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New Coated Wire Sensors for Potentiometric Determination of Gemifloxacin in Pure Form, Pharmaceutical Formulations and Biological Fluids

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A simple, accurate and precise potentiometric method was developed for the determination of gemifloxacin mesylate (GFX). Three ion selective coated wire sensors have been constructed from the incorporation of (GFX) with the ion-pairing agents phosphotungstic acid (PTA), phosphomolybdic acid (PMA) and Ammonium reineckate salt (ARS). The three sensors show nearly Nernestian response over the concentration range $1.0x10^{-7}$-$1.0 x10^{-2}$ mol L^{-1} of the drug with slopes of 56.14±0.08, 57.66±0.14 and 55.06±0.32 mV $decade^{-1}$ for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively. The electrodes exhibit a fast dynamic response of 30, 15 and 20 s for a period of 30, 35 and 25 days for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively. The sensors exhibit good selectivity for GFX with respect to some inorganic cations, amino acids and some pharmacologically related compounds. The electrodes display stable potential response in the pH range 6-9 which indicates the applicability of these electrodes in the specified range. The method is accurate and precise as indicated by the mean % recoveries 99.49±0.52, 99.56±0.41 and 99.41±0.45 for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively. The proposed method was successfully applied for the determination of GFX in pure form, its pharmaceutical formulations and biological fluids.

Keywords: Gemifloxacin mesylate; Ion-selective electrodes; Coated wire sensors; Potentiometric determination; Dosage forms; Biological fluids

1. INTRODUCTION

Gemifloxacin mesylate (Figure 1), chemically known as [(R, S) -7- [(4Z)-3-(aminomethyl)-4-(methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-1, 8-naphthyridin -3-carboxylic acid mesylate]. It is a new antibiotic and a member of the fluoroquinolone class of

antibacterial drugs recently approved by the Food and Drug Administration (FDA) for the treatment of acute bacterial exacerbation of chronic bronchitis and community-acquired pneumonia caused by certain bacteria [1]. GFX has also shown potent activity against other major pathogens involved in respiratory tract infections, including Haemophilus influenza and the atypical organisms, Legionella pneumophila, Chlamydia spp., and Mycoplasma spp. [2]. Furthermore, the compound has shown potent activity against many organisms that cause urinary tract infections. The adverse reaction profile is similar to that of older members of this class [3].

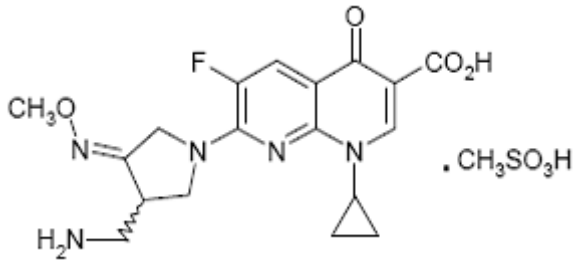

Figure 1. Chemical structure of gemifloxacine mesylate

A number of analytical methods have been reported for the determination of GFX in its pharmaceutical dosage forms and biological samples. These are including high performance liquid chromatography (HPLC) [4-9], high performance liquid chromatography coupled with mass spectrometry [10], stability indicating using capillary electrophoresis and reversed-phase liquid chromatography [11,12], gas chromatography-mass spectrometry [1], spectrophotometry [13-17], spectrofluorimetry [18], voltammetry [1,19] and chemiluminescence [20]. From the literature survey, it was found that there is no potentiometric method has been reported yet for GFX determination.

Ion-selective electrodes (ISEs) are electrochemical transducers that respond selectively, directly, and continuously to the activity of the free ion of interest in solution. They are characterized by low cost, easy to fabricate, accuracy, and can be used without previous extraction of samples. Because of these merits, the use of ISEs is increasing day by day in medicinal, environmental, agricultural and industrial fields [21, 22]. The aim of this study is to develop and validate simple, selective and sensitive coated wire electrodes for the determination of (GFX) in pure form, dosage forms and biological fluids.

2. EXPERIMENTAL

2.1. Instrumentation

The electrochemical measurements were carried out with HANNA instrument pH-211 microprocessor pH-meter and Metrohm pH-meter Model 744 for measuring pH. Saturated calomel electrode (SCE) was used as external reference electrode.

