



Research article

Novel all-solid contact Copper (II) - selective sensor based on Cefoperazone and poly(3,4-ethylenedioxythiophene) (PEDOT) as conducting polymer

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Abstract

A potentiometric all-solid contact copper (II) selective sensor based on Cefoperazone as a neutral carrier was developed. The electrode was prepared by coating the membrane solution containing PVC, plasticizer, and carrier on the surface of gold wire electrode. The coated gold wire electrode (CGWE) exhibited a linear response of 31.01 ± 0.1 mV/decade over the range of 1.0×10^{-8} – 1.0×10^{-2} Cu (II) mol.L⁻¹, and lower detection limit (LDL) 4.0×10^{-9} mol.L⁻¹. The solid-contact Cu (II) solid electrode with conducting polymer poly (3,4-ethylenedioxythiophene) (PEDOT), as intermediate layer has been successfully used to detect ions at nanomolar level concentrations. The electrode has a response time between 5-10 s and was suitable for Cu (II) determination in aqueous solution over pH range (4.0–7.0). It was found to be selective towards Cu (II) ions over other common cations and the relevant potentiometric selectivity coefficients were calculated. The analytical utility of the proposed electrode was also demonstrated.

Introduction

Copper is considered the third most abundant essential trace heavy metal ion in the human body as it plays an important role in various biological and metabolism processes [1-4]. As well, it is considered an essential nutrient for plants and some of its compounds are widely used as fertilizers, bactericides, fungicides, algicides and antifouling paints [2, 5]. Moreover, due to its high electrical conductivity, chemical stability, plasticity and capacity to form alloys with many metals, copper has many applications in industrial manufacturing and catalytic processes [5-7]. On the other hand, copper is the second toxic metal to aquatic life [1, 8]. Natural sources for human exposure to copper include windblown dust, volcanoes, decaying vegetation, forest fires and sea spray [5]. As well, it is present in waters and wastewaters resulting from mining industries, refineries, paper and dyeing [1, 8]. Copper also reaches our homes through different types of home plumbing and fixtures as well as copper sulfate may be added in drinking water storage facilities to control algal growth [1, 2, 5].

Generally, the presence of trace heavy metals in the environment is an important problem that must be monitored because of their toxicity for many life forms once their concentration exceeds a certain limit [5, 7]. As for copper, the maximum permissible level set for human exposure is 2.0 mg/L [9] or 2 mg/day [7]. Increasing this exposure beyond the 15 mg/day, copper becomes toxic [7]. Excessive intake of copper by humans can cause anemia, liver and kidney damage, and stomach and intestinal irritation [1] as well as diseases such as Wilson, Menkes, MS, Alzheimer, epilepsy, melanoma and rheumatoid arthritis [10]. Furthermore, copper can be phytotoxic at high concentrations and its bioavailability and toxicity depends on the physical and chemical speciation of the metal in the matrix.

The determination of this trace metal in food, environmental samples, water and wastewater is deemed important for regulatory and precautionary reasons.

Several instrumental techniques have been used for the copper trace determination and monitoring in environmental

matrices. These include atomic absorption spectrometry, spectrophotometry, phosphorescence quenching method and chemiluminescence [2, 3, 8] as well as inductively coupled plasma atomic emission spectrometry (ICP-AES), high performance liquid chromatography (HPLC), anodic stripping voltammetry and cyclic voltammetry [8]. However, most of these methods are either time consuming, involve multiple sample manipulations and pretreatment, or require expensive instruments and qualified personnel that are hard to avail in most laboratories [3, 8]. In this respect, electro-analytical techniques are ideal because of their high sensitivity, simple of operation and low cost [3, 8]. Among these procedures, potentiometric determination using ion selective electrodes (ISEs) offers the advantages of being fast, simple in instrumentation, accurate, reproducible, highly selective towards various species with a relatively fast response for a wide dynamic range of ionic concentrations [3,12,13]. As well, it can be used in complex and colored media [7]. These characteristics have inevitably led to the development of a number of sensors for the detection of several ionic species such as K^+ , Na^+ , Hg^{2+} , Cd^{2+} , Cl^- , NO_3^- over the last few years [12, 13]. Hence, the use of ISE for Cu (II) determination offers higher selectivity, sensitivity and ease of application within a variety of environmental matrices [2, 13].

Cefoperazone (Figure 1) is a third-generation semi-synthetic cephalosporin antibiotic that is widely applied in clinical therapy [15-17].

