RESEARCH ARTICLE

New Carbon Paste Sensor for the Determination of Ciprofloxacin in the Pharmaceutical Preparations, Serum and Urine

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ABSTRACT

A quick, novel and highly accurate sensor with superior electrochemical properties have been developed to measure ciprofloxacin in pharmaceutical preparations and human fluids. Three carbon paste sensors for ciprofloxacin (CPF) were produced using the ionophore molecule ciprofloxacin-methyl orange (CPF-MO) in combination with three different plasticizers: di-butyl phthalate (DBPH), di-butyl phosphate (DBP), and tris (2-ethylhexyl)phosphate (TEHP). The slopes of sensors A, B, and C were 59.84, 44.67, and 50.49 mV/decade, respectively. The linear range was 5×10^{-5} to 1×10^{-2} M, with detection limits of 4.6×10^{-5}, 4.4×10^{-5}, and 4.9×10^{-5} M, respectively, and a lifetime of 58, 19, and 21 days. Because sensor A produces the best results, pharmaceutical and human fluids were applied using this sensor; the recovery percentages were 98, 97, 102, 95, and 97 for CPF standard, Bactiflox tablets 500 mg, ciprocin eye drop 0.3%, urine, and serum, respectively, using potential techniques.

Keywords: Carbon past sensor, Ciprofloxacin (CPF), Human fluids Methyl orange (MO), Pharmaceutical preparations.

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INTRODUCTION

Ciprofloxacin (CPF) Figure 1 is a crystalline powder with pale yellow color and slightly hygroscopic, it has a molecular formula of $C_{17}H_{18}FN_3O_3$ HCl and a molecular weight of 367.8.[1,2] CPF is a fluoroquinolone antibiotic that is used to treat a variety of bacteria.[3] This category comprises infections of the bones and joints, the belly, some types of diarrheal disease, the respiratory system, the skin, typhoid fever, and the urinary and urinary tract. It is a fluoroquinolone of the second generation with a broad spectrum of activity that often kills germs.[4] The determination of ciprofloxacin has been accomplished using a variety of analytical techniques, including ultraviolet–spectrophotometry,[5] liquid chromatography,[6] Ultraviolet-visible (UV-Vis) method,[7] and High-performance liquid chromatography (HPLC).[8-10] As with any other potentiometric sensor, the ion-selective cell can be modeled schematically as a galvanic half-cell: internal contact metal membrane solution (Sl). Similarly, the galvanic cell (with ISE) can be represented as follows: ISE solution metal (S2) liquid-junction (salt bridge) reference electrode.[11]

As illustrated in Figure 2, a novel sensor class of carbon paste sensors (CPEs) has been applied widely as potentiometric research in this area to their unmatched features, which include extraordinarily low price, ease of processing, environmental friendliness, stable response, low level determination of the solute, lack of internal solution, and potential to connect a fresh surface sensor after each utilization.[12] The purpose of this effort is to build a new carbon paste sensor that is based

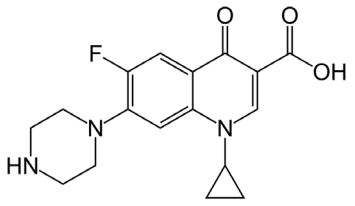

Figure 1: Chemical structure of CPF.

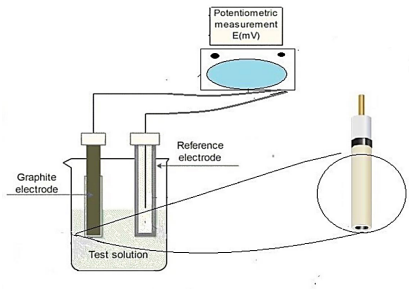

Figure 2: A schematic depiction of the carbon paste sensor cell.[12]

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on an ionophore's dissolution (CPF-MO) in a low-permeable plasticizer and the addition of graphite powder as a supporting material. The developed sensors were utilized to determine the CPF content of pharmacological dosage forms and human bodily fluids.