2.2. Materials and reagents

All chemicals used were of analytical grade. Pure grade (GFX) and its tablets (Factive® 320 mg/tablet) were supplied from Tabuk pharmaceutical. MFG. CO., Saudi Arabia. Methanol 99.9%, dioctyl phthalate (DOP) 99.0% and tetrahydrofuran (THF) 97.0% were provided by Fluka, Switzerland. Poly vinyl chloride (PVC) high molecular weight, phosphotungstic acid (PTA) 99.1%, phosphomolybdic acid (PMA) 99.9% and ammonium reineckate salt (ARS) 93.0% were purchased from Aldrich, Germany. Urine samples were obtained from healthy volunteers. Serum samples (Multi -Serum Normal, Ranbdox laboratories UK) were obtained from commercial sources.

2.3. Standard drug solution

Stock GFX solution 0.1 mol L^{-1} was prepared daily by dissolving 1.214 g of drug in 25 mL distilled water. Working solutions ranging from $1.0x10^{-7}$-$1.0x10^{-2}$ mol L^{-1} were prepared by appropriate dilution with distilled water.

2.4. Preparation of gemifloxacin ion-pair and membrane composition

The ion-pair was prepared by mixing 50 mL of 1.0 x 10^{-2} mol L^{-1} GFX and 50 mL of 1.0 x 10^{-2} mol L^{-1} PTA or PMA or ARS. The resulting precipitates were filtered, washed thoroughly with distilled water and air dried. The membranes were prepared by dissolving required amount of ion-pair, PVC and plasticizer (DOP), in 5mL tetrahydrofuran (THF). The solution mixture was poured into a Petri dish (3 cm diameter), covered with a filter paper and the solvent was allowed to evaporate slowly at room temperature.

2.5. Electrode construction

Spectroscopic pure aluminum wire of 20 mm diameter and 12 cm length was tightly insulated by polyethylene tube leaving 1.0 cm at one end for coating and 0.5 cm at other end for connection. Prior to coating, the polished surface was washed with a detergent, then rinsed with water, and dried. The sensor ending part was dipped into the coating solution. The prepared electrode was conditioned by soaking for 6 h in 1.0 x 10^{-3} mol L^{-1} GFX solution.

2.6. Electrodes calibration

The calibration of the sensors was preceded using standard solutions of (GFX) ranging from $1.0x10^{-7}$-$1.0x10^{-2}$ mol L^{-1}. All potentiometric measurements were performed using the following cell assembly: Al/ membrane/test solution//KCl salt bridge// SCE. The sequence of measurements was carried out from low concentration to higher one. The measured potential was plotted against the

logarithm of drug concentration. The sensor (s) was washed with distilled water and dried with tissue paper between measurements.

2.7. Standard addition method

The electrode was immersed into sample of 50 mL with unknown concentration and the equilibrium potential of E_1 was recorded. Then 0.1 mL of 0.1 mol L^{-1} of standard drug solution was added into the testing solution and E_2 was recorded. The concentration of the testing sample was calculated from the change of potential ΔE (E_2-E_1).

2.8. Electrode selectivity

Selectivity coefficients $K^{pot}_{GFX,j}{}^{+z}$ of the sensors towards different cations, amino acids and some pharmacologically related compounds were determined by the separate solution method [23] in which the following equation was applied:

$$\text{Log } K^{Pot}_{GFX.J}{}^{z+} = (E_2\text{-}E_1)/S + \log [GFX] - \log (J^{z+})^{1/z}$$

Where, K^{Pot} is the selectivity coefficient, E_1 is the sensor potential in 1.0 x 10^{-3} mol L^{-1} GFX solution. E_2 is the electrode potential in 1.0 x 10^{-3} mol L^{-1} solution of the interferent ion J^{Z+} and S is the slope of the calibration plot in mV.

2.9. Effect of pH

The effect of pH on the potential response of the prepared electrodes was studied using 1x10^{-3} mol L^{-1} GFX solution. The pH of this solution was adjusted between 2-12 by using suitable amounts of 0.1 mol L^{-1} NaOH or HCl solution. The potential readings corresponding to different pH values were recorded and plotted using the proposed electrode(s). The results showed that, the potential remained constant despite the pH change in the range of 6-9 which indicates the applicability of this electrode(s) in the specified range.

2.10. Determination of gemifloxacin mesylate in pharmaceutical dosage forms

2.10.1. Determination of gemifloxacin mesylate in tablets

Ten tablets (Factive® 320 mg/tablet) were finely powdered An accurate weight containing 1.214g was dissolved in 25mL distilled water to obtain a standard stock solution. Sample solutions ranging from 5.0×10^{-7}-1.0×10^{-3} mol L^{-1} (standard addition method) and 1.0×10^{-7}-1.0×10^{-2} mol L^{-1} (calibration method) were prepared by serial dilution with distilled water. These solutions were

analyzed as described above under electrode calibration and standard addition methods. The results obtained were compared to those obtained with the comparison spectrophotometric method [17].

