

## Original Research Article

# Sensing and quantification of gatifloxacin in real wastewater effluents using solid-contact ion-selective membranes

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### Abstract

**Purpose:** To determine gatifloxacin hydrochloride (GTF) levels in real wastewater effluents.

**Methods:** In the last few years, the application of membrane-sensitive electrodes in the analysis of active pharmaceutical ingredients (APIs) has become a topic of paramount importance. Two ion-selective electrodes (ISEs) were fabricated using phosphotungstic acid (PTA) and sodium tetraphenylborate (TPB) as ion combining principles, for selective and sensitive determination of gatifloxacin hydrochloride (GTF) in factory wastewater effluents. The membranes were successfully fabricated, and their performance was optimized. A validation scheme that followed IUPAC guidelines was implemented in the application of the sensors for sensitive determination of gatifloxacin hydrochloride.

**Results:** The fabricated membranes quantified the studied drug in a concentration range of 1 – 10<sup>4</sup> μM, with GTF-PTA and GTF-TPB electrodes showing gradients of 56.6 ± 0.40 and 57.8 ± 0.50 mV/decade, respectively. The fabricated sensors showed excellent working criteria in a pH range of one to five. A validation scheme was applied to the proposed method with respect to accuracy, robustness, and ruggedness. The suggested analytical procedure was effectively used for sensitive quantification of GTF in bulk form and in actual industrial water effluents.

**Conclusion:** The proposed method has been efficiently applied for the determination of GTF in wastewater samples without any sample pretreatment.

**Keywords:** Potentiometry, Gatifloxacin hydrochloride, Membrane-sensitive electrodes, Ion-pairing agents, Wastewater samples

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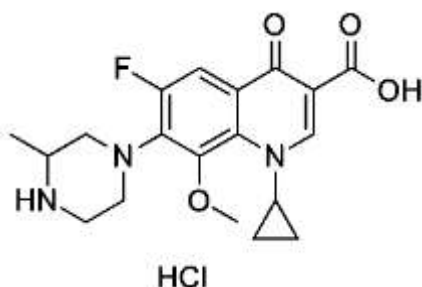
## INTRODUCTION

Globally, antibiotics are frequently used in human and veterinary medicine, and as such, their levels may be up in the environment, which increases the risk of antibiotic resistance. As

fluoroquinolones are excreted unmodified in the urine, with the likelihood of appearing in sewage systems of health institutions, they are frequently detected in surface water, especially where they have easy access to soil and water. Antibiotics negatively affect humans when they are present

in the environment, making their presence in soil or water undesirable [1].

Gatifloxacin hydrochloride (GTF), a synthetic fluoroquinolone antibiotic, is shown in Figure 1. Both Gram-positive and Gram-negative bacteria are susceptible to the action of GTF. It works by blocking bacterial cell division and inhibiting bacterial DNA gyrase which is crucial for bacterial DNA replication [2].



**Figure 1:** Chemical structure of gatifloxacin (GTF)

Different analytical methods such as spectrofluorimetry [5], spectrophotometry [3,4], high-performance liquid chromatography (HPLC) [6,7], and thin layer chromatography (TLC) [8] have been used to quantify GTF in various sample forms. On the other hand, potentiometric membrane sensors have been used to measure quinolones in dosage forms [9] or in urine [10]. It is crucial to find and keep an eye on the drugs being studied in wastewater effluents. The existence of these drugs in water samples, even in trace amounts, may pose a serious threat to human health, especially given the rise in antibiotic resistance [11].

The technique of HPLC has been used to identify fluoroquinolones in wastewater samples [12,13]. In order to pre-concentrate the analyte and exclude any interference due to the matrix effect, sample pretreatment and extraction must be completed prior to the application of LC. Therefore, it is critically necessary to develop a straightforward and affordable analytical approach for tracking the medication in environmental water samples. To address this need, membrane-sensitive electrodes should be thought of as clever instruments [14]. Liquid-contact ion selective electrodes (ISEs) have a serious problem which is evaporation of the inner solution. This results in variations in osmotic pressure, leading to damage to the membrane. Recently, an efficient method for getting around the issues with liquid-contact electrodes has emerged: solid-contact electrodes [15]. In this respect, two solid-contact electrodes were fabricated in this work. In order to create the

ISEs for sensors 1 (GTF-TPB) and 2 (GTF-PTA), sodium tetraphenylborate (TPB) and phosphotungstic acid (PTA), respectively, were used. To determine the ideal operating parameters, it was necessary to compare the working conditions.