MATERIALS AND REAGENTS

Analytical or pharmacopeia-grade substances were employed in this experiment. The solution was prepared using distilled water. Ciprofloxacin hydrochloride (CPF) was bought from Sigma-Aldrich, and the pharmaceutical formulations ciprofloxacin (bactaflox tablets) and (ciprocin eye drop) were obtained from Acino (Switzerland) and Eipico, Egypt, respectively. Fluka provided tris (2-ethyl hexyl) phosphate (TEHP) ($C_{24}H_{51}O_4P$) with a purity of 97%, di-butyl phthalate (DBPH) ($C_{16}H_{22}O_4$) with a purity of 99%, and di-butyl phosphate ($C_8H_{19}PO_4$) with a purity of 99%. We created a 0.01 M stock solution of (LiCl, KCl, NaCl, $MgCl_2$, $CaCl_2$, $ZnCl_2$, $AlCl_3$, $FeCl_3$, and $CrCl_3$). Additional diluted solutions were generated by diluting the stock solutions.

Preparation of Complex (Ionophore)

The development of the ciprofloxacin carbon paste sensor is dependent on the ionophore compound ciprofloxacin-methyl orange (CPF-MO). CPF-MO was prepared as an complex by swirling 100 mL of 0.01 M CPF solution with 100 mL of 0.01 M MO solution. Filtration, washing with millipore water, and drying for one day were used to remove the precipitate.[11]

Preparation of the Carbon Paste Sensor

Carbon paste sensors were created via combining 0.51 gm graphite powder, 0.45 gm plasticizer, and 0.04 gm CPF-MO until a uniformly wetted paste was obtained. As shown in Figure 3, the mixture was injected into the end of the syringe (1-mL). A silver wire was used to make electrical contact with the carbon paste. The carbon paste was smeared over paper to obtain a glossy look and immediately employed for potentiometric readings without preconditioning.[12,13]

Calibration Curve

The constructed sensor's calibration curve was established by transferring a suitable amount of the aqueous CPF solution (1×10^{-6} – 1×10^{-2} M), followed by immersing the CPF membrane sensor and reference sensor in the same solution and recording readings after potential stabilization. Between potentials and CPF concentrations, a calibration curve was established.

Selectivity

The separate solution method (SSM) and the match potential methods were used to determine the selectivity coefficient of potentiometric sensors toward diverse species (MPM). The following equation was utilized in the SSM method:[14]

$$K^{pot}_{A,B} = a_A^{(1 - zA/zB)} e^{(EB - EA)\, zA\, F/(R\, T)}$$

Where E_A denotes the drug's potential and EB denotes the interfering ions.

While the MPM approach employed the following equation:

$$K^{pot}_{A,B} = (a_A - a_A)/a_B$$

Preparation of Standard Solution

In distilled water, stock solutions of LiCl, KCl, NaCl, $ZnCl_2$, $CaCl_2$, $Mg(NO_3)_2.6H_2O$, $FeCl_3.6H_2O$, $AlCl_3$, and $CrCl_3.6H_2O$ were made. Subsequent dilutions of the stock solutions produced more diluted solutions. A 0.01 M CPF standard

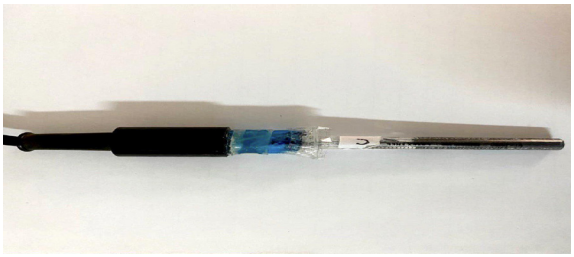

Figure 3: A Carbon Paste sensor.

