RESEARCH ARTICLE

Novel Potentiometric Sensor for Estimation of the Moxifloxacin in the Pharmaceutical Samples, Urine, and Serum

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Received: 10th October, 2022; Revised: 21st November, 2022; Accepted: 09th December, 2022; Available Online: 25th December, 2022

ABSTRACT

An easy, simple and ecofriendly process for the estimation of moxifloxacin (MFN) in the pharmaceutical samples, serum and blood. The prepared sensors contained moxifloxacin–bromophenol blue as ionphore and, tris(2-ethylhexyl) phosphate, di-butyl phthalate and di-butyl phosphate as plasticizers. The electrodes based on di-n-butyl phthalate (DBPH), Tris (2-ethylhexyl) phosphate (TEHP), and di-butyl phosphate (DBP), gave slope 44.50, 56.86 and 46.38 mV/decade, respectively. The linear concentrations were 1×10^{-5} - 1×10^{-2}, 5×10^{-5}- 1×10^{-2} and 5×10^{-5} - 1×10^{-2} M with detection limits of 9.0×10^{-6}, 4.7×10^{-5} and 4.9×10^{-5} M and a lifetime of 17, 39 and 12 days for electrodes based on DBPH, TEHP, and DBP, respectively. The best electrode was TEHP which gave the best results. The sensor that based on TEHP as plasticizer was better response and stability, it was used to estimate the moxifloxacin in pharmaceutical samples using single and multi-standard addition potentiometry.

Keywords: Bromophenol blue, Human fluids, Moxifloxacin, Pharmaceutical preparations, Sensor.

International Journal of Drug Delivery Technology (2022); DOI: 10.25258/ijddt.12.4.31

How to cite this article: Abrahem SA, Ahmad SM, Al-Phalahy BA, Novel Potentiometric Sensor for Estimation of the Moxifloxacin in the Pharmaceutical Samples, Urine, and Serum. International Journal of Drug Delivery Technology. 2022;12(4):1663-1668.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Moxifloxacin (MFN) which has the empirical formula ($C_{21}H_{24}FN_3O_4$), is (1-cyclopropyl-6-fluoro-1,4- dihydro-8-methoxy-7-[(4aS,7aS)-octahydro-6H-pyrrolo [3,4-b]pyridin-6-yl]4-oxo-3 quinolone carboxylic acid) (Figure 1).[1] It is an advanced-generation, 8-methoxyquinolone derivate of fluoroquinolone antibacterial agent that is synthetic. It was discovered in 1999.[2,3] Moxifloxacin mono-hydrochloride is a slightly yellow to yellow crystalline substance and, sold under the brand name avelox among others, is an antibiotic used to treat a number of bacterial infections.[4] Different analytical processes have been developed to estimate moxifloxacin in pharmaceutical samples, such as spectrophotometry[5] and High-performance liquid chromatography (HPLC)[6,7] methods. The applications of ISEs continue to be important in pharmaceutical analysis because these sensors offer the advantages of simple, operation, easy and low cost.[8] The aim of this research, new sensor that based on (moxifloxacin, bromophenol blue) as ion-pair in PVC plasticized with different plasticizers were prepared for the estimation of moxifloxacin in pharmaceutical samples and human fluids.

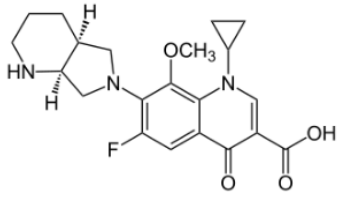

Figure 1: Structure formula of moxifloxacin.

MATERIAL AND METHODS

Equipment

An expandable ion analyzer (Orion model EA-940, USA), a pH meter (Professional Bench-top pH meter BP3001, China), Silver-silver chloride wire and saturated calomel electrode (reference electrode-Gallenkamp, USA) were used in this research. The assembly of the electrochemical cell as shown in the Figure 2.