## EXPERIMENTAL

### Instrumentation

The potentiometric measurement was performed using an electronic mV/pH meter linked to Ag/AgCl dual-junction standard electrode. Throughout the entire test, a Jenway (UK) glass electrode was utilized. Glassy carbon electrode rods (3 mm diameter) were purchased from CH Instruments, TX, USA.

### Chemicals and reagents

Bio Vision (USA) provided the GTF pure standard with CAS number (CAS # 112811-59-3) and a certificate attesting to its purity (99.92 %). Prolabo (France) was the source of TPB, PTA, HCl, sodium hydroxide, potassium chloride, AgNO<sub>3</sub>, and tetrahydrofuran (THF). Nitrophenyl octyl ether (NPOE), bis(2-ethyl hexyl) sebacate (2-EHS), and dioctyl phthalate (DOP) were supplied by Sigma, Germany. Polyvinyl chloride (PVC) of high MW grade was supplied by Fluka Chemie (Germany). Deionized water was provided by Aquatron (UK) from their water still.

### Collection of real wastewater samples, preparation, and storage

The samples were collected from a pharmaceutical plant that makes GTF tablets. Following the adjustment of pH to 3.0, the acquired samples were filtered through nylon film filters to eliminate contamination due to tiny particles. To avoid sample deterioration, the filtered samples were stored in opaque glass vials in a cold environment.

### Preparation of GTF standard solutions

A 0.01 M GTF stock solution was prepared in deionized water. Using the same solvent, judicious dilution of the GTF stock standard solution was used to create working solutions of concentrations  $1 \times 10^{-8}$  to  $1 \times 10^{-3}$  M.

### Fabrication of sensors, calibration, and optimization

PVC (0.19 g), 2-EHS (400  $\mu$ L), and sensor 1 (TPB; 0.01 g) or sensor 2 (PTA) were combined in two different petri dishes. The mixture was

dissolved in 6 mL of THF. A glassy carbon electrode was in direct contact with the THF solution, and the applied solution was allowed to evaporate completely over time. The membrane produced was conditioned by immersing in 0.01 M GTF stock standard solution for 24 h. The same GTF solution was used to store the electrodes.

After the conditioning phase, the produced sensors were calibrated by dipping them in GTF standard solutions with concentrations ranging from  $1 \times 10^{-2}$  to  $1 \times 10^{-8}$  M. The membranes were washed with deionized water in-between measurements, and typical calibration graphs were made. These plots were used to determine the unknown GTF concentrations.

The best membrane performance was achieved by researching on and modifying the factors impacting membrane performance. The competence of the electrodes was assessed in line with IUPAC's recommendations [16]. Moreover, a variety of plasticizers with various polarities were used to determine the effect of plasticizer type on membrane performance. The plasticizers were subjected to tests for optimal electrode performance. Using a  $1 \times 10^{-4}$  M GTF standard solution, the effect of pH on the performance of the membranes was examined using dropwise additions of 0.1 M NaOH or 0.1 M HCl to get various pH values.

A pH-versus-electrode potential standard graph was used to identify the ideal pH range for the built sensors. The repeatability of the prepared GTF sensors and the stability of the measured potential were observed over the course of one month. Daily calculation of potential was done with GTF at concentrations of  $1 \times 10^{-2}$ ,  $1 \times 10^{-3}$ ,  $1 \times 10^{-4}$ ,  $1 \times 10^{-5}$ , and  $1 \times 10^{-6}$  M. Gradient (in millivolts per decade) was computed for every film that was built, and the gradients obtained during calibration were compared.

The separate solution method (SSM) was used to test membrane selectivity [17]. The potential responses of the manufactured electrodes to various interferents such as various inorganic ions ( $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{NH}_4^+$ ) and structurally-related fluoroquinolones (ciprofloxacin hydrochloride and norfloxacin hydrochloride), were recorded and used to calculate PSC values for all interferents using Eq 1.

$$\text{PSC} = (E_1 - E_2)/S \dots\dots\dots (1)$$

where  $S$  stands for the examined sensor slope (mV/concentration decade),  $E_1$  is the primary ion (GTF) potential in 1.0 mM GTF, and  $E_2$  is potential in 1.0 mM interferent.

### Applications

A variety of standard GTF samples were prepared in water (tap and distilled). The pH of the prepared samples was adjusted to 3.0. The researched drug concentrations were measured using the constructed membranes, and % recovery was computed.

