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Ultrasensitive Electrochemical Approach for Gemifloxacin Mesylate Monitoring and Quantification by Different Voltammetric Methods

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The voltammetric behavior of the Gemifloxacin mesylate (GFX) on hanging mercury dropping electrode (HMDE) was studied using three different voltammetry modes. A well-defined cathodic peak was obtained in acetate buffer pH 5.0. An irreversible and diffusion controlled peak was characterized. The relationships between the current and the concentration of the investigated drug were plotted and displayed linearity over the concentration ranges of 0.01- 0.19 µg mL^{-1}, 0.006 – 0.13 µg $mL^{-1}$and 0.008– 0.27 µg mL^{-1} with minimum detection limits of 1.49, 2.06 and 2.34 *n*g mL^{-1} using DPV, SWV and CV modes, respectively. The suggested electrochemical approaches were successfully used to determine GFX in commercial products such as tablets, and the outcome data were analyzed statistically and their agreement with those from previously conducted spectrophotometric method was evaluated. The simplicity and potential sensitivity of the suggested approaches allows the assay of GFX in the bio-media. The reaction pathway was postulated.

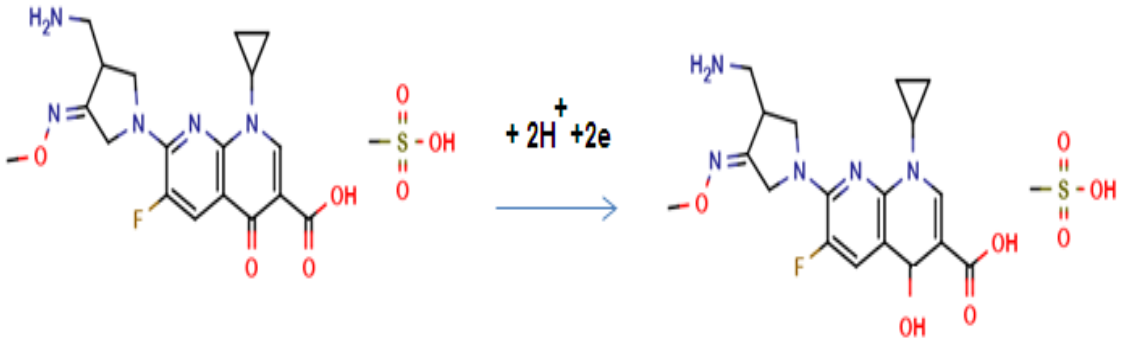
Keywords: Gemifloxacin mesylate; Electrochemical study; Three voltammetric modes; biological applications

1. INTRODUCTION

The voltammetry approaches are active techniques based on applying a controlled potential to the electrochemical cell and monitoring the outcome current flow. The electrochemical cell composed of three different electrodes, the working, reference and counter electrodes [1]. The used potential causes a change in the electroactive species concentration at the surface of the working electrode by electrochemical oxidizing or reducing it [2]. These techniques demonstrated various analytical

advantages such as excellent sensitivity to quantify organic and inorganic substances with useful and wide linear concentration ranges. Also, they can be applied using a wider temperature range, consumed very fast time of analysis (few seconds), and the chemists can study the kinetic and mechanistic parameters [3]. The analytical chemists pay their attention to use voltammetric techniques in different media to carry out elementary studies of redox reactions, adsorption processes on the surfaces and they are considered as impact and effective tools in the analysis of complex mixtures.

Gemifloxacin (GFX) is known by its powerful activity against broad spectrum bacteria [4]. Its mesylate derivative is a synthetic fluorinated quinolone which is recommended for oral administration. It was discovered by Hong et al. [5] in free base or mesylate salt (Scheme 1).



Scheme 1. Structural formula of gemifloxacine mesylate and mechanism of electrode reaction for the reduction of GFX at HMDE

The literature review addressed various analytical approaches for the estimation of GFX in pharmaceuticals and bio-samples. Among these approaches are electrochemical sensors [6], voltammetry [7,8], spectroscopic methods such as spectrofluorimetry [9-11], spectrophotometry [12-14] and chemiluminescence [15]. In addition, various chromatography and separation techniques were suggested [16-21].