2.10.2. Content uniformity assay of gemifloxacin mesylate tablets:

Ten individual tablets of Factive® 320 mg/tablet were placed in separate 100-mL measuring flasks and dissolved in 100 mL distilled water. The electrode(s) was directly immersed into 50.0 mL of each sample for three times and then washed with distilled water to reach a steady potential between the individual measurements. The mean potential was used to evaluate the content uniformity from the calibration graph.

2.11. Application to serum and urine

2.11.1 Serum

1.0 mL aliquots of serum were transferred into a series of centrifugation tubes. Aliquots of standard aqueous solution of GFX were added so that the final concentration is in the range of 1.0×10^{-7}-1.0×10^{-2} mol L^{-1}. The tubes were mixed well and 10.0 mL of diethyl ether was added to each tube and centrifuged for 2 min at 1500 rpm. Then, the deproteinated layer was transferred to a 100-mL measuring flask and complete to volume using distilled water. These solutions were analyzed as described above under electrode calibration and standard addition methods.

2.11.2 Urine

1.0 mL aliquots of urine were transferred into a seires of 100-mL measuring flasks. Aliquots of standard aqueous solution of GFX were added so that the final concentration is in the range of 1.0×10^{-7}-1.0×10^{-2} mol L^{-1}. The flasks were mixed well and completed to volume using distilled water. These solutions were analyzed as described above under electrode calibration and standard addition methods.

3. RESULTS AND DISCUSSIONS

3.1 Calibration graph and statistical data

The measuring range of a potentiometric sensor is the linear part of the calibration graph as shown in Figure 2. The critical response characteristics of coated wire electrodes were determined and the results were summarized in Table 1. The three sensors show nearly Nernestain response over the concentration range $1.0x10^{-7}$-$1.0\ x10^{-2}$ mol L^{-1} of the drug investigated. Calibration graph slopes for coated wire sensors are 56.14, 57.66 and 55.06 mV $decade^{-1}$ and standard deviations of 0.52, 0.41 and 0.45 after six replicate measurements for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively. The electrodes exhibit a fast dynamic response of 30,15 and 20 s for a period of

30, 35 and 25 days for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively, without significant change in the electrodes parameters.

Table 1. Critical response characteristics of GFX coated wire sensors

Parameter	GFX-PTA	GFX-PMA	GFX-ARS
Slope (mV decade^{-1})	56.14±0.08	57.66±0.14	55.06±0.32
Intercept	635.48	590.79	507.92
Correlation coefficient,(r)	0.9999	0.9999	0.9999
Linear range (mol L^{-1})	1.0x10^{-7} -1.0x10^{-2}	1.0x10^{-7} -1.0x10^{-2}	1.0x10^{-7} -1.0x10^{-2}
LOD (mol L^{-1})	4.68×10^{-8}	4.89×10^{-8}	5.13×10^{-8}
Response time for 10^{-3}M GFX/s	30	15	20
Lifetime/day	30	35	25
Working pH range	6 – 9	6 – 9	6 – 9
Robustness[a]	99.49±0.43	99.50±0.49	99.28±0.47
Ruggedness[b]	99.58±0.29	99.61±0.34	99.38±0.52

[a]A small variation in method parameters were carried out as pH of borate buffer (pH 7.5±1).
[b] Comparing the results by those obtained by different sensors assemblies using (Jenway 3510 pH meter)

