Journal for Technology and Science
Homepage : https://journal.antispublisher.com/index.php/IPTEKS
Email : admin@antispublisher.com

e-ISSN : 3047-4337
JOTECH, Vol. 3, No. 2, July 2026
Page 25-35

Synergy Between Bioengineered Nanoparticles and Ionic Complexes in Enhancing the Performance of Ion-Selective Electrodes: A Case Study of the Drug BHDH

Mohammed Ahmed Hameed[1], Dr. Kamal Ali Zadeh[2]
[1,2]Department of Chemistry, Lorestan University, Iran

DOI : https://doi.org/10.61796/ipteks.v3i2.468

Sections Info

Article history:
Submitted: February 15, 2026
Final Revised: March 05, 2026
Accepted: March 20, 2026
Published: April 12, 2026

Keywords:
Modified carbon paste electrodes
Bromhexine Hydrochloride (BHDH)
Lectrochemical sensors
Ion-Pair complexes
FT-IR and fluorescence spectroscopy

ABSTRACT

Objective: *The present study aims at developing novel nano – electrochemical sensors for the sensitive determination of bromhexine HCl.* ***Method:*** *The method consisted of the formation of "ion pair" complexes, (BHDH-PTA) and (BHDH-PMA), and their incorporation into bio-synthesized silver and iron nanoparticles modified carbon paste electrodes.* ***Results:*** *The analytical performance yielded a broad linear range (10−2 to 10−8 molar) and an ultra-low detection limit of 5.32 × 10−10 molar, a high response speed (3–4 seconds), and operational reliability for over a month.* ***Novelty:*** *Based on Fourier-transform infrared (FT-IR), ultraviolet-visible (UV-Vis), and fluorescence studies, the sensors were confirmed and approved as an effective tool (complexes) for pharmaceutical monitoring and medical diagnosis.*

INTRODUCTION

Electroanalytical chemistry is the bedrock in pharmaceutical control and clinical diagnosis, offering a versatile array of techniques with low cost, high precision, and speed of execution [1]. Due to the fast growth of the pharmaceutical industry, it is necessary to establish analytical methods that will be able to determine these compounds in complex matrices, at very low concentrations [2]. These compounds include; bromhexine hydrochloride (BHDH) BHDH) which is one of the most important expectorants and frequently used for the treatment of respiratory diseases linked to viscous mucus [3]. Electrochemical sensors, especially through polymer-based carbon paste electrodes, are based on the high selectivity principle to specific ions. To optimize these electrodes, they use active substances called "ion-pair complexes". This work therefore uses phosphotungstic acid (PTA) and phosphomolybdic acid (PMA) as precursors to form stable ion-responsive complexes with drug BHDH, letting the electrode display excellent ion-building capacity [4], [5], [7]. Moreover, the improvement of sensor performance has been changed through nanotechnology; nanoparticles increases surface-area-to-volume ratio and enhances electron transfer between the electrode and solution. Adopting the global trend towards green chemistry, in this study, Ag-NPs and Fe-NPs synthesized by green synthesis are used as materials to modify the surface of the electrode, with a maximum of LOD and maximum stable time of the electrode being unprecedented7[9].

In addition to the electrical characterization, a high-resolution spectroscopic characterization was performed using Fourier-transform infrared FT-IR, ultraviolet-visible UV-Vis and fluorescence spectroscopy, allowing a detailed understanding of the molecular interactions taking place and corroborating the structure of the complexes synthesized-disclosed in [10]. The combination of coordination chemistry, nanotechnology, and electroanalytical measurements creates a sophisticated approach toward smart sensors that can be fruitfully employed in pharmaceutical quality control laboratories or in hospitals to bolster patient safety and ensure accurate therapeutic dosages [12], [13], [14], [15].

RESEARCH METHOD

Preparation of Ion-Pair Compounds

Ion-Pair Compound (BHDH-PTA)

Preparation of BHDH-PTA ion-pair complex BHDH drug solution 50 mL (2×10^{-2} M) was mixed with 50 mL of PTA precipitating reagent which was prepared by dissolving PTA in 100 mL volumetric flask containing the same molar concentration. The obtained solution was stirred with glass rod and stand at room temperature for 24 h, whereupon a pink precipitate was formed.