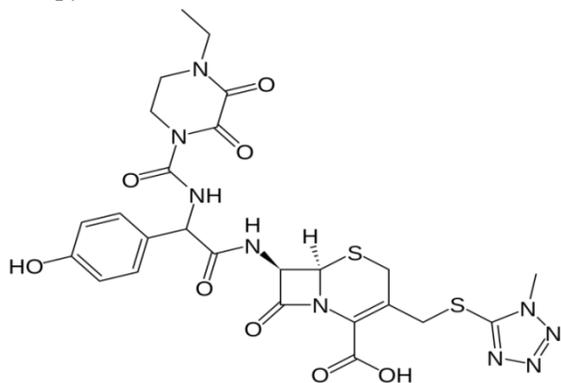


Figure 1. Chemical structure of Cefoperazone

The metal complexes of the non-cyclic cefoperazone sodium molecule have been extensively studied in order to evaluate their toxicity and biological performance [16,18]. From these studies, it was found that cefoperazone has the capability of chelate binding with different transition metals such as (Al, Cd, Co, Cu, Fe and Ni) and that the formed complexes were non-toxic and insoluble in water and sparingly soluble in common organic solvents. However, there are no reports of the use of this ionophore antibiotic (cefoperazone) for the transition metal ions detection in aqueous environmental samples or investigation concerning its suitability for such an application. Therefore, the aim of this work is to develop a CGWE incorporating cefoperazone as a neutral ligand for the determination of copper(II) in

aqueous solution. The potentiometric selectivity of the electrode towards various ions and the effect of the membrane matrix, carrier concentration, and pH were investigated and the optimal operational parameters of this sensor have been characterized. Finally, analytical applications of this developed Cu(II) ISE were investigated and the results were reported accordingly.

Experimental

Chemicals and reagents

All reagents used for the preparation of the membranes were of analytical-reagent grade and were used without further purification. Dibutyl phthalate (DBP), dioctyl sebacate (DOS), sodium tetraphenyl borate (NaTPB), tributylphthalate (TBP), high relative molecular weight Poly(vinyl chloride) PVC were purchased from Aldrich. Tetrahydrofuran (THF) was obtained from Fluka. Stock solutions of Cu(II) ion were freshly prepared by dissolving the appropriate weight of Cu(II) nitrate trihydrate salt in double distilled deionized water. All cation solutions were freshly prepared by accurate dilution from the stock solution of (0.1 mol L⁻¹). Cefoperazone sodium (Cefobid) and Materna (vitamin and mineral supplement) were obtained locally from Pfizer Co, Egypt (PFE). The Cefoperazone acid form was prepared by the addition of an equivalent amount of Cefoperazone sodium form (Cefobid) (0.1 mol L⁻¹) and HCl (0.1 mol L⁻¹) in solution. The pH response profile for the developed electrode was examined using different copper (II) ion concentrations.

Instrumentation and Apparatus

All potentiometric measurements were performed at (25 ± 1°C) using a Jenway pH/Ion meter Model (3310). A double junction Ag/AgCl reference electrode containing (3 mol L⁻¹) potassium chloride in outer and inner tubes was used as reference electrode. The pH values were determined using a combined glass-pH electrode Model Jenco (6173). All spectrophotometric measurements were made using a Jasco (USA) double beam spectrophotometer Model (V-630). FTIR spectra for Cefoperazone acid form and Cefoperazone copper complex were recorded on a Pye-Unicam type (1200) spectrophotometer using KBr discs. Thermogravimetric analysis of both ligand and metal-ligand complex was carried out using DTG-60H simultaneous DTA-TG SHIMADZU (Japan) in dynamic nitrogen and air atmospheres (20 mL min⁻¹) with a heating rate of (10°C.min⁻¹) using platinum crucibles. Melting point measurements were done using Bibby Stuart Scientific (SMP3, UK).

Preparation of PVC membrane-coated graphite electrode

The general procedure for the preparation of PVC membrane is similar to that previously described [12, 19, 20]. The electrode was prepared from a spectroscopic-grade

graphite rod (3.00 mm diameter and 10.0 mm long) after washing thoroughly with hydrochloric acid (0.1 mol L⁻¹) and ethyl alcohol and drying at 100 °C. The rod was fitted into a plastic body and connected to the pH/ion meter from the membrane free end using an insulated copper wire. The coated-graphite membrane electrode was prepared by mixing of PVC, plasticizer and anionic additives (for a total mass of 100 mg) and dissolving them in about 2.0 ml of THF. The electro active material (Cefoperazone) (0- 12 mg) was added to this mixture and the solution was mixed well. Table 1 shows the different variation in the ISE constituents and membrane content of the developed PVC membranes and the potential response obtained.