Table 1: The influence of plasticizers on the CPF sensor's characteristics

Parameters	*CPF*		
	DBPH	*TEHP*	*DBP*
Slope (mV/decade)	59.84	50.49	44.67
linear range (M)	5×10^{-5} -1×10^{-2}	5×10^{-5} -1×10^{-2}	5×10^{-5} -1×10^{-2}
pH	3–8	4–8	4–8
Life time (days)	58	21	19
Response time (min.) at 10^{-2} and at 10-6 M	0.6 , 2.7	2.6 5.8	1.2 2.8
LOD (M)	4.6×10-5	4.9×10-5	4.4×10-5
Correlation coefficient (R)	0.9984	0.9922	0.9990

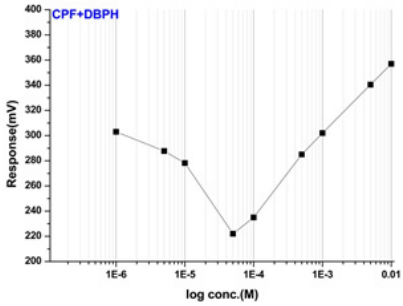

Figure 4: Calibration curve of (CPF-MO/DBPH) first sensor.

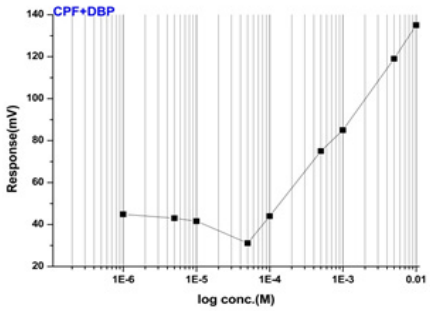

Figure 5: Calibration curve of (CPF-MO/DBP) second sensor.

Table 2: The measured selectivity coefficient for various interfering ions with a (CPF-MO/DBPH) sensor.

Conc.(M)	$K_{A,B}$								
	Na^{+}	K^{+}	Li^{+}	Ca^{+2}	Mg^{+2}	Zn^{+2}	Al^{+3}	Cr^{+3}	Fe^{+3}
1×10^{-2}	0.04	0.05	0.07	1.1×10^{-4}	1.4×10^{-4}	2.4×10^{-4}	2.2×10^{-5}	3.1×10^{-5}	2.3×10^{-5}
5×10^{-3}	0.02	0.06	0.04	1.3×10^{-4}	1.2×10^{-4}	2.3×10^{-4}	2.0×10^{-5}	3.5×10^{-5}	2.9×10^{-5}
1×10^{-3}	0.03	0.02	0.04	1.6×10^{-4}	1.6×10^{-4}	2.1×10^{-4}	2.3×10^{-5}	3.4×10^{-5}	3.7×10^{-5}
5×10^{-4}	0.06	0.08	0.07	1.7×10^{-4}	2.3×10^{-4}	2.5×10^{-4}	2.4×10^{-5}	2.3×10^{-5}	2.8×10^{-5}
1×10^{-4}	0.09	0.08	0.09	2.2×10^{-4}	2.4×10^{-4}	2.6×10^{-4}	2.8×10^{-5}	2.7×10^{-5}	2.6×10^{-5}
5×10^{-5}	0.16	0.10	0.11	2.5×10^{-4}	2.8×10^{-4}	2.8×10^{-4}	3.6×10^{-5}	3.7×10^{-5}	3.8×10^{-5}
1×10^{-5}	0.21	0.29	0.27	2.9×10^{-4}	3.1×10^{-4}	2.9×10^{-4}	4.9×10^{-5}	4.5×10^{-5}	4.7×10^{-5}
5×10^{-6}	0.35	0.33	0.34	3.2×10^{-4}	3.2×10^{-4}	3.2×10^{-4}	8.8×10^{-5}	7.2×10^{-5}	5.4×10^{-5}
1×10^{-6}	0.41	0.36	0.39	3.5×10^{-4}	5.5×10^{-4}	3.4×10^{-4}	6.7×10^{-5}	7.8×10^{-5}	5.7×10^{-5}

Table 3: Direct approach for estimating pharmaceutical applications and human fluids.

