decade. Also, a wider linear response range and higher sensitivity were reached when the MWCNTs were present in the composition of the electrode. However, increasing the amount of the MWCNTs higher than 10 % in the composition of the carbon paste caused a long response time of the sensor and decreased its sensitivity. It is probably due to the high surface area formed on the electrode surface that

Table 1 Optimization of the carbon paste compositions

Electrode no.	Plasticizer	Ion association (%)	Graphite powder (%)	MWCNTs (%)	TiO_2 (%)	Slope (mV/decade)
1	51 % 2-NPOE	0.0	49.0	0.0	0.0	11.32±0.30
2	51 % 2-NPOE	0.5	48.5	0.0	0.0	36.20±0.20
3	51 % 2-NPOE	1.0	48.0	0.0	0.0	38.10±0.20
4	51 % 2-NPOE	1.5	47.5	0.0	0.0	42.22±0.13
5	51 % 2-NPOE	2.0	47.0	0.0	0.0	41.87±0.40
6	51 % 2-NPOE	1.5	42.5	5.0	0.0	47.15±0.10
7	51 % 2-NPOE	1.5	37.5	10	0.0	52.68±0.22
8	51 % 2-NPOE	1.5	32.5	15	0.0	50.86±0.10
9	51 % 2-NPOE	1.5	32.5	10	5.0	56.81±0.21
10	51 % 2-NPOE	1.5	30.5	10	7.0	59.55±0.10
11	51 % 2-NPOE	1.5	28.5	10	9.0	59.52±0.10
12	51 % 2-NPOE	0.0	44.0	0.0	5.0	15.91±0.23

may offer special opportunities for the capturing ions on the electrode surface [23, 28].

Recently, there is a considerable interest in using titanium dioxide (TiO_2) nanoparticles as a modifier since they have excellent chemical and physical properties; they have been used in sensor preparation, coating, solar cell, and other applications [36, 37]. TiO_2 nanoparticles have been incorporated with other compounds such as graphite powder and carbon nanotubes to make modified electrodes in the electrochemical analysis of some biologically important compounds [47–51], because they have high surface area, good biocompatibility, and relatively good conductivity, and also, they provide more active sites at the electrode surface and also improve the stability of the electrode. In this study, it was observed from Table 1 that the Nernstian slope of the proposed sensor first rapidly increased by increasing the content of TiO_2 nanoparticles in the paste up to about 7 % and then started to level off and even slightly decreased with the higher loadings. This is because the sites for adsorption increased with the increase in the percentage of TiO_2 nanoparticles in the modified sensor, while the excess of TiO_2 nanoparticles increases the resistance of the electrode. Hence, a 7.0-wt% TiO_2-modified CPE was used throughout this work.

Effect of the plasticizer

Plasticizers are important constituents and influence the detection limit, selectivity, and sensitivity of the ion selective electrodes [52–58]. Furthermore, the nature of the plasticizer affects both the dielectric constant of the paste and the mobility of the target species [59]. Therefore, the influence of the polarity of the plasticizer on the cation selectivity of the paste was investigated. In exploration for a suitable plasticizer for constructing the present electrode, five plasticizers with different polarities, including 2-NPOE, DOP, DBP, DOS, and DOPh, were used into the structure of this electrode. The results obtained indicate that 2-NPOE has a great polarity (ε_r=24) and high lipophilicity to avoid exudation and to considerably affect dissolution of ion associations within the paste. This effect is due to increasing its partition coefficient and providing a suitable mechanical property compared with low polarity plasticizers [60].

The suggested strategy of the sensing process

The strategy of the study presented herein was based on the fact that hyoscine butylbromide (HYBB) behaves as cation of the quaternary ammonium compound. This fact suggests the use of anionic ion exchangers, forming water-insoluble ion association complexes. Ammonium reineckate as an anionic exchanger was used for the preparation of water-insoluble ion associate with HYBB. The high lipophilicity and remarkable stability of this complex suggested its selective use as electroactive materials in the paste matrix for the determination of HYBB [39]. HYBB reacted with ammonium reineckate to form stable 1:1 water-insoluble ion association complex, with low solubility product and suitable grain size precipitate [39]. As we know, the ion association complex used in ion selective electrodes should have rapid exchange kinetics and adequate formation constants in the paste [42]. In addition, for entrapping the ions sensed or in the extraction of target ions from the aqueous solution to the organic paste phase and increasing the partition coefficient and providing a suitable mechanical property of the paste, a suitable plasticizer is needed [60–62], where 2-NPOE was used in the study.