Once the reaction is complete, the mixture is filtered and residual precipitate is washed times with distilled water to degrease it. The resultant precipitate was subsequently washed with methanol and dried in air for three days, and the obtaining solid kept for later use to prepare the electrodes. Its sediment is identical to the ion-association complex formed. The infrared spectrum of the Complex synthesized is shown in Figure (1).

.

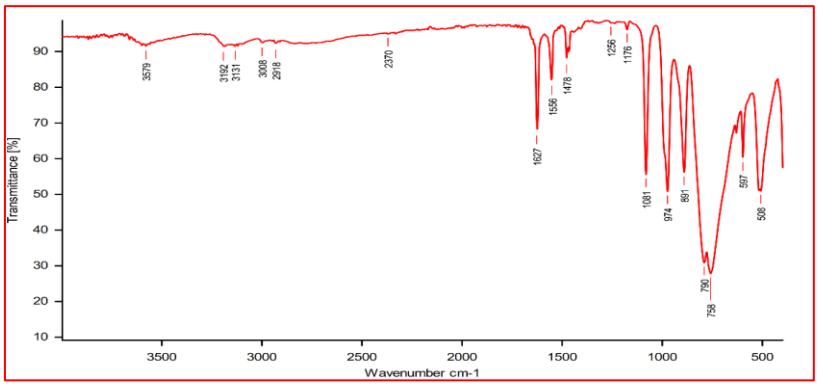

Figure 1. Shows the ion pair BHDH-PTA's FT-IR spectra.

Ion-Pair Compound (BHDH-PMA)

Ionic-pair complex (BHDH-PMA) was obtained by mixing 50 mL of BHDH drug solution of 2×10^{-2} M with 50 mL of prepercipitating reagent PMA (same concentration) in a 100 mL flask. The resulting slurry was stirred well with a glass rod and left at 25 °C for 24 h. Since, in this period, there was a yellow-color precipitate, it indicates the formation of int. ion-association complex.

The mixture was then filtered, and the resulting precipitate was washed multiple times using distilled water to remove unreacted reagents and contaminants. The freeze-dried complex was then air-dried for 3 days and stored at room temperature until used for the electrode preparation. The precipitate was collected which is the obtained ion-association complex and measured the infrared spectrum this is showed in (Fig.2) the infrared spectrum of complex that prepared.

.

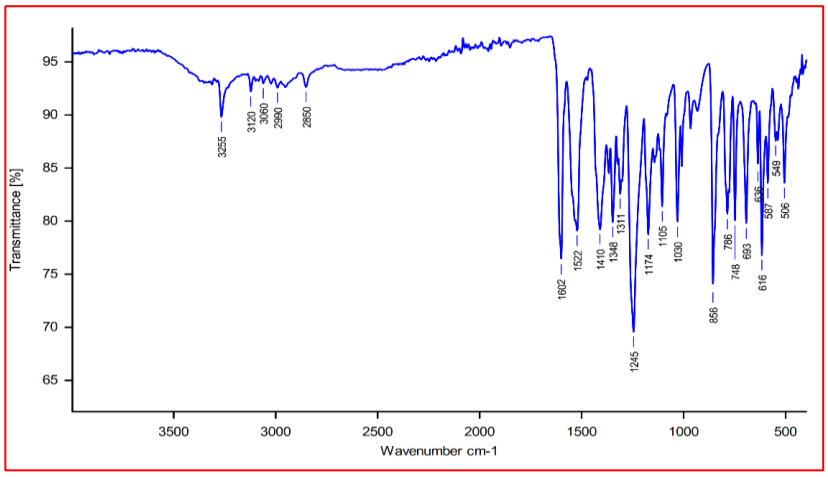

Figure 2. FT-IR spectrum of ion pair BHDH-PMA.