The working surface of the electrode was polished after preparation and rinsed with water and ethanol before being allowed to dry. Before its initial use, the rod was dipped in the membrane solution in THF for about 2.0 s according to the IUPAC recommendations [21] and was allowed to dry leaving the PVC layer coating. This operation was repeated for (12-20) times in order to obtain a proper layer thickness and was then left overnight to completely dry at room temperature. The electrode was conditioned by soaking it in 1.0 x10⁻³ mol L⁻¹ Cu (II) nitrate solution for 24 hours.

Electrochemical measurement and Calibration of the ion-selective sensor

The ion-selective electrodes were calibrated by immersing them in conjunction with Ag/AgCl reference electrode in a 100-mL beaker containing 50.0 mL of Cu (II) ion solutions and the pH was adjusted to 4.8 using acetate buffer, according to the obtained optimal pH range. The performance of each electrode was investigated by measuring its potential in Cu(II) nitrate solutions in range of (1.0×10⁻⁷ mol L⁻¹ - 1.0×10⁻² mol L⁻¹) at constant pH. After stirring the solutions at room temperature (25°C), the potentials were monitored and recorded after stabilization to ± 0.5mV. A calibration curve was constructed by plotting the recorded potentials as a function of log [Cu(II)]. The employed galvanic cell can be represented as: Ag/AgCl/ 3.0 mol L⁻¹ KCl / sample solution / IS-membrane.

Selectivity of ISE and the influence of interfering ions

The influence of some inorganic cations on the selectivity of the developed sensor was investigated. The selectivity coefficients were estimated using Nicolsky–Eisenman equation:

$$\log K_{A,B}^{pot} = \frac{(E_B - E_A) Z_A F}{2.303RT} + \left(1 - \frac{Z_A}{Z_B}\right) \lg a_A$$

Potentiometric selectivity coefficients ($K_{A,B}^{pot}$) describing the preference by the membrane for an interfering ion B relative to Cu²⁺ was determined by the separate solution method (SSM). In this method, the concentrations of a cell comprising an ion selective electrode and a reference

electrode (ISE cell) were adjusted within two separate solutions, one containing the ion A of the activity a_A (but no B), the other containing the ion B (but no A) with an activity as high as to achieve the same measured cell voltage [21]. From any pair of activities a_A and a_B giving the same cell

voltage, the value of ($K_{A,B}^{pot}$) may be calculated. The potentiometric selectivity coefficients of the proposed electrodes are provided in Table 2.

Preparation of copper (II) Cefoperazone complex: determination of structure and stoichiometry

Cu (II) Cefoperazone complex was prepared by the step wise addition of (0.1 mol L⁻¹) copper nitrate solution to a stirred solution of an equivalent amount of (0.1 mol L⁻¹) Cefoperazone sodium form. The obtained complex - a yellowish-green precipitate- was filtered and washed with (0.1 mol L⁻¹) NaOH solution and dried. The molar ratio method was used to deduce the stoichiometry of the formed Cu-complex [22]. FTIR and TGA techniques were also used to explain the stoichiometry, formation and confirmation of the formed Cu-Cefoperazone complex.

Analytical application of developed sensor in some pharmaceutical formulations

Ten Materna tablets (vitamins/antibiotic and mineral supplement) were ground in a porcelain mortar, and the equivalent of one tablet was accurately weighed and dissolved in 500 mL double distilled water containing 1 mL of conc. H₂SO₄. After filtration into a volumetric flask, the filtrate was completed to 1000 mL with double distilled water and the pH was adjusted to 4.8 using acetate buffer. The concentration of Cu(II) in these tablet formulation was determined both by the developed sensor and spectrophotometrically using dithizone method [22] and the results were statistically compared.

Results and Discussion

Effect of pH

The influence of pH of the test solution on the potential response of the membrane sensor was tested within the pH range 2–12 and the results are shown in Figure 2. The pH response for sensor electrode #4 was examined using different concentrations of Cu(NO₃)₂ solutions (1.0×10⁻³ mol L⁻¹, 1.0×10⁻⁴ mol L⁻¹ and 1.0×10⁻⁵ mol L⁻¹). From Figure 2, it was observed that the measured potentials remained unchanged over the pH range of 4.0–7.0. As well, it was observed that as the concentration of the Cu ion in solution decreased, the measured potentials slightly decreased. Similar potential response vs. pH was obtained for Cu(II) sensors produced using other neutral carriers by other researchers [1, 3, 6, 14, 25].