Reagents and Solutions

All of the substances utilized in this study were of analytical quality. For the production of the solution, millipore water was employed. Standard moxifloxacin was acquired from

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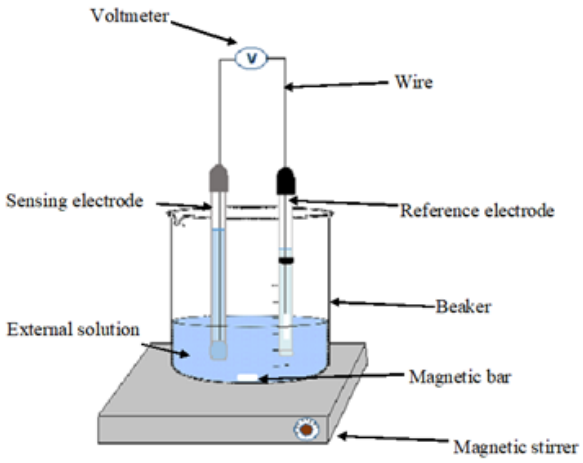

Figure 2: Diagram of ISE cell.[9]

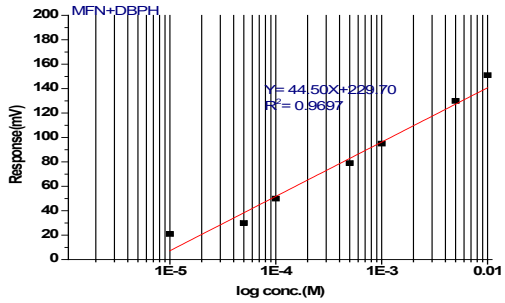

Figure 3: Linear curve of sensor A

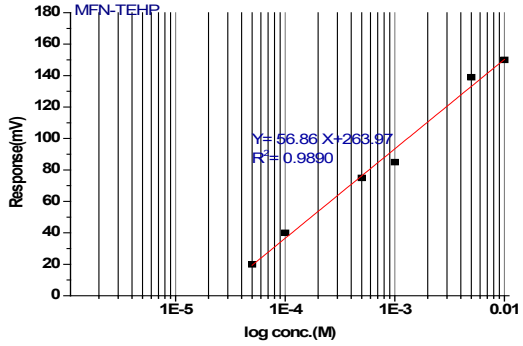

Figure 4: Iinear curve of sensor B

Sigma-Aldrich. India's Cipla Ltd supplied the pharmaceutical formulations moxifloxacin tablets and ocular drops. Bromophenol blue 98% (BPB) was supplied by Fluka, di-butylphthalate 99% (DBPH), tris (2-ethylhexyl)phosphate 99% (TEHP), and di-butyl phosphate 98% (DBP) were supplied by Ferak, and poly(vinyl) chloride and tetrahydrofuran were obtained by Fluka, AG, Switzerland LiCl, KCl, NaCl, $MgCl_2$, $CaCl_2$, ZnC_{l2}, $AlCl_3$, $FeCl_3$, and $CrCl_3$ ($1*10^{-2}$) M stock solution was created. The stock solutions were subsequently diluted to produce further diluted solutions.

Procedure

Synthesis of Ion Pair

Preparation of a moxifloxacin sensor utilizing moxifloxacin-bromophenol blue (MFN-BPB) as an ion pair. The (MFN-BPB) ionfore was prepared by stirring together 100 mL of a 0.01M solution of MFN and 100 mL of a 0.01 M solution of BPB. The formed precipitate was further filtered, rinsed with millipore water, and dried at 60°C.[10]

Preparation of Sensor

Davis *et al.*[11] report the hardening process of moxifloxacin into the matrix sensor. Add 0.040 g of the complex, 0.360 g of plasticizer, and 0.17 g of polyvinyl chloride as support, then add 7 mL of tetra hydro furan with stirring until the formation of the viscous solution.

Calibration Curve

The calibration of the electrode was preceded using standard solutions of MFN ranging from (1×10^{-2}-1×10^{-6}) M. The sequence of measurements was carried out from low concentration to a higher one. The measured potential was plotted against the logarithm of MFN concentration (Figure 3-5).[12]

Estimation of Selectivity Coefficient Factor

A SSM[13] was used for the $K_{A,B}$ measurement, which calculated according to equation (1):

$$\log K^{pot}_{A,B}=(E_B-E_A)/S+(1-z_A/z_B)\log a_A \quad \ldots\ldots\ldots\ldots\ldots\ldots(1)$$

E_A, E_B; z_A, z_B; and a_A, are the potentials, charge numbers, and activities for the primary A ion, respectively, at $a_A = a_B$.