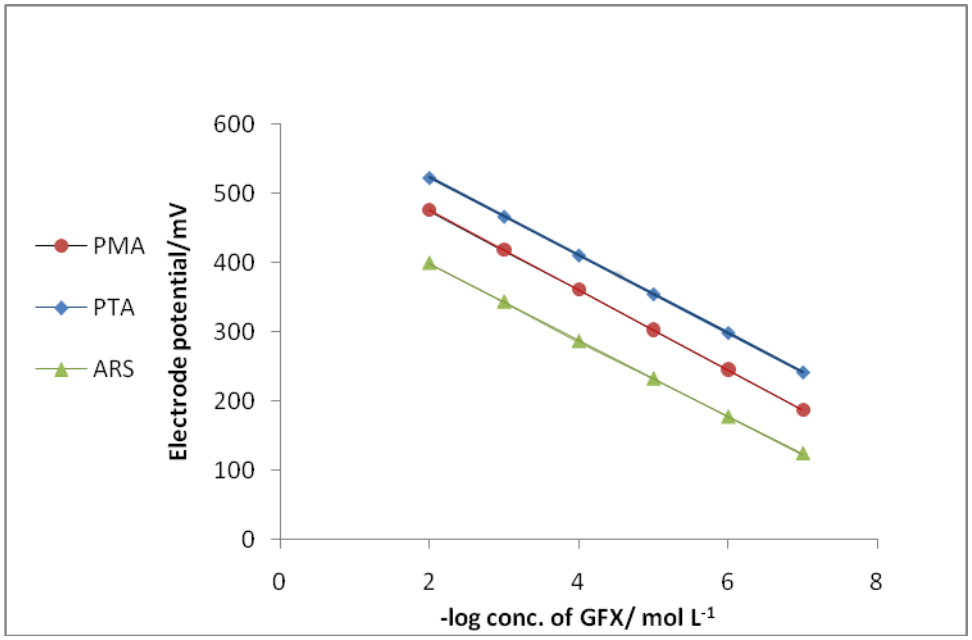

Figure 2. Typical calibration graphs of GFX

3.2 Effect of pH

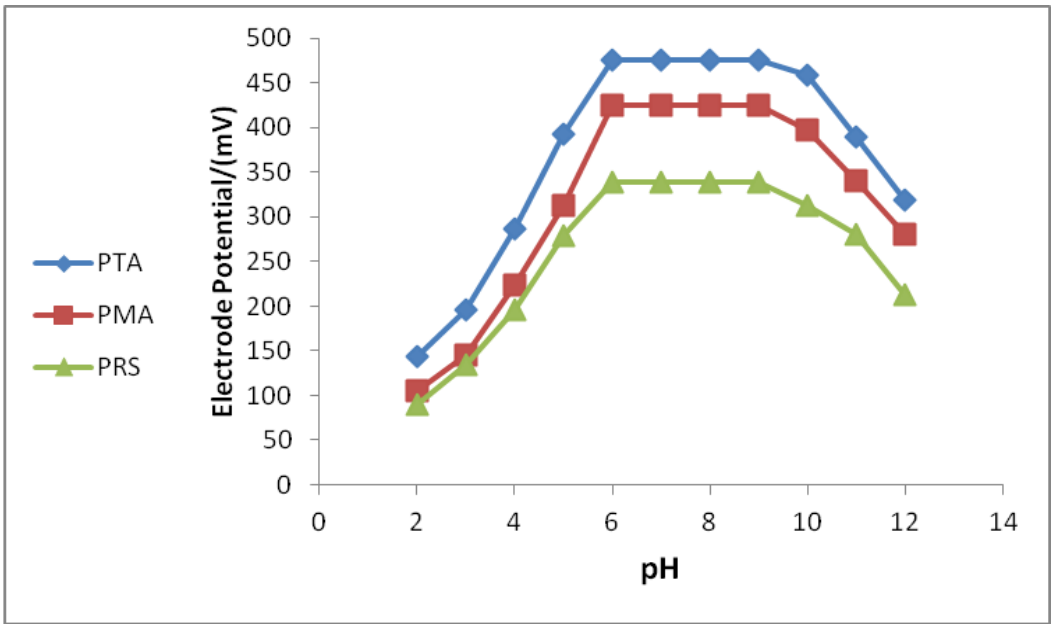

Figure 3. Effect of pH on GFX electrode potential

To examine the effect of pH on the response of the three sensors, the potential was measured at a specific concentrations of GFX solution (1.0×10^{-3} mol L^{-1}) from the pH value of 2.0 up to 12.0 (0.1 mol L^{-1} NaOH or 0.1 mol L^{-1} HCl solution were employed for the pH adjustment). The results showed that the potential remained constant despite the pH change in the range of 6 – 9, which indicates the applicability of these electrodes in the specified pH range (Figure 3). Below pH 6, the potential of the electrode increased with the increase of analyte acidity which may be described to extraction of H^+ ions by membrane. While at pH more than 9, the response of the electrode decreased which may be attributed to increase of OH^- concentration [24].