Fabrication of Coated Carbon Sensor (I)

A coated carbon sensor was fabricated with a pure carbon rod (4 cm long, 4 mm in diameter) inserted into a polyethylene tube, where one end of the carbon rod was exposed to the atmosphere and the rest of the rod was vegetatively enclosed by polyethylene tube that was a good insulator to electrolytic test. The exposed tip was dip coated seven times in a membrane cocktail containing BHDH-PTA ion-pair complex (190 mg).

The composition of the membrane was as follows: 0.15 g BHDH-PTA ion-pair, 0.006 g silver nanoparticles (Ag-NPs), 0.35 mL tributyl phosphate (TBP; plasticizer), and polyvinyl chloride (PVC) dissolved in tetrahydrofuran (THF). The deposited membrane was dried for 1 min after each dipping cycle to ensure homogeneous formation of the films.

The bath was maintained at 3×10^{-3} M of BHDH by immersing the prepared sensor for 24 h, while the other side of the rod was electrical insulated and was linked to a copper wire that was connected to the potentiometric measurement device.

Preparation of Coated Carbon Sensor (II)

The second coated carbon sensor was prepared in the same manner with a pure carbon rod tightly inserted into the center of the polyethylene tube with one terminal open to coating a membrane. This was achieved by (1) dipping the exposed end into the membrane mixture seven times, which included 190 mg of BHDH-PMA ion-pair complex.

The composition of membrane cocktail consisted of 0.14 g of BHDH-PMA ion-pair, 0.0055 g of Fe-NPs, 0.35 mL of TBP, and PVC dissolved in THF. Following each immersion, the membrane deposited was incubated for 1 min to dry before the next coating step.

The prepared sensor was then gold coated for (3×10^{-3} M BHDH solution) for 24 h, One end of the rod without gold film was insulated and was connected to a copper wire to ensure electrical contact with the potentiometric set-up.

RESULTS AND DISCUSSION

Study of the Best Experimental Conditions for Electrode (I)

In the second part of this study, the analytical features of the prepared sensor were examined after the fabrication of the nanostructured coated carbon electrode and preactivation in 1×10^{-3} M BHDH solution.

An optimization process was performed to evaluate experimental parameters affecting detection, such as solution pH, temperature, response time, linear concentration range, electrode slope, and correlation coefficient. In addition, the analytic performance of the sensor regarding operational life, sensitivity, precision, limit of detection, selectivity behavior and the real analytic applications were assessed. Electrode performance was evaluated from the potential (mV).

Response Time of Electrode (I)

The response time represents the period required for the electrode to attain a stable potential after contact with the analyte solution. It is considered one of the most important dynamic parameters for evaluating electrode performance. Several factors may affect the response behavior, including solution viscosity, temperature, and the rate at which the sample is measured or transferred.

pH impact on electrode (I)

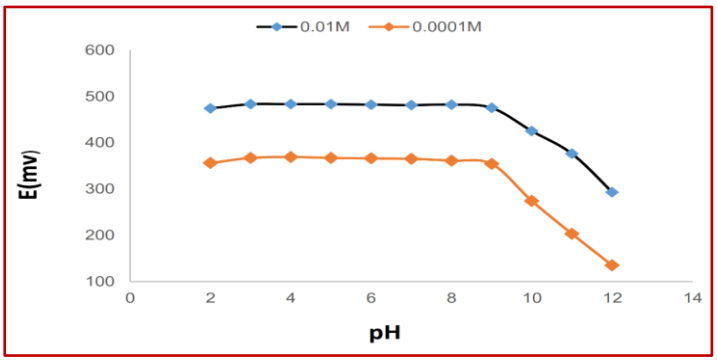

Figure 3. Impact of pH on the responses of nano graphite electrode(I).