The $K_{A,B}$ were measured by the MPM[14,15] according to equation(2):

$$K^{pot}_{A,B}=a_A/(a_B)^{zA/zB} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(2)$$

Table 1: Plasticizer effect on the parameter of MFN sensor.

Parameters	*DBPH*	*TEHP*	*DBP*
Slope (mV/decade)	44.50	56.86	46.38
LOD (M)	9.0×10^{-6}	4.7×10^{-5}	4.9×10^{-5}
Linear conc. (M)	1×10^{-5} - 1×10^{-2}	5×10^{-5}- 1×10^{-2}	5×10^{-5} - 1×10^{-2}
Response time(min.)	0.7 at $1*10^{-2}$ 3.2 at $1*10^{-6}$	1.5 at $1*10^{-2}$ 3.6 at$1*10^{-6}$	1.3 at $1*10^{-2}$ 5.8 at $1*10^{-6}$
Life time (day)	17	39	12
pH	4–7	4–8	5–7
R	0.9847	0.9945	0.9958

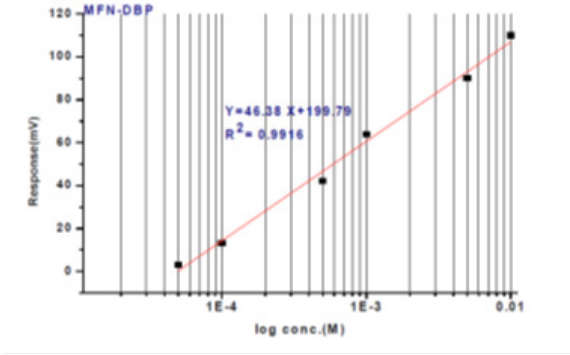

Figure 5: Linear curve of sensor C

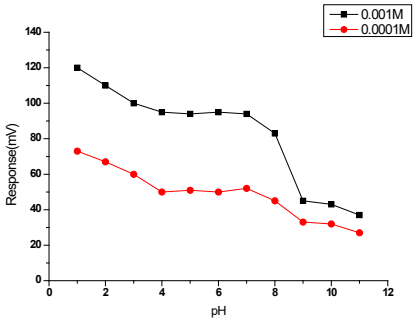

Figure 6: Effect of pH for A sensor

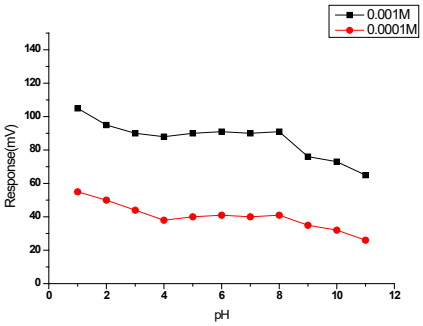

Figure 7: Effect of pH for B sensor

Determination of MFN in Human Fluids

Samples of human fluids were extracted from a healthy person, and 0.25 mL of MFN standard was added to 25 mL volumetric flask and completed to the mark with millipore water, before the potentiometric analysis.[16]

RESULT AND DISCUSION

New sensors were prepared for the estimation of MFN in the pharmaceutical samples, serum and urine, the characterization of these electrodes based on the ion-pair using different plasticizers were described. As depicted in the images, three plasticizers were used to study the MFN sensors' reaction to plasticizers: DBPH, tris (2-ethylhexyl)phosphate, and di-butyl phosphate (3,4 and 5). It was necessary to add plasticizers to dissolve the ion-exchanger and tune sensors permittivity and mobility of the complex to achieve a sensor with the optimum selectivity and sensitivity (Table 1).

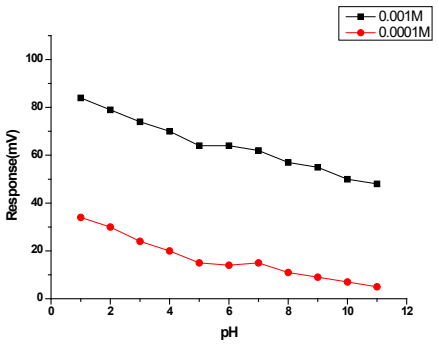

Figure 8: Effect of pH for C sensor

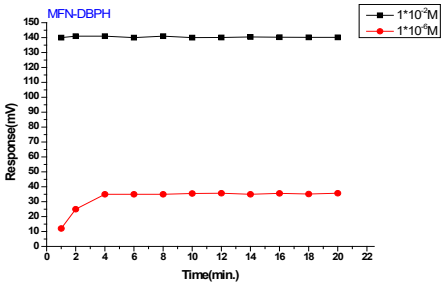

Figure 9: Response time of sensor A.