Drug	*Original conc.(M)*	*Found conc.(M)*	*RSD% n=3*	*RC%*	*RE%*
pure of ciprofloxacin	1×10^{-4}	1.03×10^{-4}	0.952	103.0	3.0
Bactiflox (500 mg)	1×10^{-4}	1.02×10^{-4}	0.564	102.0	2.0
Ciprocin (0.3% eye drop)	1×10^{-4}	0.96×10^{-4}	0.531	106.0	-4.0
Urine	1×10^{-4}	1.06×10^{-4}	0.638	106.0	6.0
Plasma	1×10^{-4}	1.04×10^{-4}	0.987	104.0	4.0

Table 4: Standard potentiometric method for estimating the standard, medicinal application, and human fluids.

Drug	*Original conc.(M)*	*Found conc.(M)*	*RSD% n= 3*	*RC%*	*RE%*
pure of ciprofloxacin	1×10-4	0.98×10-4	0.432	98.0	-2.0
Bactiflox (500 mg)	1×10-4	0.97×10-4	0.418	97.0	-3.0
Ciprocin (0.3% eye drop)	1×10-4	1.02×10-4	0.322	102.0	2.0
Urine	1×10-4	0.95×10-4	0.876	95.0	-5.0
plasma	1×10-4	0.97×10-4	0.788	97.0	-3.0

Table 5: Volume at the intercept with the X axis and calculation of the concentration C_U(M) using the (MSA) method for the (CPF-MO/DBPH) sensor.

Drug	*Original Conc. (M)*	*V(ml)at intercept*	*CU (M)*	*RC%*	*RE%*
pure of ciprofloxacin	1.0×10^{-4}	0.0990	0.99×10^{-4}	99.0	-1.0
Bactiflox (500 mg)	1.0×10^{-4}	0.0970	0.98×10^{-4}	98.0	-2.0
Ciprocin (0.3% eye drop)	1.0×10^{-4}	0.0980	0.99×10^{-4}	99.0	-1.0
Urine	1.0×10^{-4}	0.0950	0.96×10^{-4}	96.0	-4.0
plasma	1.0×10^{-4}	0.0970	0.98×10^{-4}	98.0	-2.0

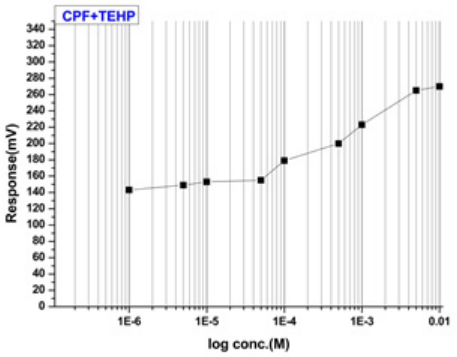

Figure 6: Calibration curve of (CPF-MO/TEHP) third sensor.

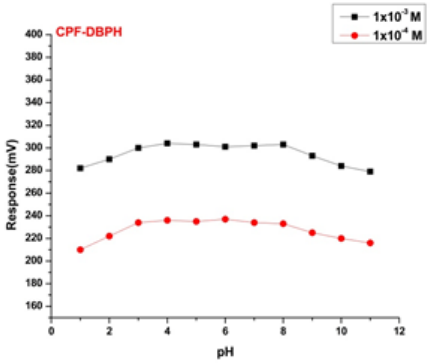

Figure 7: Effect of pH for (CPF-MO/DBPH) sensor.

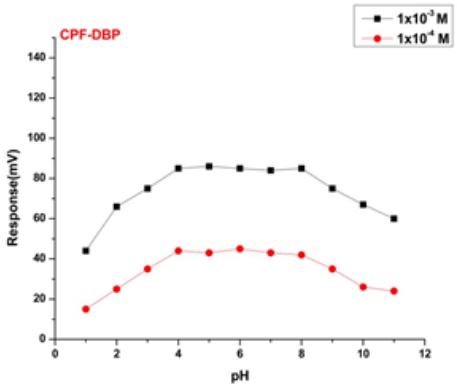

Figure 8: Effect of pH for (CPF-MO/DBP) sensor.