Real wastewater samples were also evaluated using the built-in sensors. The concentrations of analyzed samples were obtained from the standard calibration curves. After employing solid-phase extraction, the results obtained using the suggested approach were compared with those obtained using a reference method [6].

## RESULTS

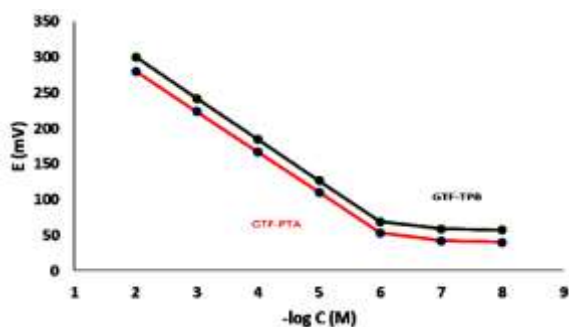
### Effectiveness of membranes

The characteristics of the electrodes were assessed with respect to criteria which are shown in Table 1. A near-optimal Nernstian behavior was attained from 1.0 to  $10^4$   $\mu\text{M}$ . The slopes of sensors 1 and 2 were  $57.8 \pm 0.50$  and  $56.6 \pm 0.40$  mV/decade, respectively. Typical calibration plots are shown in Figure 2.

**Table 1:** Characteristics of the electrodes

Characteristic	Sensor 1	Sensor 2
Gradient (mV/decade)*	57.8±0.50	56.6±0.40
Time taken to respond (sec)	10-20	10-20
pH range	1.0 -5.0	1.0-5.0
Range of concentration ( $\mu\text{M}$ )	$1 \times 10^{-6}$ - $1 \times 10^{-2}$	$1 \times 10^{-6}$ - $1 \times 10^{-2}$
Stability (days)	21	21
Accuracy	99.41±0.64	100.14±0.71
Detection limit ( $\mu\text{g/mL}$ )	0.24	0.24
Ruggedness <sup>†</sup>	98.98*±1.21	99.78*±1.43
Robustness	100.56*±1.54	100.63*±0.93

\*Mean of 5 measurements. <sup>†</sup> Relative to values obtained for various sensors using Hanna digital ion-analyzer



**Figure 2:** Standard curve of potential against  $-\log$  concentration for GTF sensors at pH 3.0

Using IUPAC criteria [16], the performance of the produced membranes was assessed. A number of performance aspects were taken into consideration, including response time, ideal pH range, linearity, impact of plasticizer type, and limit of detection. The effect of plasticizer type was determined through experiments using 2-EHS, DOP, and NPOE which had different polarities. The plasticizer that produced the best results was 2-EHS.

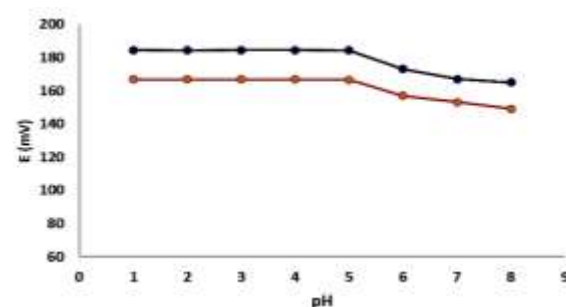
The junction of the two extrapolated linear segments of the standard curve represents the limit of detection [16]. Detection limits  $\leq 0.24 \mu\text{g/mL}$  depicted excellent sensitivity (Table 1). The performance of the produced sensors was impacted by medium pH. The pH range of 1.0 to 5.0 was found to have the optimum electrochemical response (Figure 3).

By establishing calibration plots and evaluating attributes of the sensors every day, the lifetime of the sensors was investigated. When no potential changes ( $< 3.0 \text{ mV}$ ) were noticed and calibration attributes were taken into account, the duration of the 2 produced sensors was 3 weeks (Figure 4). The response time, which measures the period required by fabricated electrode to reach a constant value (1 mV) following increase in sample level by ten folds, is a crucial factor in evaluating the performance of membranes [16]. The response time of the fabricated sensors was found to be 15 sec.