According to the above explanations based on the synergic effect due to the combination of MWCNTs, titania nanoparticles, the ion-exchange site with plasticizer agent can provide excellent electrochemical platforms for target drug sensing due to the combination of the enlarged active surface area and strong adsorptive capability of the nanomaterials, increased in conductivity and sensitivity, and good compactness of the sensing layer compared to traditional liquid membrane electrodes, as well as the specific complexing ability of the modifier.

The surface morphologies of the prepared CPEs

Figure 1 shows SEM images for bare CPE and modified CPE with nanomaterials. As can be seen at the surface of CPE (Fig. 1a), the layer of irregular flakes of graphite powder was present and isolated with each other. After the nanomaterials were added to the carbon paste, it can be seen that materials were distributed on the surface of electrode with a special three-dimensional structure (Fig. 1b). A significant improvement in the surface structure of the modified CPE is observed.

Electrochemical impedance spectroscopy (EIS) study of the prepared potentiometric sensors

EIS is a powerful technique to study the conductivity properties of the surface of modified electrodes. For investigation of the effects of carbon nanotubes and TiO_2 nanoparticles on the conductivity property of the prepared potentiometric electrode surface, EIS measurements were done. The semicircle diameter of the Nyquist plot reflects the electron transfer resistance (Rct). Nyquist diagrams of $[Fe\ (CN)_6]^{3-/4-}$ solution containing 0.1 M KNO_3 at different electrodes (bare CPE and modified CPEs) are shown in Fig. 2. According to this figure, curve a represents the impedance spectrum of bare CPE. Curves b and c show the impedance spectrum of the modified CPE with carbon nanotubes and modified with carbon nanotubes and TiO_2 nanoparticles, respectively. As can be seen from this figure, the semicircle diameter decreases from curve a to curve c. So, the semicircle diameter comparison of these curves clearly shows that charge transfer resistance decreased when carbon paste is modified with 10 % CNT or modified with CNT and TiO_2 nanoparticles. As it is shown, the best result for modification of the carbon paste electrode was obtained in the presence of CNTs and TiO_2 nanoparticles. By increasing the conductivity, the dynamic working range and response time of the sensor improve. If the transduction property of the sensor increases, the potential response of the sensor improves to Nernstian values.

Emf measurements

The emf measurements with the suggested modified CPE were carried out with the following cell assemblies:

> Ag, AgCl(s), KCl (3 mol L^{-1})/sample solution/modified carbon paste electrode

Calibration graph was obtained by plotting the potential, *E*, versus the logarithm of the HYB ion concentration.

Measuring range and detection limit

Measuring range and detection limit (DL) for the determination of HYBB by the prepared CPE was evaluated using linear curve fitting based on IUPAC recommendations. The electrode shows a linear response of $y=59.55x+902.8$ with $R^2=0.998$ to the concentration of HYB ion in the range of 3.00×10^{-8} to 1.00×10^{-2} mol L^{-1} (Fig. 3). Under the optimum conditions, the calibration curve was plotted. Also, DL is defined as the concentration of the HYB ion obtained when the linear regions of the calibration curves are extrapolated to the baseline potentials. In this study, the detection limit of the suggested CPE was 8.50×10^{-9} mol L^{-1}.

Effect of pH

The most important factor in the functioning of most ion selective electrodes is the pH value of the test solution. In order to investigate the effect of pH on the potential response of the electrode, the potentials were measured for a 1.00×10^{-3}-mol-L^{-1} solution of HYBB ion having different pH values. The pH varied from 1.50 to 10.5 by the addition of dilute solutions of HNO_3 or NaOH. The potential variation as a function of pH is plotted in Fig. 4. The composition of the electrode was kept constant during all experiments. The results obtained indicate that the potential remains constant over