Temperature Impact on electrode(I)

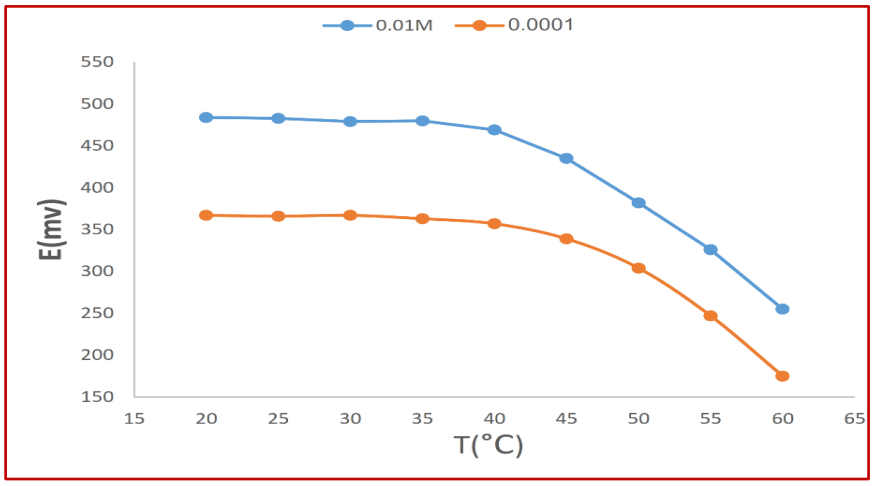

Figure 4. The electrode (I) is affected by temperature.

Life time of electrode(I)

The present study revealed that the prepared electrode exhibited a stable operational lifetime of nearly 33 days. Beyond this duration, the electrode response showed a negative deviation, which can be explained by the leaching of the electroactive material and the plasticizer from the polymeric membrane matrix. These results are illustrated in Figure (5).

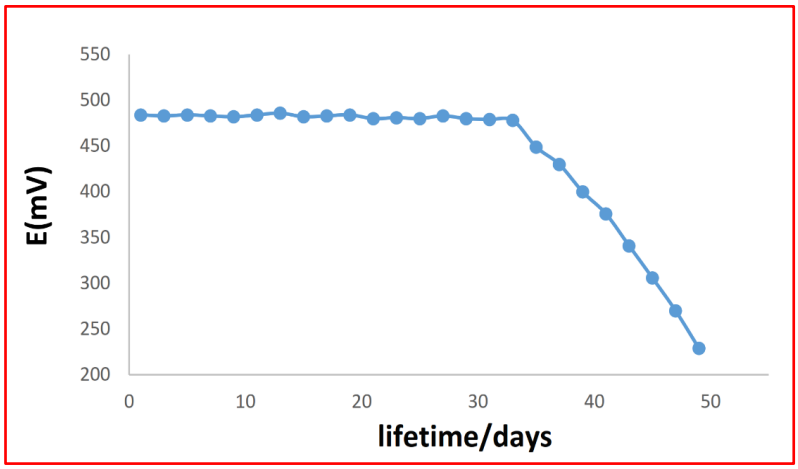

Figure 5. Life time of electrode

Detection limit for electrode (I)

$$LOD=\frac{3.3\times SD\times C}{E_{ave}}...Eq.2$$

Accuracy and precision for electrode (I)

Recording of the possible values for 6 replicate readings at each concentration, we achieved RSD% and percentage of recovery data confirming a high sensitivity and a high accuracy of the proposed method.

Characterization of the best conditions found for the polarity for electrode (II)

After the preparation of the nanocoated electrode on a graphite rod, it was immersed in a 1×10^{-3} M drug solution for a certain period, then the performance of the fabricated nanoelectrode was measured systematically. In the study, some parameters such as pH, temperature, response time, concentration range, slope and correlation coefficient were evaluated. Electrode lifetime, accuracy, reproducibility, detection limit, and selectivity, as well as practical applications are other analytical aspects which have also been discussed. It was evaluated for all in mV unit as per method for potential measurements.

Response time of electrode (II)

Influence of pH on electrode (II)

The electrode response began to rise in response to the increasing acidity of the analyte solution below pH 3.0. The interaction of the membrane with hydrogen ions has been shown to cause] an unstable or irregular response. In contrast, a potential drop was observed at pH > 9.0. That is, likely due to a lack of the non-protonated secondary amino group, thereby lowering the amount of ionized species in solution.