3.3 Selectivity of the electrode

The influence of some inorganic cations, amino acids and some pharmacologically related compounds on GFX sensors was investigated using separate solution method [23]. The results obtained (Table 2) reflect a very high selectivity of the investigated electrodes for the GFX cation. The mechanism of selectivity is mainly based on the streospecificity and electrostatic environment, and is dependent on how much matching is present between the locations of the lipophilic sites in the two competing species in the bathing solution side and those present in the receptor of the ion-pair [25]. As shown in Table 2, the electrodes exhibit good tolerance towards inorganic cations and amino acids.

The interference of ciprofloxacin and sparfloxacin as some pharmacologically related compounds with GFX was studied. On using (GFX-PTA) sensor, ciprofloxacin and sparfloxacin slightly interfered during the determination of GFX; while on using the sensors (GFX-PMA, GFX-ARS), ciprofloxacin and sparfloxacin did not interfere with GFX determination.

Table 2. Selectivity coefficients K^{pot} of the GFX coated wire sensors calculated by the separate solution method ($1x10^{-3}$ M of both GFX and the interferent) at 25ºC

Interferent	-log $K^{pot}_{GFX,J}{}^{z+}$	-log $K^{pot}_{GFX,J}{}^{z+}$	-log $K^{pot}_{GFX,J}{}^{z+}$
	GFX-PTA	GFX-PMA	GFX-ARS
Thymidine	$1.1x10^{-4}$	$2.5x10^{-4}$	$9.7x10^{-3}$
Glutamine	$1.2x10^{-4}$	$1.9x10^{-4}$	$6.1x10^{-3}$
Serine	$2.1x10^{-4}$	$4.9x10^{-5}$	$1.9x10^{-3}$
Cystine	$1.2x10^{-3}$	$3.5x10^{-4}$	$3.9x10^{-4}$
Uracil	$5.0x10^{-3}$	$1.8x10^{-3}$	$3.5x10^{-3}$
Ornithine	$8.2x10^{-3}$	$2.7x10^{-3}$	$1.7x10^{-3}$
Thymine	$10x10^{-3}$	$1.8x10^{-4}$	$1.5x10^{-3}$
Histadine	$3.8x10^{-4}$	$2.8x10^{-4}$	$1.2x10^{-3}$
Glycine	$9.4x10^{-4}$	$2.7x10^{-4}$	$2.6x10^{-4}$
Cu^{2+}	$1.6x10^{-3}$	$7.2x10^{-5}$	$1.4x10^{-3}$
Ca^{2+}	$9.1x10^{-5}$	$1.7x10^{-4}$	$4.9x10^{-4}$
Na^{+}	$2.6x10^{-4}$	$2.1x10^{-5}$	$1.1x10^{-3}$
NH_4^{+}	$9.4x10^{-4}$	$1.7x10^{-4}$	$1.9x10^{-3}$
Zn^{2+}	$1.5x10^{-4}$	$4.7x10^{-4}$	$8.2x10^{-3}$
Ni^{2+}	$1.9x10^{-4}$	$1.7x10^{-5}$	$5.4x10^{-4}$
Cd^{2+}	$1.4x10^{-4}$	$7.5x10^{-5}$	$7.2x10^{-4}$
Mn^{2+}	$1.0x10^{-3}$	$1.1x10^{-4}$	$1.2x10^{-3}$
K^{+}	$9.1x10^{-5}$	$2.4x10^{-4}$	$2.3x10^{-3}$
Mg^{2+}	$3.5x10^{-4}$	$2.3x10^{-4}$	$3.5x10^{-4}$
Sn^{2+}	$4.7x10^{-4}$	$6.7x10^{-4}$	$4.6x10^{-4}$
Ciprofloxacin	$2.3x10^{-2}$	$4.3x10^{-4}$	$8.2x10^{-4}$
Sparfloxacin	$1.2x10^{-2}$	$1.7x10^{-4}$	$1.0x10^{-3}$

3.4 Life-time Study

GFX electrodes lifetime was estimated with the calibration curve, periodical test of a standard solution ($1.0x10^{-7}$–$1.0x10^{-2}$ mol L^{-1}) and calculation of its response slope. For this purpose, three sensors were employed and the calibration graphs were plotted after optimum soaking time of 6 h in 1.0 $x10^{-3}$ mol L^{-1} GFX solution. The slopes of calibration curves were 56.14, 57.66 and 55.06 mV $decade^{-1}$ at 25 ºC for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively. The electrodes were continuously soaked on 1.0 $x10^{-3}$ mol L^{-1} solution of GFX for about 35 days. The calibration plot slopes decreased slightly to be 50.09, 52.40 and 51.63 mV $decade^{-1}$ after 30, 35 and 25 days for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively. This reveals that soaking of sensors in the drug solution for a long time has a negative effect on the response of membrane. The same effect appears after working with the sensors for a long time. The regeneration of the electrodes was tried simply by reformation of the ion-pair on the external gel layer of membrane [26].