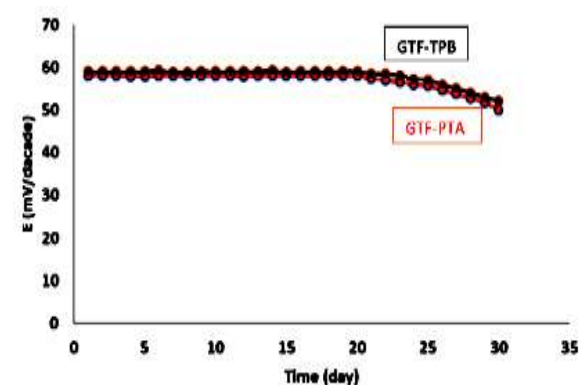
The accuracy of the procedure was evaluated using the synthesized membranes over a range

of GTF concentrations. The robustness of the procedure was assessed by measuring how well the analytical assay handled minor changes in the working environment. In order to measure the reproducibility of the procedure, its toughness was also evaluated. Table 1 depicts these characteristics. The choice of the created sensors is a considered crucial decision factor because it emphasizes their suitability for assessing real wastewater specimens.

The separate solution method (SSM) was used to evaluate the selectivity of the manufactured membranes [17]. The potentiometric selectivity coefficients (PSCs) of the electrodes in the presence of various interferents (various inorganic ions and structurally-related fluoroquinolones) are displayed in Table 2. The results show that the developed sensors had high selectivity for the medication under study.



**Figure 3:** Influence of pH on GTF membrane sensor potential response



**Figure 4:** GTF membrane sensor stability at 25 °C

**Table 2:** PSCs of the GTF selective sensors as measured using separate solution procedure

Interfering factor	GTF-TPB	GTF-PTA
Na <sup>+</sup>	$1.5 \times 10^{-3} \pm 0.43$	$1.6 \times 10^{-3} \pm 0.83$
K <sup>+</sup>	$2.2 \times 10^{-4} \pm 0.53$	$2.3 \times 10^{-4} \pm 0.55$
NH <sub>4</sub> <sup>+</sup>	$1.2 \times 10^{-4} \pm 0.93$	$1.2 \times 10^{-4} \pm 1.21$
Ciprofloxacin hydrochloride	$2.1 \times 10^{-3} \pm 0.78$	$2.2 \times 10^{-3} \pm 0.33$
Norfloxacin hydrochloride	$3.1 \times 10^{-4} \pm 0.44$	$3.2 \times 10^{-4} \pm 0.35$

Values are mean  $\pm$  SD (n =5)

### Water samples spiked with GTF

Results revealed that the produced electrodes worked well for measuring GTF in samples of water (distilled and tap) that had been mixed with definite amounts of the targeted medication. Table 3 displays the findings, which demonstrate the high degree of accuracy of the approach.

**Table 3:** Sensitivity of electrodes in measurement of GTF in spiked water specimens

Sample	Percentage recovery	
	Sensor 1	Sensor 2
Distilled H <sub>2</sub> O	99.89±0.78	99.75±0.56
Tap H <sub>2</sub> O	100.77±0.46	99.45±0.43

Values are mean ± SD (n =5)

### GTF levels in actual pharmaceutical wastewater

Operating circumstances were optimized for optimum membrane performance. Thereafter, the sensors were used to carefully analyze a variety of samples taken from a pharmaceutical factory wastewater discharge without any prior processing. An important advantage of the analytical strategy was the lack of sample pre-treatment. A comparison was done between the resultant data and data from a standard assay [6] (Table 4).

**Table 4:** Measurement of GTF levels in actual drug factory wastewater specimens (µg/mL)

Specimen Number	Sensor 1	Sensor 2	Reference Method [6]*
1	35.02 ± 0.78	35.12 ± 0.67	34.97 ± 0.56
2	15.05 ± 0.84	15.31±0.34	15.56 ± 0.32
3	51.78 ± 0.69	51.25 ± 0.79	51.55 ± 0.45
4	27.53 ± 0.86	27.89 ± 0.45	27.13 ± 0.78
5	10.05 ± 0.43	10.31±0.56	10.56 ± 0.86
6	20.33 ± 0.55	20.36 ± 0.93	20.29 ± 0.68

Data are expressed as mean ± SD (n=5). \*RP-HPLC-method using Hypersil C8 column (0.250m x 4.6mm x 5 mm) as stationary phase, and 0.02 M phosphate buffer pH 3.0 (adjusted with 1 mL triethylamine and phosphoric acid) and methanol (42:58 v/v) as mobile phase at flow rate 1.5 mL/min, with UV-detection at 270 nm

## DISCUSSION

The importance of detection and evaluation of environmental pollution has been highlighted in recent years. Potentiometric electrodes have many advantages over other techniques used in the analysis of wastewater effluents, including HPLC, because they are simple to use and inexpensive, and they have advantages such as

great selectivity and non-requirement for pretreatment of samples [18]. This study created two membrane-sensitive electrodes that may be utilized to quantify GTF accurately and selectively in unpretreated real effluent water. The operation of the electrodes was modified to achieve ideal conditions. The performance parameters: working pH, linearity ranges, selectivity, lifespan, and response time were evaluated in accordance with the IUPAC recommendations [16].