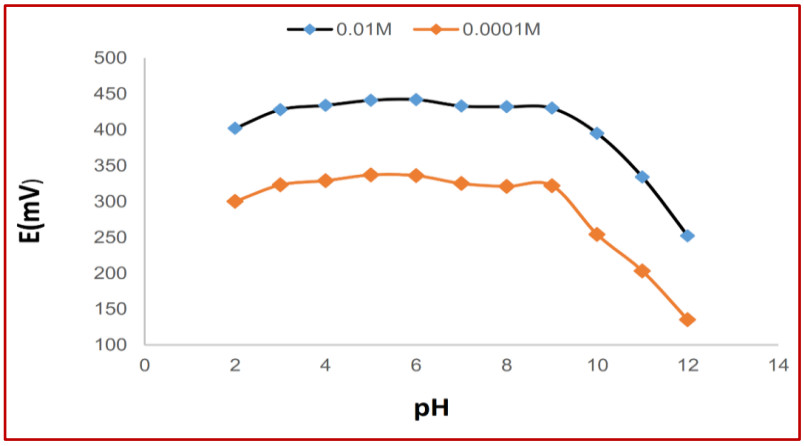

Figure 6. Shows how pH affects the nano graphite electrode's (II) reactions.

Effect of Temperature on Electrode (II)

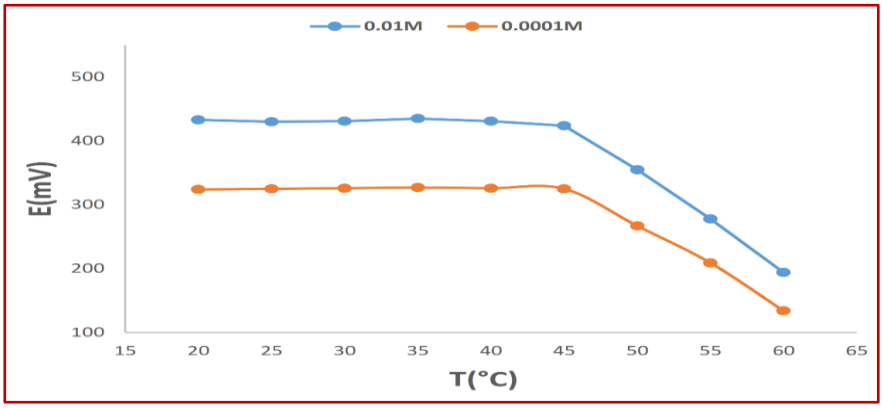

Figure 7. Impact of temperature on the electrode (II).

Life time of electrode (II)

The outcomes are depicted in Figure (8).

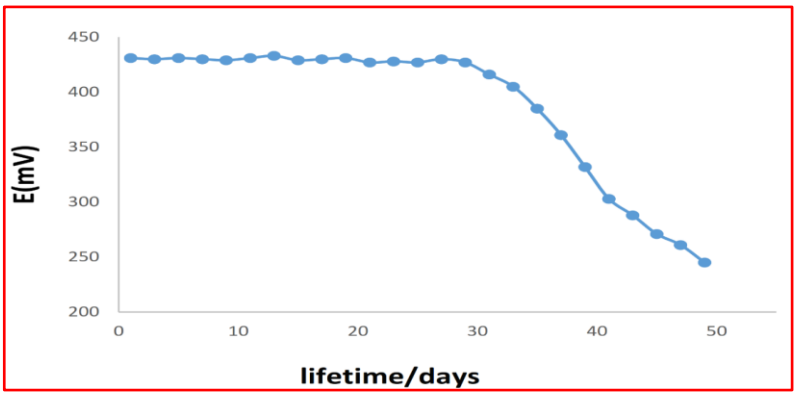

Figure 8. Life time of electrode (II)

Calibration plot

The slope is near the theoretical value (59.2 mV/decade) calculated from the Nernst equation for the monovalent ion