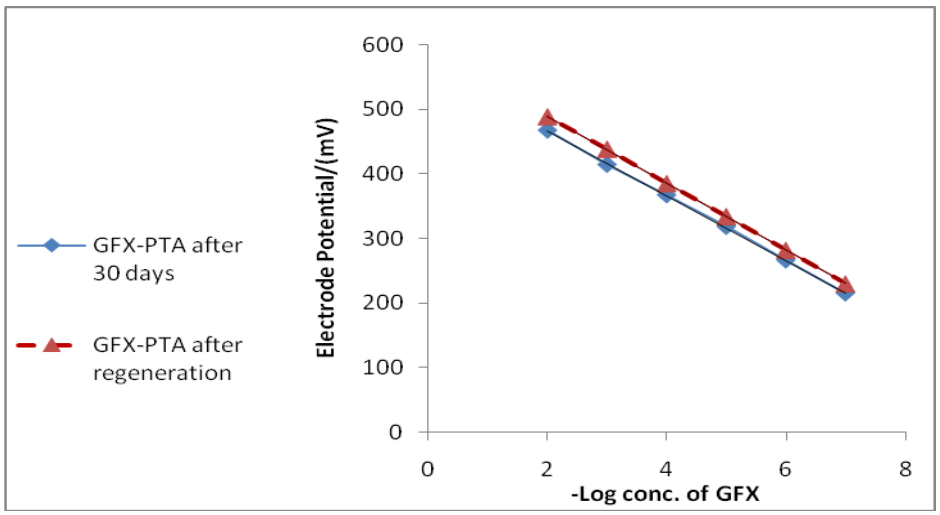

Figure 4. Regeneration of GFX-PTA coated wire electrode

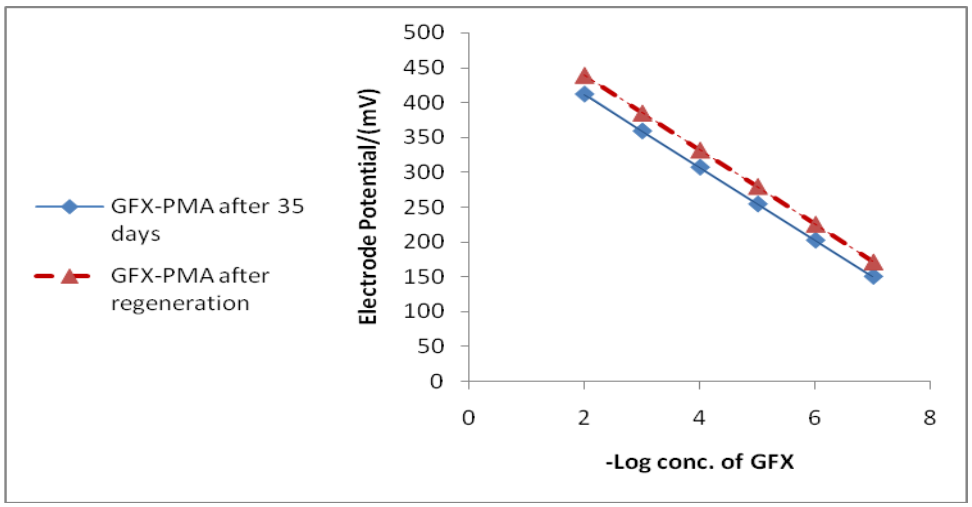

Figure 5. Regeneration of GFX-PMA coated wire electrode

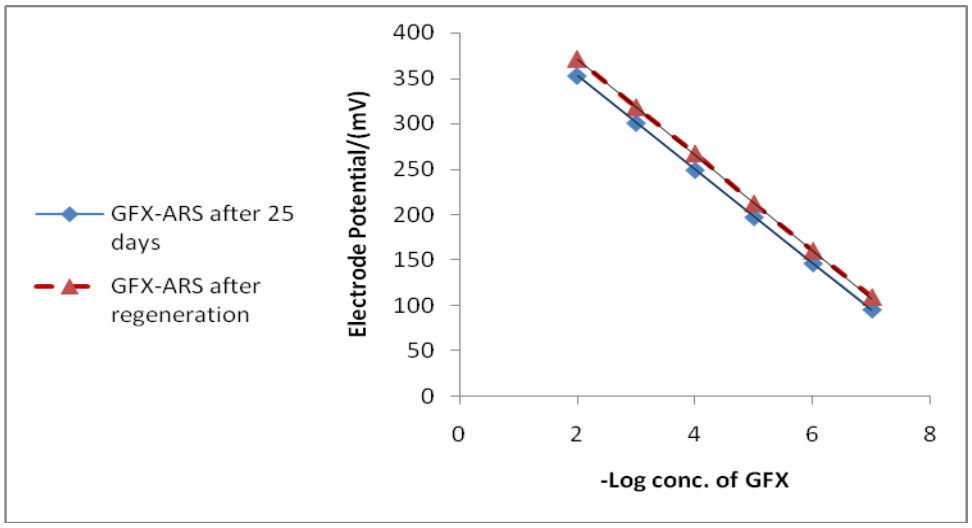

Figure 6. Regeneration of GFX-ARS coated wire electrode

The regeneration of the (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors was successfully achieved by soaking the exhausted electrodes for 24 h in solutions of $1.0x10^{-2}$ $molL^{-1}$ phosphotungstic acid (PTA), phosphomolybdic acid (PMA) and ammonium reineckate (ARS), followed by soaking for 3 h in $1.0x10^{-2}$ mol L^{-1} GFX solution. (Figures 4-6) , shows the calibration graphs for exhausted sensors (slope 50.09, 52.40 and 51.63 mV $decade^{-1}$) for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively, and for the same sensors after regeneration (slope 51.69, 53.26 and 52.54 mV $decade^{-1}$).

3.5 Quantification of gemifloxacin

The investigated sensors were found to be useful in the potentiometric determination of GFX in pure solutions by calibration graph and standard addition method.The results obtained were listed in Table 3. The results obtained were compared with a reference UV- spectrophotometric method [17], as shown in Table 3. Statistical analysis [27] of the results obtained by the proposed and comparison methods using Student's t-test and variance ratio F-test, showed no significant difference between them regarding accuracy and precision, respectively. (Table 3)

Table 3. Analysis of GFX in pure form and dosage forms by the proposed and reported methods