Generally, the variability of the measured potentials below pH 4.0 may be attributed to the protonation of the ligand in

the membrane phase, which results in the loss of its ability to form a complex with Cu^{2+} ions [3, 6]. As well, it was reported that at lower pH, the protonation of nitrogen atoms present on some ligands may result in the improper functioning of the membrane electrode towards Cu^{2+} ion [23]. This interference of H^+ ions may be due to the high rate of H^+ ions diffusion from the sample solution towards the membrane matrix (ability to extract H^+ ion) where they interact with the ionophore and its protonation results in a decreased selectivity for Cu(II) ions [3,4,6,14]. Thus, in this case the electrode response reflected an increase in the H^+ ions in solution. At higher pH (>7.0), on the other hand, the potential drop may be attributed to the formation of hydroxyl-complexes of Cu^{2+} in solution. However, the sensing behavior of the membrane electrode remained unchanged when used in low to high concentration and vice versa. The stability and reproducibility of the electrode was also tested and the long-term study revealed no significant changes in the performance of the PVC electrode over a period of two months.

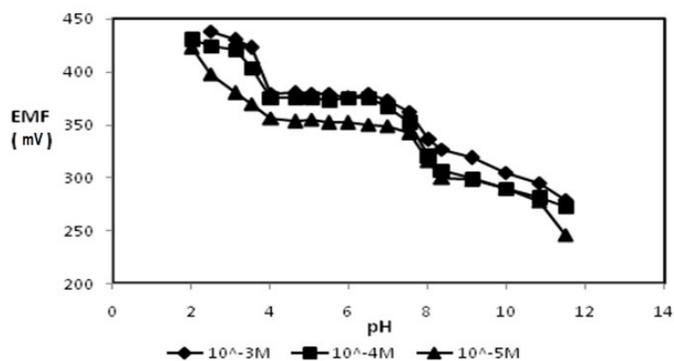


Figure 2. The effect of the solution pH upon the potential response of the developed Cu(II) ion selective electrode in the presence of different Cu(II) ion concentrations (1×10^{-3} M, 1×10^{-4} and 1×10^{-5} M).

The effect of membrane composition

Some important features of the PVC based membranes that significantly influences its selectivity and sensitivity are the nature and amount of ionophore, the properties of the plasticizer, the plasticizer/PVC ratio and the nature of additives used [4,14, 23]. As well, it is well recognized that the sensitivity, selectivity, linearity, and other analytical characteristics of the CGE depends significantly upon the membrane composition [3, 24]. The performance and characteristics of several membranes prepared and their composition are summarized in Table 1. It can be seen from these results that sensor #4 showed an improved slope (31.01 mV/decade), a larger linear concentration range for ion detection (1.0×10^{-6} mol L^{-1} to 1.0×10^{-2} mol L^{-1}) and a lower detection limit (LDL) of 4.0×10^{-7} mol L^{-1} . The results also indicate that such sensitivity was achieved by using 10 mg of the ionophore, 60 mg of DOS as plasticizer and 30 mg PVC. It has to be noted that increasing the ionophore

content above the optimum did not improve upon the electrode sensitivity and detection limit.

However, within that optimal composition (sensor #4) no (NaTPB) was included. Thus, the improvement in sensitivity of the developed electrode may be a result of the type of plasticizer added and not the presence of the lipophilic negatively charged additives such as NaTPB. It was reported that the plasticizer to be used in membranes should exhibit high lipophilicity, high molecular weight, low tendency for exudation from the polymer matrix, low vapor pressure and high capacity to dissolve the substrate and other additives present in the membrane [5]. As well, plasticizers must not have functional groups that may compete with the carriers as they may affect the chelation with the primary ion [21]. Moreover, it was reported that the response characteristics of ion-selective electrodes were largely affected by the nature and amount of plasticizer [14, 21]. This may be due to the influence of the plasticizer on dielectric constant /polarity of the membrane phase, the mobility of the ionophore molecules and the state of ligands. As well, the addition of plasticizers was reported to not only improve the workability of the membranes, but also contribute significantly towards the improvement in the working concentration range, stability and shelf life of the sensor [5]. In conclusion, the optimal composition of sensor # 4 was used thereafter to study various operational parameters of the electrode: the working concentration range, sensitivity, selectivity.

Table 1 and (Figures 3, 4)

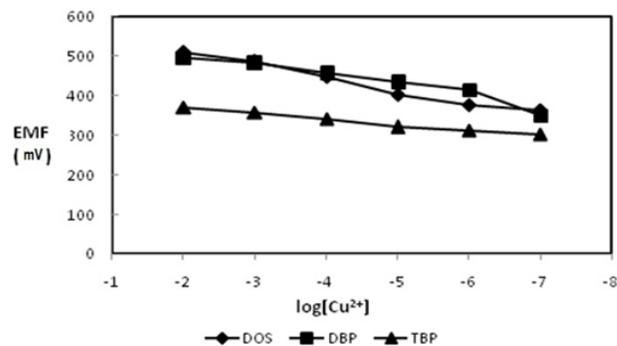


Figure 3. The calibration curve of 10% ionophore with various type of plasticizer.