To evaluate how plasticizers affected membrane function, three plasticizer types were utilized (NPOE, 2-EHS, and DOP). The finest electrochemical sensor performance was produced by the plasticizer 2-EHS, and its manufactured membranes responded most closely to Nernstian behavior in terms of potential slope. This is due to the fact that the polarities of GTF and 2-EHS are similar.

The detection limits of the developed membranes demonstrate their exceptional sensitivity, which is appropriate for the application. They also showed quick reaction times over a variety of drug levels. These attributes are very crucial components for efficient detection and evaluation of GTF in real specimens utilizing manufactured sensors.

The produced membranes had consistent electrochemical behavior over the pH range of 1.0 to 5.0. The calibration curves indicated a considerable deviation from linearity at pH levels higher than five. Non-Nernstian slopes were seen because the decreased solubility of the drug resulted in weaker GTF ionization at higher pH levels.

The created electrodes showed outstanding stability over a three-week period, thereby indicating the values of TPB and PTA as ion-combining agents that may be used to create sensitive electrodes for measuring GTF in many types of materials. However, the stability of the fabricated sensors was drastically decreased after 21 days.

The validation approach illustrated the precision, toughness, and resilience of the suggested method. Different GTF samples were tested using the produced electrodes to assess the accuracy of the method. To demonstrate that the recommended procedure could be employed even if the experimental conditions varied somewhat, robustness and ruggedness were also carefully evaluated to establish repeatability of the method. The results obtained for these factors indicated exceptional membrane performance, as seen in Table 2.

The selectivity of the suggested method should be thoroughly examined, to be certain that the cited procedure will work even if there are multiple interferents in the actual samples. Sensor selectivity is influenced by the constituent parts of the membrane, solvent used, and the ratio of plasticizer to PVC matrix [19]. Lipophilic ionic sites enhance interfacial ion-exchange kinetics. Ionic sites TPB and PTA have been introduced to membranes that are sensitive to cations in order to provide greater selectivity and sensitivity. Preconditioning involves combining TPB or PTA with the quaternary nitrogen in GTF to a stage of equilibrium when the electrode is ready to measure level of the drug under study. Polyvinylchloride continues to be the standard regular matrix for carrier-based ISEs. Solvent polymeric membranes (plasticizers), which are needed for ion sensors, are constructed with a background of approximately 66: 33 % ratio of membrane solvent-to-PVC. The presence of this amount of plasticizer makes it possible to enhance ion mobility and provide ideal membrane physical characteristics [20].

Selectivity has a key role in ISE performance. The stereo-specificity and lipophilicity of the two competing species in the sample solution side and ion exchanger receptor are the key determinants of selectivity [21]. Several interfering substances that are frequently found in drug industry effluent water were investigated. Various inorganic salts were utilized as interferents. Additionally, fluoroquinolones with chemical structures similar to GTF (ciprofloxacin hydrochloride and norfloxacin hydrochloride) were studied. The calculated PSCs showed that the built-in membranes displayed exceptional selectivity.

The suggested method is distinct since there has not been much work done on the potentiometry detection of GTF in real wastewater effluents. In comparison with the other analytical approaches employed for GTF analysis, the non-requirement for sample pre-treatment indicates the uncomplicated nature of the method. Moreover, the suggested procedure is very economical because the cost per sample is low. A steady and quick potential response was attained over large concentration and pH ranges, indicating the suitability of use of the suggested method for GTF analysis in real wastewater effluents.

## CONCLUSION

The produced electrodes have been successfully used for GTF quantification in actual samples of wastewater effluents without sample

pretreatment. The membranes are useful for quick, easy, sensitive, and selective quantification of GTF in actual wastewater effluents without sample preparation.

## DECLARATIONS

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### *Ethical approval*

None provided.

### *Availability of data and materials*

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### *Conflict of Interest*

No conflict of interest associated with this work.

### *Contribution of Authors*

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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