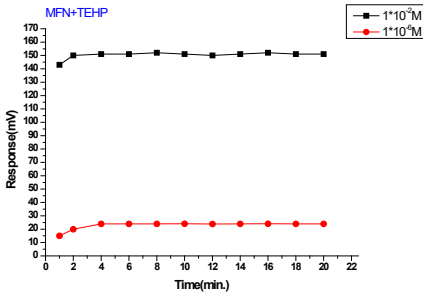

Figure 10: Response time of sensor B.

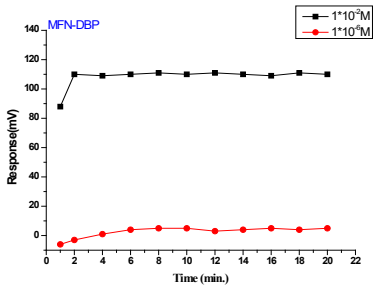

Figure 11: Response time of sensor C.

pH Effect

The effect of pH on the sensor's potential was determined by measuring the cell's potential at MFN concentrations of $1*10^{-4}$ and $1*10^{-3}$ M. Several drops of (0.1 M) HCl or NaOH were added to alter the pH of the solution. At the low pH the potential of the electrodes increased, this is because the electrode was

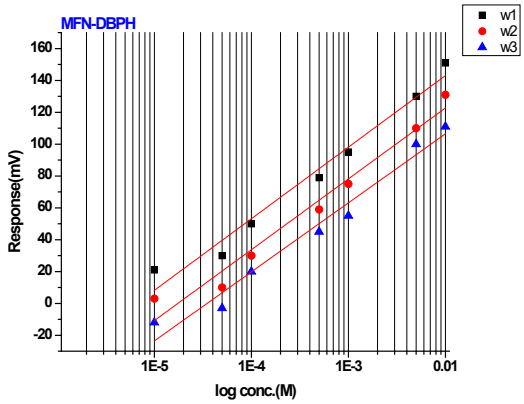

Figure 12: Lifetime of sensor A.

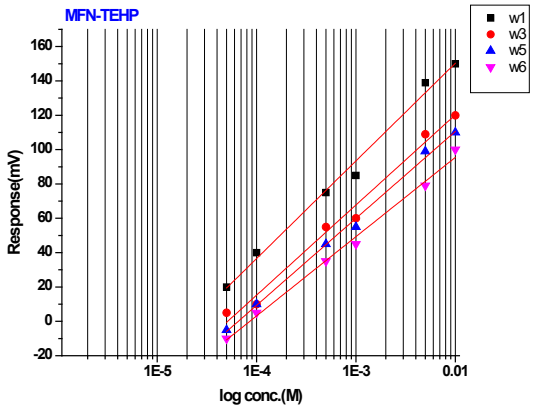

Figure 13: Lifetime of sensor B.

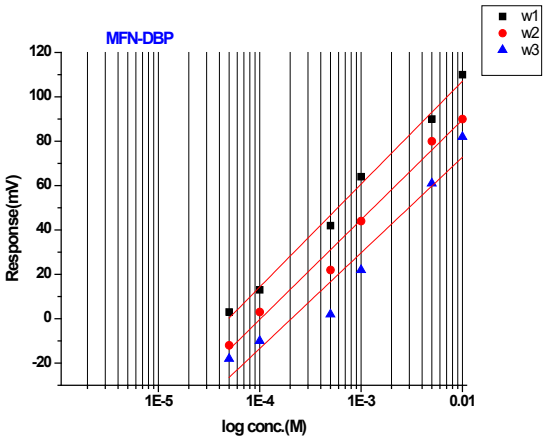

Figure 14: Lifetime of sensor C.