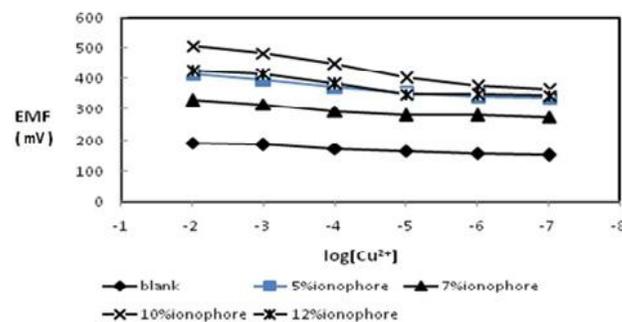


Figure 4. Calibration curve of various ionophore ratio with DOS plasticizer

Table 1. Data indicating the effect of varying the membrane composition upon the its performance and characteristics

Sensor No	PVC (mg)	DOS (mg)	TBP (mg)	DBP (mg)	Ionophore (mg)	NaTPB (mg)	Slope (mv/decade)	LDL (mol L ⁻¹)	Linear range (mol L ⁻¹)
0	33.4	66.6	0.0	0.0	0.0	0.0	12.3	7x10 ⁻⁴	2x10 ⁻³ -1x10 ⁻²
1	47.5	47.5	0.0	0.0	5.0	0.0	18.9	9x10 ⁻⁶	1x10 ⁻⁵ -1x10 ⁻³
2	31.7	63.3	0.0	0.0	5.0	0.0	16.5	2x10 ⁻⁶	1x10 ⁻⁵ -1x10 ⁻²
3	31.0	62.0	0.0	0.0	7.0	0.0	11.3	9x10 ⁻⁶	1x10 ⁻⁵ – 1x10 ⁻³
4	30.0	60.0	0.0	0.0	10.0	0.0	31.01	4x10 ⁻⁷	1x10 ⁻⁶ – 1x10 ⁻²
5	30.0	0.0	0.0	60.0	10.0	0.0	27.3	9x10 ⁻⁷	1x10 ⁻⁵ – 1x10 ⁻²
6	30.0	0.0	60.0	0.0	10.0	0.0	14.2	8x10 ⁻⁶	2x10 ⁻⁵ – 1x10 ⁻²
7	29.6	59.4	0.0	0.0	10.0	1.0	5.75	1x10 ⁻⁵	8x10 ⁻⁴ – 1x10 ⁻⁴
8	29.3	58.7	0.0	0.0	10.0	2.0	27.6	1x10 ⁻⁶	1x10 ⁻⁵ – 1x10 ⁻⁴
9	29.0	58.0	0.0	0.0	10.0	3.0	12.9	5x10 ⁻⁵	1x10 ⁻⁴ – 5x10 ⁻²
10	29.3	58.7	0.0	0.0	12.0	0.0	17.3	8x10 ⁻⁶	1x10 ⁻⁵ – 1x10 ⁻²

Response time

The dynamic response time for any ion-selective electrode is an important factor that determines the analytical applicability of the sensor [7, 25]. The practical response time of the proposed electrode was recorded by changing the concentration of Cu²⁺ in a series of solution ranging from 1.0 x10⁻⁶ to 1.0 x10⁻² mol L⁻¹. The average time required for the membrane electrode to reach a steady potential response within ±1mV of the final equilibrium value after successive immersion in a series of Cu²⁺ solutions, each having a 10-fold difference in concentration, was between 20-30 s. This is most probably due to the fast exchange complexation-decomplexation kinetics of Cu(II) ions with the ionophore at the test solution-membrane interface [4]. However, it has to be noted that at lower concentrations, the response time reached 30 s for a copper concentration of 1.0×10⁻⁵ mol L⁻¹, which is similar to observations made by Ardakani et al. [6]. As well, it was observed that the sensing behavior of the membrane electrode did not depend on whether the potentials were recorded from low to high concentrations or vice versa.