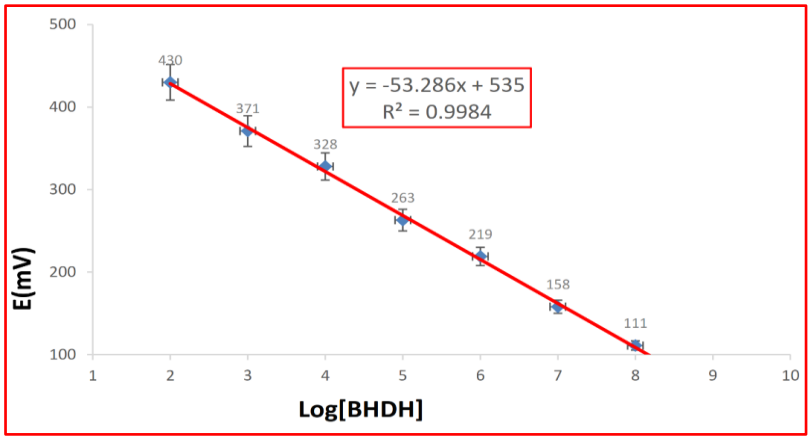

Figure 9. BHDH using nano graphite (II).

Study of Ion-Pair Compounds (BHDH-PMA): UV–Vis Absorption and Fluorescence spectra

Figure 10 displays the absorption and fluorescence emission spectra of Compound 2 in the polar aprotic solvent, acetonitrile.

The first absorption band extends to the near-UV between 340–400 nm and was remarkably intense in the UV–Vis absorption spectrum (left). This can be attributed to the π→π* electronic transition on the conjugated coumarin chromophore.

The dominant emission peak in the fluorescence emission spectrum (right) is at ~462 nm, relatively intense, and approximately spectrally broad. This is assigned to the S_1 excited state, which has primarily π→π* character.

A large Stokes shift may indicate considerable geometric rearrangement in the excited state (possibly associated with ring planarization and increased intramolecular

charge transfer (ICT)). Since that kind of behavior minimizes the self-absorbed effects, it is good.

In addition, the absorption and emission bands exhibit significant bathochromic (red) shifts in acetonitrile. Such spectral behavior exhibits positive solvatochromism which establishes the solvation effect on the electronic structure of the compound.

These results thus corroborate that Compound 2 acts as a useful sensor and probe for polar microenvironments as further assessed using solvatochromic descriptions.

Acetonitrile Solvent

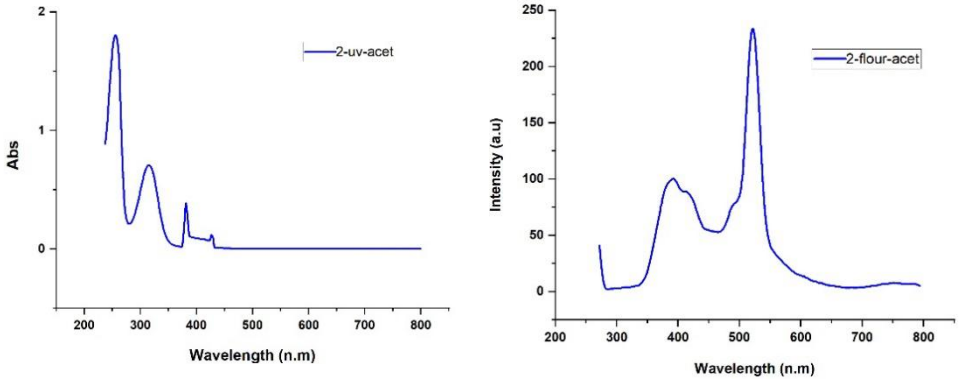

Figure 10. UV–Vis absorption spectrum (left) and fluorescence emission spectrum (right) of the ion-pair compound (BHDH–PMA) in acetonitrile.

Figure 3-14: The absorption and fluorescence emission spectra of Compound 2 in chloroform.

The characteristic absorption band (centered at ~335 nm) in the UV–Vis absorption spectrum (left), ascribed to the π→π* electronic transition, is medium-intense. Moreover, a shallow shoulder can be seen around 370 nm which may be tentatively ascribed to an n→π* transition and/or an intramolecular charge transfer (ICT) contribution. The extinction in visible region is negligible.