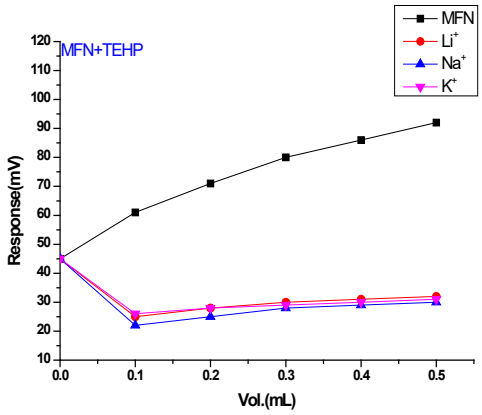

Figure 15: Selectivity of electrode B for mono-cations by MPM.

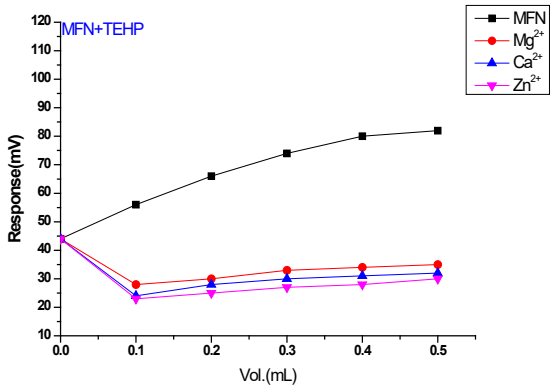

Figure 16: Selectivity of electrode B for di-cations by MPM.

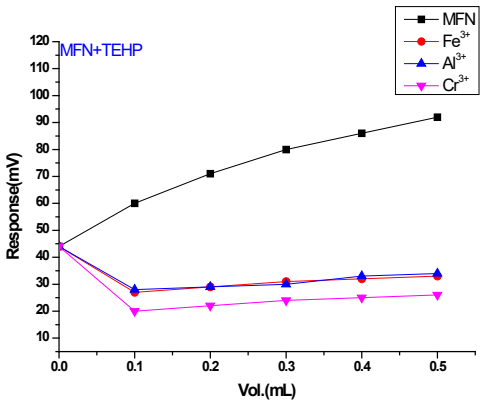

Figure 17: Selectivity of electrode B for tri-cations by MPM.

respond to the H^+ ions. While at high pH levels the potential of the electrodes drops sharply because of the poisoning of membrane due to the formation of white precipitation.[17] From Figures 6-8 it can notice that MFN sensor does not respond to pH changes in the range (5–7).

Response Time and Lifetime

After immersing the prepared sensor and the reference sensor in $1*10^{-6}$ and $1*10^{-2}$ M of MFN solution, the proposed electrodes attained stable potentials after 0.7, 1.5, and 1.3 minutes at $1*10^{-2}$ M and after 3.2, 3.6, and 5.8 minutes at ($1*10^{-6}$ M) for electrodes A, B, and C, respectively. The results were represented in Figures (9-11). The lifetime of the three electrodes were measured and found that it was 17, 39 and 12 day for electrode A, B and C, respectively. After this time the slope tends to decrease and the LOD tends to increase because of the leaching of ion pair from the membrane to the external solution.[18] The results were plotted in Figures 12-14.

Table 2: Selectivity coefficient of sensor B.

Conc. (M)	$K_{A,B}$								
	Li^{+}	Na^{+}	K^{+}	Ca^{2+}	Mg^{2+}	Zn^{2+}	Al^{3+}	Fe^{3+}	Cr^{3+}
$1*10^{-2}$	7.13×10^{-3}	4.77×10^{-3}	5.67×10^{-3}	5.67×10^{-4}	5.80×10^{-3}	6.21×10^{-3}	2.44×10^{-3}	3.67×10^{-3}	7.90×10^{-3}
$5*10^{-3}$	1.67×10^{-3}	3.11×10^{-3}	4.32×10^{-3}	3.35×10^{-4}	4.77×10^{-3}	5.17×10^{-3}	3.99×10^{-3}	4.75×10^{-3}	8.61×10^{-3}
$1*10^{-3}$	2.33×10^{-3}	1.87×10^{-3}	2.45×10^{-3}	2.74×10^{-4}	3.99×10^{-3}	4.99×10^{-3}	4.81×10^{-3}	5.87×10^{-3}	9.76×10^{-3}
$5*10^{-4}$	4.58×10^{-2}	3.67×10^{-2}	3.69×10^{-2}	1.89×10^{-2}	5.67×10^{-2}	3.53×10^{-2}	5.83×10^{-4}	9.88×10^{-4}	7.89×10^{-4}
$1*10^{-4}$	9.35×10^{-2}	5.32×10^{-2}	5.97×10^{-2}	4.78×10^{-2}	7.99×10^{-2}	2.18×10^{-2}	6.79×10^{-4}	7.83×10^{-4}	6.15×10^{-4}
$5*10^{-5}$	2.55×10^{-2}	7.81×10^{-2}	7.45×10^{-2}	6.69×10^{-2}	8.38×10^{-2}	2.01×10^{-2}	4.39×10^{-4}	5.19×10^{-4}	4.69×10^{-4}
$1*10^{-5}$	1.38×10^{-2}	8.99×10^{-2}	9.14×10^{-2}	8.74×10^{-1}	9.59×10^{-1}	1.93×10^{-1}	6.72×10^{-5}	3.66×10^{-5}	8.23×10^{-5}
$1*10^{-6}$	1.14×10^{-1}	2.56×10^{-1}	4.27×10^{-1}	5.20×10^{-1}	8.41×10^{-1}	7.75×10^{-1}	7.85×10^{-5}	2.78×10^{-5}	5.20×10^{-5}