Potentiometric selectivity

Overall, the most important characteristic that determines the extent of utility of any sensor in real sample measurements is ion selectivity as well as the influence of interfering ions on the response behavior of the electrode [1, 25]. Therefore, ligands used as ionophores in an ISE must be selective for an ion over other metal ions; have a rapid exchange kinetics and be sufficiently lipophilic to prevent leaching of the ligand into the solutions surrounding the electrode [1, 3, 26]. The selectivity of the membrane electrode #4 and SSM has been recommended only when the electrode produces a Nernstian response to both principal and interfering ions [21]. It is important to point out that the concentration level of the interfering ion, which the electrode can tolerate, depends upon the numerical value of the selectivity coefficient. In other words, the smaller the value of the selectivity coefficient, the higher the concentration of interfering ion(s) which can be tolerated by

the sensor. From the data in Table 2, it is evident that the developed electrode exhibited a significant and high selectivity towards Cu²⁺ relative to several other common transition metal ions. (Table 2).

Table 2. Selectivity data of the Cu(II) ion-selective electrode (sensor no. 4) based on ionophore Cefoperazone

Interfering ion	$K_{A,B}^{pot}$
Hg ²⁺	0.411 x 10 ⁻³
Pb ²⁺	1.079 x 10 ⁻³
Ca ²⁺	5.960 x 10 ⁻⁴
Mn ²⁺	3.059 x 10 ⁻⁴
Co ²⁺	2.841 x 10 ⁻⁴
Ni ²⁺	2.449 x 10 ⁻³
Cd ²⁺	8.020 x 10 ⁻³
Al ³⁺	5.951 x 10 ⁻⁴

Characterization of copper-Cefoperazone complex

The study of the formation of Cu-cefoperazone and its structural properties has been the focus of interest for a number of years by some researchers [16,18,27,28]. This was due to the fact that the formed metal complex did influence its antimicrobial activity, toxicity, resistance to hydrolysis and other biological and chemical properties in order to reduce the doses [29]. As well, it has been reported that Cephalosporins chelation with metals(II) tends to make the ligand to act as a more powerful and potent bacterial agent . In this respect, Cu(II) ions were reported to catalyze the hydrolysis of cephalosporin molecules and increase its catalytic effect through the formation of Cu(II) complexes in weakly acidic medium in the human body and thus decrease the dose.

The spectrophotometric study of the uncomplexed ligand and Cu-ligand complex indicated the prevalence of two peaks ($\lambda = 268$ nm and 298.5 nm) for the former and peaks at ($\lambda = 274$ nm (A=0.546) and $\lambda = 338$ nm (A=0.468)) for the latter. The adsorption maxima of the uncomplexed ligand at ($\lambda = 268$ nm) was reported to be associated with a $\pi \rightarrow \pi^*$ transition due to molecular orbital energy levels originating in the NC-S moiety while that at ($\lambda = 298.5$ nm) was related

to the $\pi \rightarrow \pi^*$ transition within the tetrazole moiety [16]. The shifted absorption band at 274 nm was reported to be induced by bonding $\sigma(\text{N}) \rightarrow$ antibonding with $d_{x^2-y^2}(\text{Cu})$ charge transfer, an observation which confirms the formation of RN-Cu complexes [30]. As well, the shift from 298.5 nm to 338 nm was indicative of the bonding of Cu(II) to both HN- and CO- in ligand complex molecule [31].

The molar ratio method was used to determine the metal to ligand stoichiometry of the formation of Cu-ligand complex and the absorbance was measured at $\lambda = 338$ nm. A plot of the results indicated that the formed metal complex had a 1:1 stoichiometry with respect to metal and electro-active material. Previous studies have indicated that cefoperazone (Cephalosporin antibiotic) forms stable 1:1 complex with Cu^{2+} [16,18] with which the current findings are in agreement.