The fluorescence emission spectrum (right) shows a dominant emission peak around450nmand a marked vibronic fine-structure, characteristic of emission from a locally excited(LE) state. Another, much weaker band emerges around 650 nm, which could be correlated with minimal excimer formation.

The account for sizable difference between the ground and also excited states, the determined Stokes shift is approximately 115 nm (≈ 6200 cm^{-1}). The spectral position in chloroform is situated at an intermediate position as compared to the spectra in benzene and acetonitrile, consistent with positive solvatochromic behavior and indicates a nearly linear dependence on solvent polarity.

Solvatochromic Interpretation

Since the ICT excited state of Compound 2 is highly tunable, it can be considered as a novel solvatochromic probe for probing media of intermediate polarity.

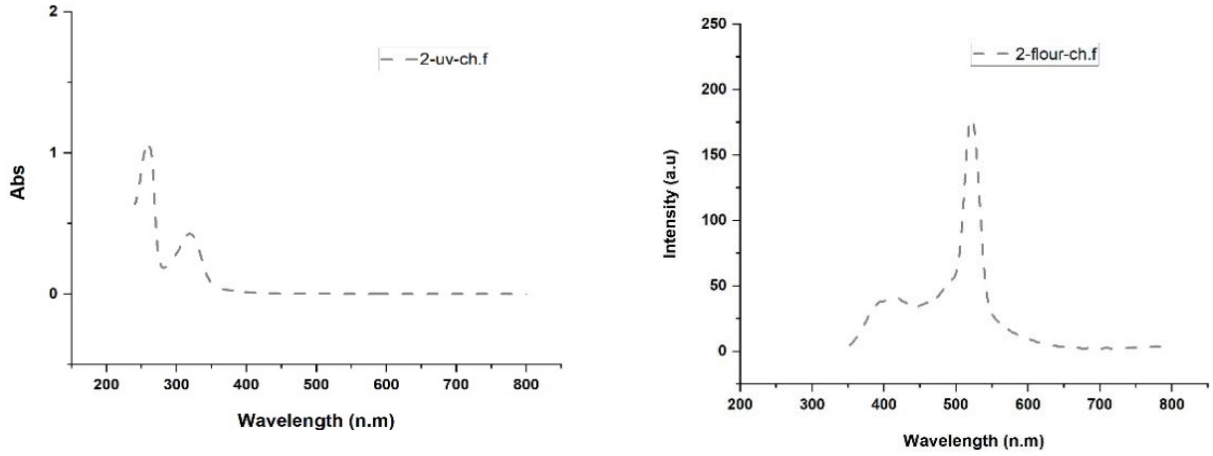

Figure 11. UV-Vis absorption spectrum (left) and fluorescence emission spectrum (right) of Ion-Pair Compounds (BHDH-PMA) in chloroform solvent.

Applications

Several applications can be derived from testing the drug and experimenting with silver ferric nitrate, including the following: drug analysis in factories, where it is used as an alternative for testing the concentrations of active ingredients in pharmaceutical preparations such as tablets and syrups... etc. It has been shown to provide stability and consistency of the active ingredient under various storage conditions, including temperature and over time. It can also be used as a nanosensor, serves as a good drug carrier, and has other chemical applications.

CONCLUSION

Fundamental Finding: Combining BHDH–PTA and BHDH–PMA ion-pair complexes as carbon paste electrodes with green synthesized nanoparticles resulted in composite materials with remarkable electroanalytical properties. The sensors exhibited a wide linear concentration range, rapid potentiometric responses, acceptable operational lifetimes, high accuracy, and sensitivity. **Implication:** The sensors demonstrated high precision, low relative error, and high recovery percentages, indicating their suitability for pharmaceutical monitoring and medical applications. They also showed high sensitivity, with detection limits in the range of 10^{-10} M, making them effective for detecting low concentrations of bromhexine HCl in pharmaceutical products. **Limitation:** The operational lifetimes of the electrodes were limited to 33 days (Electrode I) and 29 days (Electrode II), which may restrict long-term usage. Additionally, the response time varied slightly between electrodes, with slight differences in performance. **Future Research:** Future studies can focus on improving the electrode lifetimes and refining the response times of the sensors. Further exploration into the application of these sensors for detecting other pharmaceutical drugs and extending their use in clinical diagnostics would be beneficial.