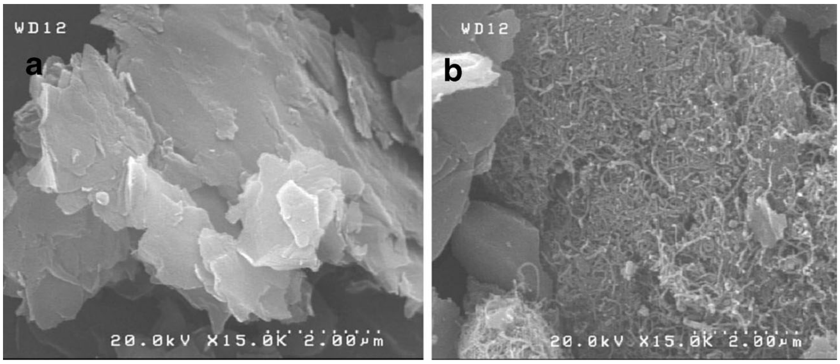

Fig. 1 SEM images for bare CPE (**a**) and suggested modified CPE (**b**)

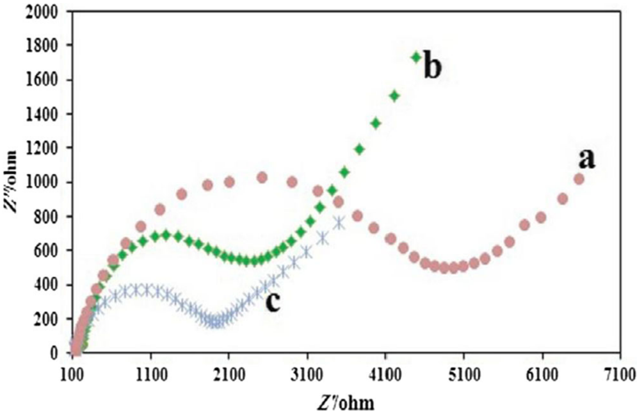

Fig. 2 Impedance plots for different electrodes in $Fe(CN)_6^{3-/4-}$ containing 0.1 M KNO_3: *a* bare CPE, *b* modified CPE with CNTs, and *c* modified CPE with CNTs and TiO_2 nanoparticles

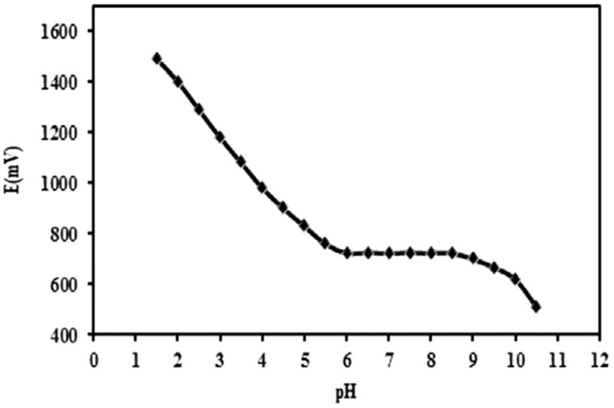

Fig. 4 Effect of pH on cell potential of the modified electrode at 1.00×10^{-3} mol L^{-1} HYBB solutions

the pH range of 6.00–8.50. The acidic (pH<6.00) and basic (pH>8.50) regions exhibit a jump (drift) of the potential of the suggested hyoscine-sensitive carbon paste electrode compared to the pH range of 6.00–8.50 where the potential remains stable. Thus, the electrode works satisfactorily in the pH range of 6.00–8.50. However, there is an observed drift at pH values lower than 6.00 which may be due to H^+ ion interference. On the other hand, the potential decreases gradually at pH values higher than 8.50, which may be attributed to the formation of the free hyoscine base in the test solution.

Response time of the electrode

The response time of the ion selective electrodes is an important factor for any analytical application. In the case of all electrodes, the average response time was defined as the required time for the electrodes to reach a cell potential of 90 % of the final equilibrium values after successive immersions in a series of solutions each having a tenfold concentration difference. The response time of the electrode was evaluated (according to IUPAC definition) by measuring the time required to achieve a 90 % value of steady potential for a HYBB solution. A response time of about 5 s was obtained for this electrode.

Stability of the electrode

The long-term stability of the proposed modified HYBB sensor was investigated by periodically recalibrating in standard solutions and calculating the slope of the optimized sensor over a period of 1 month in a working concentration range of 3.00×10^{-8}–1.00×10^{-2} mol L^{-1} HYBB solutions. During this period, the sensor was used daily over an extended time period (1 h per day). The results exhibited that the slope of the electrode responses was reproducible (with a RSD<0.5 %) and no significant drift was observed for this period of time.