FTIR analysis of the ligand cefoperazone sodium and Cu(II)-cefoperazone the complex was undertaken to help identify and determine the coordination sites that could be involved in chelation (Figure 5A and 5B). The spectra of the mixed-ligand Cu(II) complex revealed a broad band in the region $\sim 3430\text{--}3470$ cm^{-1} , which may be attributed to the stretching vibration of OH group [29,32]. As well, the presence of a broad band ($3285\text{--}3520$ cm^{-1}) in the spectra of metal complex was associated with coordinated and/or lattice water molecules [33], a fact that was supported by thermal analysis data. Moreover, the presence of the two peaks at (3430.74 cm^{-1}) and (1513.85 cm^{-1}) was indicative of the fact that the functional groups involved in the Cu-complex formation were $\text{C}=\text{O}$ and N-H [31]. On the other hand, the appearance of the two bands assigned for $\nu(\text{C}=\text{O})_{\beta\text{-lactam}}$ and $\nu(\text{C}=\text{O})_{\text{amide}} + \nu(\text{C}=\text{O})_{\text{ester}}$ frequencies at $1774\text{--}8$ cm^{-1} and $1674\text{--}7$ cm^{-1} , respectively, that were not shifted in both the ligand and the complex spectra may indicate that these groups were not involved in metal coordination [34]. The appearance of the band at 1615 cm^{-1} was reported to correspond to the complexation of the carboxylate with the metal(II) ions thus indicating coordination through that group [16]. The band observed between $1380\text{--}1385$ cm^{-1} was assigned to $\nu(\text{COO})_s$ in the complex suggesting unidentate binding of the carboxylate group to the metal [28]. Other bands observed for the formed metal complex at the region between $540\text{--}550$ cm^{-1} were attributed to $\nu(\text{Cu-O})$ [28]. As well, (M-N) stretching vibrations recorded between $450\text{--}490$ cm^{-1} range in the metal complex provided evidence that the tetrazole moiety was bonded to the metal ion through the nitrogen atom [16,27,31]. The non-ligand band in the regions of $430\text{--}460$ cm^{-1} and $510\text{--}520$ cm^{-1} were observed and were assigned to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ modes, respectively [33-36]. As well as the band at 428 cm^{-1} was reported to be indicative of the Cu-N stretching vibration [31]. This coordination between the beta-lactam ring through its N atom may be explained by the fact that N contained unshared electron pair that were potentially available for coordination with the

metal ion [29]. As well, it was reported that for cephalosporin, side chains may be involved in the coordination of hetero-cycles which may increase the stability of such formed metal complexes [29].

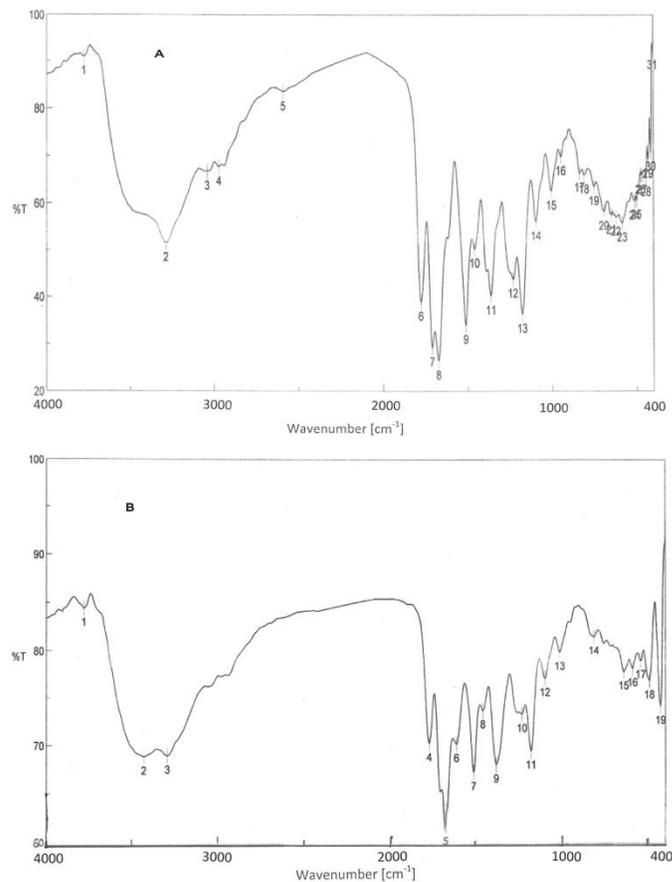


Figure 5. FTIR spectra for Cefoperazone sodium (A) and Cu- Cefoperazone complex (B)

The stability of the metal-ligand complex was investigated using thermal gravimetric analysis (TGA) of both the uncomplexed and complexed ligand under nitrogen atmosphere at the heating rate of $10^\circ\text{C}/\text{min}$. This technique (TGA) was reported to be helpful in indicating the presence of water or solvent molecules associated within the coordination sphere or in crystalline form [37]. The results of the TGA analysis indicated a (4.27%) weight loss at 90°C , which corresponded to the loss of two lattice water molecules from the composition of the hydrate. The present results are accordance with those reported by Fuliaş et al. [32, 38] who indicated that a weight loss within the range $50\text{--}150^\circ\text{C}$ was indicative of the loss of dehydration water molecule. At 160°C , a 6.41% weight loss was obtained which corresponded to the loss of -OH and H_2O coordinated molecules. This is in accordance with Singh and Singh [37] and Anacona and Osorio [27] findings which reported that the endothermic decomposition of cephalosporins within the $150\text{--}180^\circ\text{C}$ range was due to the loss of coordinated water molecule and at that stage no hydrate water or other solvent molecules were present. This thermal behavior was also reported to be characteristic of metal in cephalosporins in

which were metals were strongly bonded /coordinated with water these molecules and that this process of their release required such high temperatures [34]. Finally, the data indicate that there was a 83.02% weight loss obtained within range of (200-600°C), which may be attributed to the loss of ligand or its total decomposition [32, 34, 36]. Above 650°C, it was reported that there was no further weight change which was indicative that the remaining residue was the metal oxide [29, 34, 36, 38].