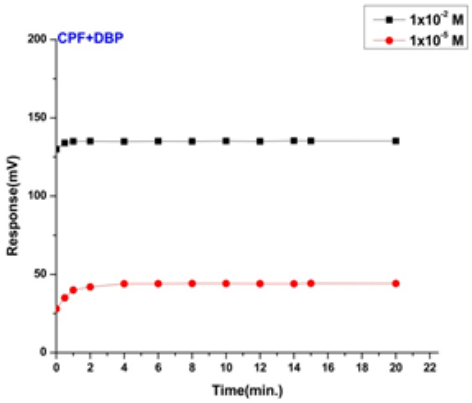

Figure 11: Response time of (CPF-MO/DBP) sensor.

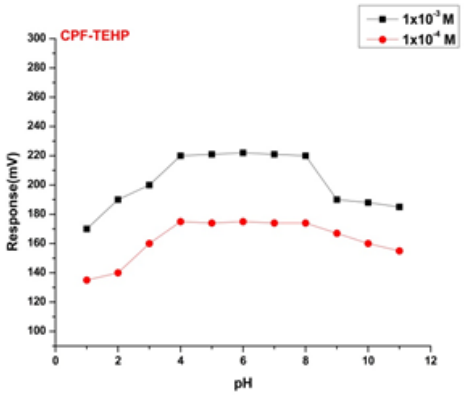

Figure 9: Effect of pH for (CPF-MO/TEHP) sensor.

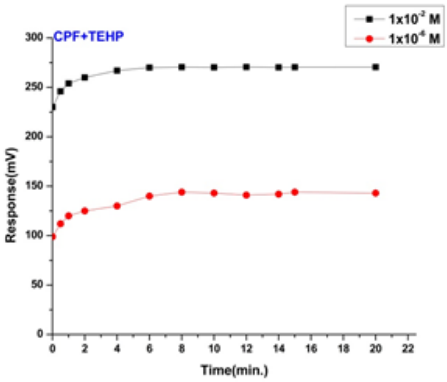

Figure 12: Response time of (CPF-MO/TEHP) sensor.

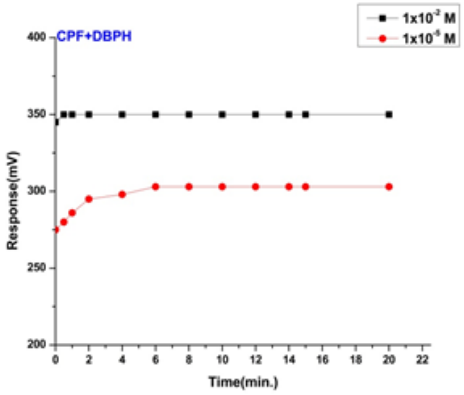

Figure 10: Response time of (CPF-MO/DBPH) sensor.

solution was made by dissolving 0.1269 g standard into the solution and diluting it to a volume of 25 mL. The remainder of the CPF standard solutions was made by further diluting the stock solution.

Sample Analysis

The direct method, which involved administering a sample with concentrations ranging from 1.0×10^{-6} to 1.0×10^{-2} M and measuring the potential to construct the calibration curve. The voltage was applied after each increment and the CPF concentration in a drug sample was calculated using the conventional addition method. 0.1-mL of 1×10^{-2} M CPF was introduced to 10 mL of a sample containing varying concentrations of 1×10^{-4} M CPF.

CPF Determination in Human Fluids

In a 25 mL volumetric flask, added 2.5 mL urine and serum filled with distilled water and subjected to potentiometric analysis.[15]

RESULTS AND DISCUSSION

Influence of Plasticizers

Three plasticizers were used to explore the effect of plasticizers on the response of the CPF sensor: DBPH, tris-(2-ethylhexyl) phosphate (TEHP), and diastolic blood pressure (DBP), as depicted in Figures 4 to 6. To optimize the prepared sensor's selectivity and sensitivity, plasticizers were used to dissolve the complex and to alter the sensor's permittivity and ion-exchanger mobility.[14]