Sample	Statistical Parameter	GFX-PTA		GFX-PMA		GFX-ARS		Reported method[17]
		Calibration Method*	standard addition method*	Calibration method	standard addition method	Calibration method	standard addition method	
pure form	Mean ±S.D	99.49±0.52	99.38±0.51	99.56±0.41	99.40±0.50	99.41±0.45	99.64±0.37	99.50±0.75
	n	6	6	6	6	6	6	6
	Variance	0.27	0.26	0.17	0.25	0.20	0.14	0.56
	%SE**	0.21	0.21	0.17	0.20	0.18	0.15	0.75
	%RSD	0.52	0.52	0.41	0.50	0.45	0.37	0.30
	t-test	0.03(2.23)*	0.33(2.23)*	0.17(2.23)*	0.28(2.23)*	0.25(2.23)*	0.42(2.23)*	(2.23)*
	F-test	2.07(5.05)*	2.15(5.05)*	3.29(5.05)*	2.24(5.05)*	2.80(5.05)*	4.00(5.05)*	(5.05)*
FACTIVE ® Tablets (320 mg GFX/tablet)	Mean ±S.D	99.46±0.45	99.61±0.33	99.55±0.40	99.67±0.31	99.32±0.48	99.58±0.58	99.38±0.39
	n	6	6	6	6	6	6	6
	Variance	0.19	0.11	0.16	0.096	0.23	0.33	0.15
	%SE**	0.18	0.14	0.16	0.13	0.19	0.23	0.16
	%RSD	0.45	0.33	0.40	0.31	0.49	0.58	0.39
	t-test	0.33 (2.23)*	1.08(2.23)*	0.75 (2.23)*	1.41(2.23)*	0.24 (2.23)*	0.71 (2.23)*	(2.23)*
	F-test	1.27(5.05)*	1.36(5.05)*	1.07(5.05)*	1.67(5.05)*	1.5(5.05)*	2.2 (5.05)*	(5.05)*

*The Figures in parentheses are the tabulated t- and F- test at p = 0.05[27]
**%Error= %RSD/√n

3.6 Method validation

The linearity, limit of detection, selectivity, precision, accuracy and ruggedness/robustness were the parameters used for the method validation. For linearity and limit of detection as mentioned before, the investigated drug (GFX) was measured using GFX-electrodes over the concentration range 1×10^{-7} -1×10^{-2} mol L^{-1} at lower limit of detection 4.68 $\times10^{-8}$, 4.89×10^{-8} and 5.13×10^{-8} mol L^{-1} for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively.