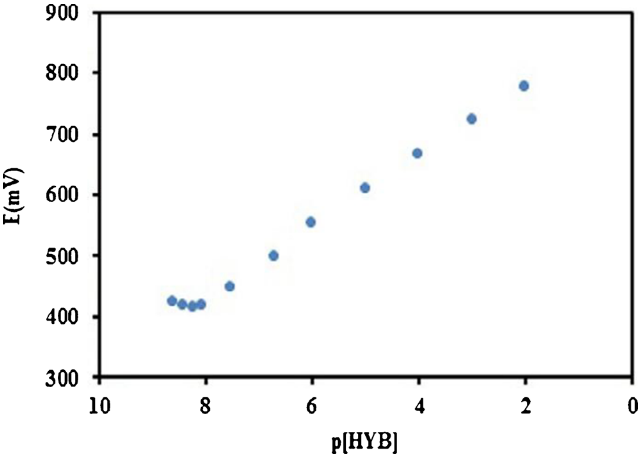

Fig. 3 Calibration curve of the HYBB-modified carbon paste electrode (electrode no. 10)

Table 2 Selectivity coefficient ($K_{i,j}$) for various interfering compounds for HYBB selective carbon paste electrode

Interference (*j*)	$K_{HYBB,j}$	Interference (*j*)	$K_{HYBB,j}$
Pb^{2+}	3.58×10^{-4}	Cs^+	5.47×10^{-4}
Cu^{2+}	4.39×10^{-4}	K^+	9.13×10^{-5}
Zn^{2+}	1.13×10^{-5}	Na^+	1.27×10^{-5}
Ni^{2+}	5.34×10^{-4}	NH_4^+	1.42×10^{-3}
Co^{2+}	1.47×10^{-5}		
Mn^{2+}	6.37×10^{-4}		
Sr^{2+}	1.23×10^{-4}		
Mg^{2+}	2.47×10^{-5}		
Ba^{2+}	6.41×10^{-5}		
Ca^{2+}	6.33×10^{-5}		
Cr^{3+}	4.91×10^{-5}		

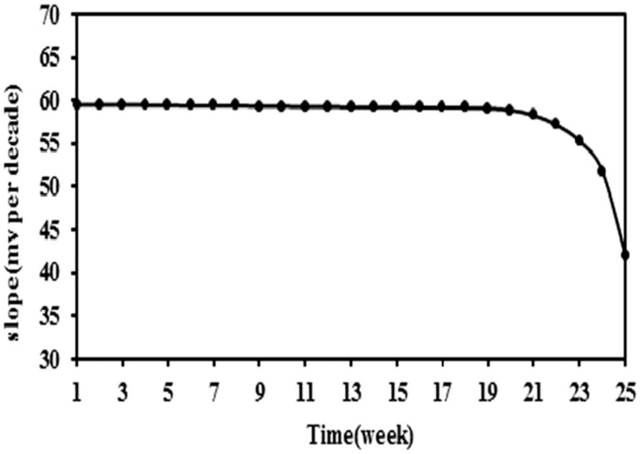

Fig. 5 The lifetime of the HYBB-modified carbon paste electrode (electrode no. 10)

Selectivity and interference

Selectivity, which describes ion selective electrode specificity toward the target ion in the presence of interfering ions, is the most important characteristic of these devices. The potentiometric selectivity coefficients of the HYB^+ sensor were evaluated by the matched potential method (MPM) [63]. According to this method, the potentiometric selectivity coefficient is defined as the activity (concentration) ratio of primary (A) and interfering (B) ions that give the same potential change under identical conditions. At first, a known activity of the primary ion (a'_{A}) solution is added into a reference solution that contains a fixed activity (a_{A}) of primary ions, and the corresponding potential change (ΔE) is recorded. Next, a solution of an interfering ion (B) is added to the reference solution until the same potential change (ΔE) is recorded. The change in potential produced at the constant background of the primary ion must be the same in both cases. It is given by the expression:

$$K^{\mathrm{pot}}_{\mathrm{A,\,B}} = \frac{a'_{\mathrm{A}} - a_{\mathrm{A}}}{a_{\mathrm{B}}}$$

The resulting values of the selectivity coefficients are given in Table 2. According to this table, all interfering compounds applied in this study would not affect the selectivity of the present sensor. On the other hand, this sensor displays significantly high selectivity for the HYB ion.