REFERENCES

[1] C. Reichardt and T. Welton, Solvents and solvent effects in organic chemistry. John Wiley & Sons, 2010.

[2] F. Kh. S. Niyari, "Synthesis of asymmetric mixed-chelate copper (II) complexes with N,N-dialkyl N′-2-furanylethylenediamine and acetylacetonato ligands and investigation of their solvatochromism," M.Sc. thesis, University of Mazandaran, 2011.

[3] E. O. Voit, H. A. Martens, and S. W. Omholt, "150 years of the mass action law," PLoS Comput. Biol., vol. 11, no. 1, p. e1004012, 2015.

[4] C. Reichardt, "Empirische parameter der Lösungsmittelpolarität," Angew. Chemie, vol. 77, no. 1, pp. 30–40, 1965.

[5] Z. Hu, S. Tan, R. Mi, X. Li, D. Li, and B. Yang, "Solvent-controlled reactivity of Au/CeO_2 towards hydrogenation of p-chloronitrobenzene," Catal. Letters, vol. 148, no. 5, pp. 1490–1498, 2018.

[6] J. L. Kneebone, W. W. Brennessel, and M. L. Neidig, "Intermediates and reactivity in iron-catalyzed cross-couplings of alkynyl Grignards with alkyl halides," J. Am. Chem. Soc., vol. 139, no. 20, pp. 6988–7003, 2017.

[7] F. Hosseinpour, "Investigation of solvatochromic properties and solvation behavior in several deep eutectic solvents (DESs) and their mixtures with water," M.Sc. thesis, University of Damghan, 2021.

[8] P. Kumar Malik, M. Tripathy, and S. Patel, "D-π-A molecular probe to unveil the role of solute–solvent hydrogen bonding in solvatochromism, location-specific preferential solvation and synergistic effects in binary mixtures," ChemistrySelect, vol. 5, no. 12, pp. 3551–3566, 2020.

[9] M.-O. Simon and C.-J. Li, "Green chemistry oriented organic synthesis in water," Chem. Soc. Rev., vol. 41, no. 4, pp. 1415–1427, 2012.

[10] Z. V. Parkouhi, "Investigation of green synthesis of imidazo[1,2-a]pyridines and study of their solvatochromic effects," M.Sc. thesis, Noshirvani University of Technology, Babol, 2018.

[11] J. P. Cerón-Carrasco, D. Jacquemin, C. Laurence, A. Planchat, C. Reichardt, and K. Sraïdi, "Solvent polarity scales: determination of new ET(30) values for 84 organic solvents," J. Phys. Org. Chem., vol. 27, no. 6, pp. 512–518, 2014.

[12] M. S. Zakerhamidi and S. Shahrabi, "Solvatochromic solvent polarity parameters for the characterisation of some cyanobiphenyl nematic liquid crystals," Liq. Cryst., vol. 40, no. 9, pp. 1195–1201, 2013.

[13] M. J. Kamlet and R. W. Taft, "The solvatochromic comparison method. I. The β-scale of solvent hydrogen-bond acceptor (HBA) basicities," J. Am. Chem. Soc., vol. 98, no. 2, pp. 377–383, 1976.

[14] M. Schmeisser, P. Illner, R. Puchta, A. Zahl, and R. van Eldik, "Gutmann donor and acceptor numbers for ionic liquids," Chem. Eur. J., vol. 18, no. 35, pp. 10969–10982, 2012.

[15] V. Gutmann, "Empirical parameters for donor and acceptor properties of solvents," Electrochim. Acta, vol. 21, no. 9, pp. 661–670, 1976.

***Mohammed Ahmed Hameed (Corresponding Author)**
Department of Chemistry, Lorestan University, Iran
Email: alhamedalhamed75@gmail.com

Kamal Ali Zadeh
Department of Chemistry, Lorestan University, Iran