The precision of the method was calculated in terms of (intraday and interday). The %RSD values of intraday and interday studies for the repeated determination were less than 2% which indicating good precision (Table 4).

Table 4. Precision of the proposed method for the determination of GFX in pure form

Conc.(mol L^{-1})	GFX-PTA			GFX-PMA			GFX-ARS		
	Recovery %	%RSD*	Error**%	Recovery %	%RSD	Error%	Recovery %	%RSD	Error**%**
Intraday precision									
$1.0x10^{-6}$	99.89 ± 0.31	0.31	0.18	99.61 ± 0.26	0.26	0.15	99.56 ±0.34	0.35	0.19
$1.0x10^{-5}$	99.20 ± 0.41	0.41	0.24	99.73 ± 0.50	0.50	0.29	99.53 ±0.61	0.61	0.35
$1.0x10^{-4}$	99.75 ± 0.50	0.50	0.29	99.42 ±0.63	0.63	0.36	99.58 ±0.52	0.52	0.30
Interday precision									
$1.0x10^{-6}$	99.78 ±0.35	0.35	0.20	99.64 ±0.57	0.58	0.33	99.39±0.59	0.59	0.34
$1.0x10^{-5}$	99.20 ±0.20	0.20	0.12	99.33 ±0.50	0.51	0.29	99.67±0.50	0.50	0.29
$1.0x10^{-4}$	99.33 ±0.38	0.38	0.22	99.25 ±0.50	0.50	0.29	99.33±0.63	0.63	0.36

*%RSD= *(S.D/Mean) 100*
**%Error= %RSD/√n

The robustness of proposed method was carried out by using borate buffer pH 7.5±1 and the percentage recoveries were 99.49±0.43,99.50±0.49 and 99.28±0.47 for (GFX-PTA), (GFX-PMA) and (GFX-ARS) coated wire sensors, respectively, The reproducibility upon using another model of pH-meter (Jenway 3510) was indicated by the results obtained in Table 1.

3.7. Analytical applications

3.7.1 The sensor response in pharmaceutical formulation

In order to evaluate the analytical usefulness of the proposed potentiometric method, GFX was determined in its tablets. The results obtained were in good agreement with those obtained by the published spectrophotometric method [17]. Table 3 shows the results of analysis of GFX in its tablets.

Statistical analysis [27] of the result obtained by the proposed and the comparison methods shows no significant difference between the two methods as regards to accuracy (t- test) and precision (F-test).

3.7.2 The sensor response in biological fluids

Allen et al [28] reported that GFX is rapidly absorbed after oral administration and maximum concentrations of the drug substance (C_{max}) in plasma increased linearly with dose. C_{max} was achieved approximately 1 h after dosing and the mean C_{max} values were found as 1.48±0.39 μg mL^{-1} following a single oral dose of 320 mg GFX.

The high sensitivity of the proposed method allowed the determination of GFX in biological fluids. The nominal content of drug in spiked serum and urine was determined using the calibration and standard addition methods. The potential of the GFX sensors showed no significant difference of response time between aqueous solution of pure drug and its spiked biological fluids. The obtained results shown in Table 5 were satisfactory accurate and precise.

Table 5. Determination of GFX in spiked human serum and urine by the GFX electrode.

Sample	GFX-PTA		GFX-PMA		GFX-ARS	
	Calibration Method*	standard addition method*	Calibration Method*	standard addition method*	Calibration Method*	standard addition method*
Urine	99.48±0.38	99.55±0.58	99.46±0.54	99.71±0.29	99.30±0.51	99.50±0.39
Serum	99.54±0.36	99.35±0.33	99.49±0.48	99.35±0.33	99.47±0.38	99.35±0.33

** Mean±S.D of six determinations*

4. CONCLUSION

The potentiometric method developed for the determination of GFX is simple, accurate, easy to operate and inexpensive; making it an excellent tool for the routine determination of GFX in quality control laboratories. Also, it provides a fast assay of GFX in its pharmaceutical preparations without interference from excipients. The method was also applied to spiked serum and urine samples without any interference from the matrix. Hence the proposed methods can be used for routine analysis of GFX in pharmaceutical industries, hospitals and research laboratories.

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