Analytical Applications

The optimized developed electrode was used to determine the amount of copper in pharmaceutical drug (Materna) which was labeled to contain 2 mg Cu/tablet. The results obtained were compared to the standard Dithizone spectrophotometric method for Cu(II) determination [22]. The potential of the sample measured by the electrode provided a Cu concentration = 3.00×10^{-5} mol L⁻¹ which was equivalent to 1.90638 mg/ tablet (accuracy 95.31%). Spectrophotometrically, the concentration of copper in the same sample was 3.10×10^{-5} mol L⁻¹ which was equivalent to 1.9699 mg/ tablet (98.49%). However, while the accuracy of spectrophotometric method was slightly higher than that

of the ion selective electrode, the developed ISE has a noted advantage over due to the simplicity of the technique and speed of detection.

Comparison of the proposed electrode with previously reported electrode

The performance a characteristic of the proposed sensor was compared with those of the best previously prepared copper sensors and the results are indicated in Table 3. From the interference study, it was obvious that the proposed sensor has no interference from many ions which cause serious interference for other similar electrodes. As well, the sensor has a wide working concentration range, and a comparably better lower limit of detection and a good response time. It has to be noted that the current sensor set-up did not employ a lipophilic additive yet its sensitivity depended upon the used plasticizer properties and offered a good selectivity and sensitivity relative to solid state ISE prepared by Pérez et al. [11]. As well, no synthesis of the ionophore was required and the produced sensor provided the largest slope (mV/decade), a good limit of detection, fast response time and a good accuracy and stability. Table (3).

Table 3. Analytical parameters for some reported copper-selective PVC-membrane sensors

<i>Ionophore</i>	<i>Detection limit (M)</i>	<i>Linear range (M)</i>	<i>Slope (mV/decade)</i>	<i>Response</i>	<i>Stability</i>	<i>pH range</i>	<i>Ref.</i>
Azathioether crowns containing a 1,10-phenanthroline sub-unit	8.0×10^{-6}	$1 \times 10^{-5} - 1 \times 10^{-1}$	29.4	15 s	3 months	2.5-5.5	[25]
2-acetylpyridine-(1 <i>R</i>)-(-)-fenchone azine ligand	4.0×10^{-6}	$1.0 \times 10^{-5} - 1.0 \times 10^{-1}$	30.0	≤20s	3 months	4.0-5.0 & 6.0-10.0	[4]
1, 8-Bis(2-hydroxynaphthalaldimino)3, 6-dioxaoctane	1.0×10^{-6}	$3.3 \times 10^{-6} - 1.0 \times 10^{-2}$	29.0	10-15 s	21 days	4.0-8.0	[6]
2-mercaptobenzoxazole	2.0×10^{-6}	$5.0 \times 10^{-6} - 1.6 \times 10^{-2}$	29.2	<10 s	2 months	4-6	[26]
Cefaroparzone	4.0×10^{-7}	$1 \times 10^{-6} - 1 \times 10^{-2}$	31.01	20-30 s	2 months	4.0-7.0	this study

Conclusion

In the present work, a new copper (II) ion-selective polymeric membrane electrode based on Cefoperazone as a neutral carrier was successfully developed. The coated graphite electrode exhibited linear response with Nernstian slope of 31.01 mV per decade within the copper ion concentration range of $1.0 \times 10^{-6} - 1.0 \times 10^{-2}$ mol L⁻¹. The developed sensor had a lower detection limit of 4.0×10^{-7} mol L⁻¹. The electrode was found to be selective for Cu(II) ions over some common ions such as Hg²⁺, Pb²⁺, Ca²⁺, Mn²⁺, Co²⁺, Cd²⁺, Ni²⁺ and Al³⁺ and this was affirmed by the calculation of their potentiometric selectivity coefficients. The electrode is suitable for the determination of Cu (II) in

aqueous solutions over a wide pH range (4.0-7.0). The analytical utility of the proposed electrode was demonstrated and its application for the determination of copper in real samples and in some pharmaceutical formulations was reported.

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