Influence of pH

The influence of pH on the sensor's potential was examined by measuring the cell's potential in CPF solutions at 1×10^{-4} and 1×10^{-3} M concentrations. As demonstrated in Figures 7 to 9,

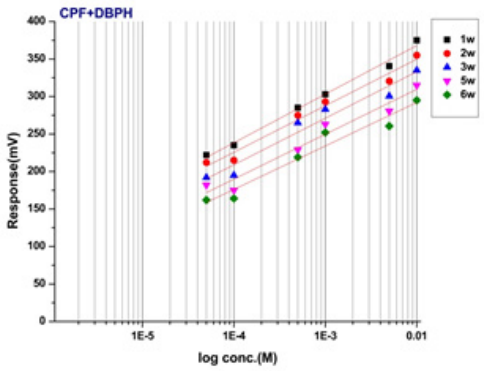

Figure 13: Life time of (CPF-MO/DBPH) sensor.

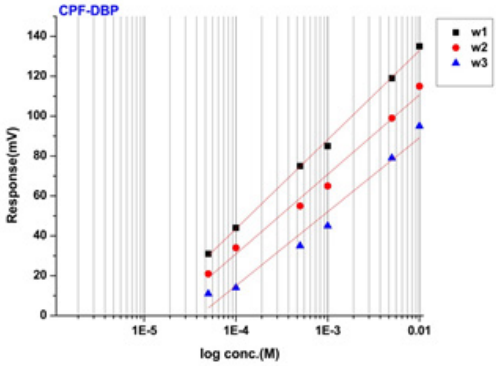

Figure 14: Life time of (CPF-MO/DBP) sensor.

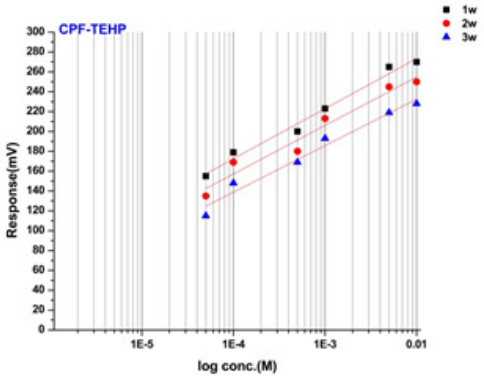

Figure 15: Life time of (CPF-MO/THEP) sensor.

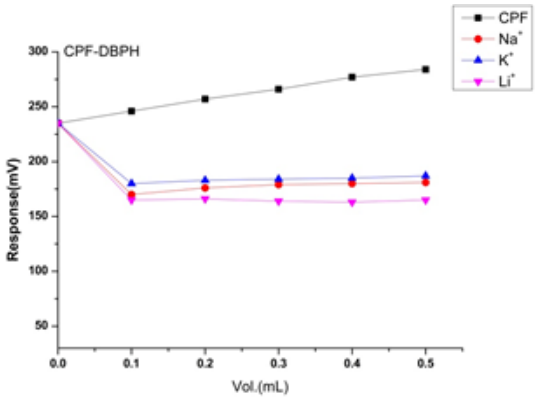

Figure 16: Selectivity for (CPF-MO/DBPH) monocations as determined using the match potential approach.

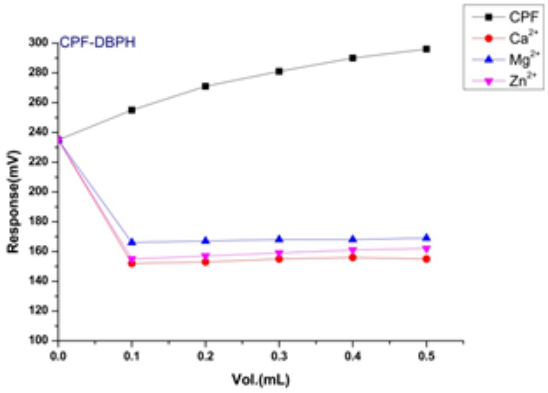

Figure 17: Selectivity for (CPF-MO/DBPH) di-cations as determined by the match potential approach.