Table 3: Standard addition procedure for pharmaceutical formulations and human liquids utilizing the B sensor.

Drug	*Taken conc.(M)*	*Founded conc.(M)*	*RSD% n=3*	*RC%*	*RE%*
Standard moxifloxacin	$1*10^{-4}$	$0.96*10^{-4}$	0.764	96	-4
Moxiflox tablet (400mg)	$1*10^{-4}$	$1.03*10^{-4}$	0.921	103	3
Moxicip eye drop	$1*10^{-4}$	1.02	0.89	102	2
Urine	$1*10^{-4}$	$1.06*10^{-4}$	1.23	106	6
Serum	$1*10^{-4}$	$1.05*10^{-4}$	1.03	105	5

Table 4: Multi-standard additions method for the pharmaceutical applications and human fluids by B sensor.

Drug	*Taken conc. (M)*	C_U *(M)*	*RC%*	*RE%*
Standard moxifloxacin	$1*10^{-4}$	0.992×10^{-4}	99.2	1.8
Moxiflox tablet (400mg)	$1*10^{-4}$	1.02×10^{-4}	102	1
Moxicip eye drop	$1*10^{-4}$	1.01×10^{-4}		
Urine	$1*10^{-4}$	1.03×10^{-4}	103	3
Serum	$1*10^{-4}$	1.02×10^{-4}	102	2

Selectivity

Using the (SSM) and (MPM), the interferences of certain inorganic cations (Li^{+}, Na^{+}, K^{+}, Mg^{+2}, Ca^{+2}, Zn^{+2}, Al^{+3}, Cr^{+3} and Fe^{+3}) were examined. The selectivity coefficient values for (SSM) were computed using the Nickolsky–Eisenman equation 19 and recorded in Table 2.[19]

Fewer values of $K_{A,B}$ were obtained leads to no interfering of these inorganic cations on the sensor B response[20]. Figures 15-17 shows the results of selectivity by (MPM)

Analytical Techniques

The sensor B was successfully utilised to assess MFN in standard medicine, pharmaceutical formulation (tablets, eye drop), and human fluids (serum, urine), as indicated in Tables 3 and 4.

In accordance with the usual addition procedure, the concentration of MFN was measured by adding 0.1 mL of $1*10^{-2}$ M MFN to 10 mL of $1*10^{-4}$ M. Using the following equation 3, the change in potentials measurements was measured after each addition:

$$C_x = C_s V_s / [(V_x + V_s) \times 10^{\Delta E/s} - V_x] \quad \ldots\ldots(3)$$

C_x and V_x was the conc. and volume of unknown sample, respectively. C_s and V_s was the conc. and volume of standard solution, respectively. S was the slope value of the calibration curve and ΔE was the change in the potential of the electrode.[21,22]

CONCLUSION

In this research, the novel three sensors of MFN was prepared based on poly vinyl chloride (PVC) membrane as supporting and the ion-exchanger that MFN-BPB, using three different plasticizers: DBPH, TEHP and DBP. It was a sensitive, straightforward, rapid, and cost-effective approach for determining MFN in its pure dosage, pharmaceutical samples, and human fluids. With a time stability of upto 39 days, the B sensor has a strong performance.

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