Table 4 Results of determination of HYBB in its formulation in aqueous solution

Sample	Added (mg)	Found[a] (mg)	Recovery (%)
Tablet	–	9.81±0.21	–
	2	11.84±0.17	101.5
	4	13.76±0.23	98.8
Suppository	–	9.95±0.19	–
	2	11.92±0.19	98.5
	4	13.98±0.13	100.8

[a] Average of four replicable measurements

Lifetime of the electrode

Another important factor of the ion selective electrodes is the lifetime of the sensor that is generally evaluated in these methods. The lifetime of the proposed modified HYBB sensor was evaluated by periodically recalibrating the potentiometric response to HYB ion in a series of standard HYBB solutions. After the conditioning step, the sensor repeatedly calibrated four times during a period of 25 weeks, and its responses are depicted in Fig. 5. The proposed sensor was gently washed with distilled water, dried, and stored at room temperature when not in use. As can be seen in Fig. 5, before 20 weeks, no significant change in the performance of the sensor was observed. There was a slight gradual decrease in the slopes from 59.55 to 58.93 mV/decade. This shows that the lifetime of the proposed HYBB sensor was about 5 months.

Precision and accuracy of the method

The precision of the method was checked by the analysis of four replicates of the sample, expressed by RSD% at the limit of quantification range, which was <1 %. Also, the accuracy was expressed in terms of percentage deviation of the measured concentration from the actual concentration. The obtained results are within the acceptable range of <1 %.

Table 3 Comparison of some characteristics of the suggested electrode with previously reported hyoscine butylbromide ISEs

DL (mol L^{-1})	Linear range (mol L^{-1})	Slope (mV/decade)	Response time (s)	Lifetime (weeks)	Reference
8.50×10^{-9}	3.00×10^{-8}–1.00×10^{-2}	59.55	~5	20	Suggested electrode
4.90×10^{-7}	1.00×10^{-6}–1.00×10^{-2}	51.51	20–30	5–6	[39]
3.00×10^{-6}	1.00×10^{-5}–1.00×10^{-2}	57.00	~10	4	[64]
1.80×10^{-7}	1.00×10^{-6}–1.00×10^{-2}	54.57	20–30	6–8	[65]

Table 5 Results of determination of HYBB in biological samples in aqueous solution

Sample	Added (M)	Found[a] (M)	Recovery (%)
Blood serum	–	N.D.	–
	1.50×10^{-7}	1.52×10^{-7} (±0.17)	101.3
	1.50×10^{-5}	1.48×10^{-5} (±0.14)	98.7
	1.50×10^{-3}	1.44×10^{-3} (±0.21)	96.0
Urine	–	N.D.	–
	1.50×10^{-7}	1.45×10^{-7} (±0.12)	96.7
	1.50×10^{-5}	1.43×10^{-5} (±0.22)	95.3
	1.50×10^{-3}	1.54×10^{-3} (±0.16)	102.7

N.D. not detected

[a] Average of four replicate measurements

Response characteristics

The response characteristics of the suggested electrode in this study are compared with some previously reported hyoscine butylbromide selective electrodes in Table 3. As shown in the table, the suggested electrode represents a wider dynamic range compared to all of the reported sensors and a near-Nernstian slope compared to the other sensors. Also, it has a very short response time and long lifetime in comparison to all of the other sensors.

Analytical applications

In order to test the analytical applicability of the suggested sensor, it has been applied for the determination of HYB ions in different kinds of pharmaceutical formulations and biological samples. The potentiometric determination of HYBB in its powdered tablets and suppository was carried out by the standard addition method. The results are given in Table 4. According to this table, the satisfactory recoveries and the good agreement between the obtained value and the manufacturer's value for tablet and suppository indicated that the proposed method had great potential in the practical sample analysis (manufacturer's value was given as 10 mg per tablet).

The suggested HYB carbon paste sensor was also successfully applied to obtain recoveries of HYBB in blood serum and urine samples. The analysis was performed by the standard addition technique. The results are given in Table 5. According to these results, the sensor provides a good alternative for the determination of HYBB in biological samples.

Conclusion

In the present study, a new nanocomposite material made from mixing MWCNTs with TiO_2 nanoparticles was used to fabricate a highly sensitive, stable, and robust electrode which was used for sensing HYBB. The performance of HYBB carbon paste potentiometric sensor can be highly improved by using MWCNTs as better signal transducers and also using TiO_2 nanoparticles to improve of the surface structure of modified CPE and as better signal transducers too. The suggested potentiometric modified CPE in comparison with the PVC membrane sensor shows better responses in terms of sensitivity, dynamic concentration range, detection limit, Nernstain slope, response time, lifetime, and mechanical stability.

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