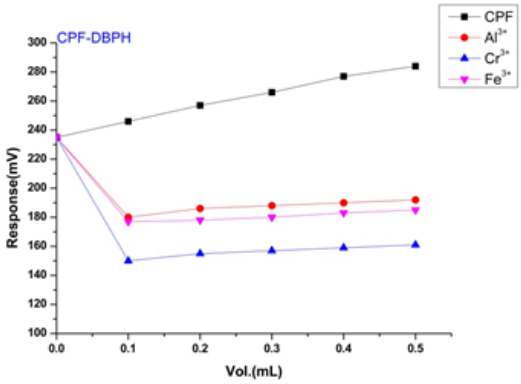

Figure 18: Selectivity for (CPF-MO/DBPH) tri-cations as determined using the match potential approach.

the pH was changed as described in Table 1 by adding a few drops of 0.1 M HCl or NaOH, the CPF sensor was respond to pH fluctuations in the range of 3 to 8.

Response Time and Lifetime

The sensor response time was defined as the time required for the CPE and reference electrode to reach a stable potential after immersion in 1×10^{-6} and 1×10^{-2} M of CPF solution, respectively, as illustrated in Figures 10 to 12. The sensor's lifetime was determined after five weeks of operation (Figures 13-15). The slope diminishes and the detection limit increases after this time interval, and the calibration curve is created using a succession of standard solutions ranging in concentration from 1×10-6 to 1×10-2 M of CPF[16,17] after immersion in 1×10^{-6} and 1×10^{-2} M of CPF solution, respectively, as illustrated in Figures 12 to 14. The sensor's lifetime was determined after five weeks of operation. The slope diminishes and the detection limit increases after this time interval, and the calibration curve is created using a succession of standard solutions ranging in concentration from 1×10^{-6} to 1×10^{-2} M of CPF.[16,17]

As a result of the obtained data, it was observed that the slope of the (CPF-MO/DBPH) sensor response gradually decreases from (59.84) mV/decade to (49.12) mV/decade. These results demonstrate that the (CPF-MO/DBPH) sensor is suitable for use six weeks after manufacturing with acceptable efficiency. After this time period, the (CPF-MO/DBPH) sensor becomes less sensitive to CPF, possibly due to the slow leaching of the complex from the paste into the external solution.[18]

Selectivity

The interferences of several inorganic cations were investigated using the separate solution method and the match potential method. These cations included Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, Al^{3+}, Cr^{3+}, and Fe^{3+}. The values of the selectivity coefficients are shown in (Figures 18) and Table 2. Because the drug solution and the interfering cation have the same potential at 5 or 10 mV, the selectivity coefficients cannot be established (Figures 16 to 18).

Monovalent cations have a higher selectivity coefficient than divalent and trivalent cations, which may be owing to differences in permeability, mobility and ionic size. The following is the order of selectivity.

trivalent < divalent < monovalent

CPF Application in Pharmaceutical Samples and Human Fluids

The proposed sensor was successfully used to determine CPF in pharmaceutical samples such as tablets and eye drops, as well as human fluids such as plasma and urine using the direct methodology and standard addition method; the acquired findings are reported in Tables 3 to 5.

The CPF concentration was calculated using the standard addition method by adding 0.1 mL of 1×10^{-2} M CPF to 10 mL of 1×10^{-4} M. Following each addition, the following equation (18-20) was used to record the change in potential readings:

$$C_x = C_sV_s / [(V_x + V_s) \times 10^{\Delta E/s} \_ V_x]$$

In compared to the standard addition method, the multi standard addition approach produces more precise and accurate results, as illustrated in the table above. This could be because the normal work style, in comparison to the multi standard addition method, eliminates the dilution component during solution preparation.[19-21] As a result, errors are reduced.

CONCLUSION

The suggested CPF-sensor enables quantification of CPF medicine in bulk CPF, pharmaceutical samples such as tablets and ocular drops, and human fluids such as plasma and urine. It was a clever, precise, quick, and cost-effective maneuver. Over a number of weeks, the sensor has demonstrated exceptional performance.

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