The objective of this study is the exploiting of three different electrochemical modes to determine GFX in its tablets and spiked bio-fluids using hanging mercury dropping electrode (HMDE).

2. EXPERIMENTAL

2.1 Apparatus

This study was conducted using a 797 VA Computrace, (Metrohm, Switzerland), the device was connected to Dell Dell computer which programed by control software (VA Computrace 2.0). The pH of supporting electrolytes was adjusted using HANNA pH-211- Romania pH-meter.

2.2 Materials and reagents

Tabuk pharmaceuticals, MFG. Co., Saudi Arabia supplied GFX and its tablets (Factive® 320 mg/tablet). The following reagents were used: Britton-Robinson (B-R) buffers (0.08 mol L^{-1}), of pH 2-

12, acetate buffer (0.2 mol L^{-1}), of pH 2.75 - 5.5, phosphate buffer (0.1 mol L^{-1}) of pH 5.8 - 8, and borate buffer (0.1 mol L^{-1}) of pH 7.6-12.3, were prepared using distilled water [22], and used as supporting electrolytes. Commercial serum samples (Multi-Serum Normal, Ranbdox Laboratories UK) were deproteinated using acetonitrile (BDH Ltd, Pool, UK). The urine samples were gained from healthy volunteers and informed consent was taken before starting this study.

2.3 Analytical procedures

2.3.1 Analysis of standard GFX

To carry out the analysis of GFX, the voltammetric cell was cleaned and dried and 25 mL of acetate buffer of pH 5 was added as supporting electrolyte, followed by the addition of the required working solutions of GFX. Nitrogen gas was used for 5 min to purge the test solution. The voltammograms were recorded using DPV, SWV and CV modes. The peak current was plotted as a function of concentration of GFX to construct the calibration graphs.

2.3.2 Analysis of GFX in Tablets

In order to analyze GFX in the tablets, not less than five of FACTIVE® tablets (320 mg/tablet) were weighed and finely powdered. Approximately, 50 mL of a standard solution 1.0×10^{-3} mol L^{-1} was prepared in distilled water under sonication for 30 min, filtered and the volume was accomplished by the same solvent. The test solutions were analyzed using the same procedure as previously described.

2.3.3 Analysis of GFX in bio-media

The analysis of GFX in spiked serum samples was conducted by spiking the serum with different aliquots of GFX solution and 0.1 mL of previously spiked serum was transferred to centrifuged tubes. Approximately, 1.0 mL of acetonitrile was added, the vortex was done for 1 min then, centrifuged for 10 min at 1500 rpm. 0.1 mL volume of clear supernatant was transferred into the voltammetric cell containing a 25 mL acetate buffer of pH 5, so that the final concentration is in the range of (23.9 – 398, 11.90 – 270) $\times10^{-3}$µmol L^{-1} and 16 – 557×10^{-3} µmol L^{-1} for DPV, SWV and CV, respectively.

2.3.4 Analysis of GFX in Spiked Urine

The spiked urine samples with the required concentrations of GFX standard solution were prepared. Then, the final concentration was adjusted using 25 mL of acetate buffer of pH 5 to the ranges of (23.9 – 398, 11.90 - 270 and 16 – 557) $\times10^{-3}$ µmol L^{-1} for DPV, SWV and CV, respectively.

3. RESULTS AND DISCUSSION

The voltammetric reduction of GFX at the HMDE was investigated in the pH range 2.7-12.0 using DPV, SWV and CV. Only cathodic peak is obtained between pH 4-9, 2.7-10 and 4.5- 10 for DPV, SWV and CV, respectively. The DP, SW and CV voltammograms of 7.94×10^{-2} µmol L^{-1} GFX in acetate buffer at pH 5 were recorded (Figure 1).

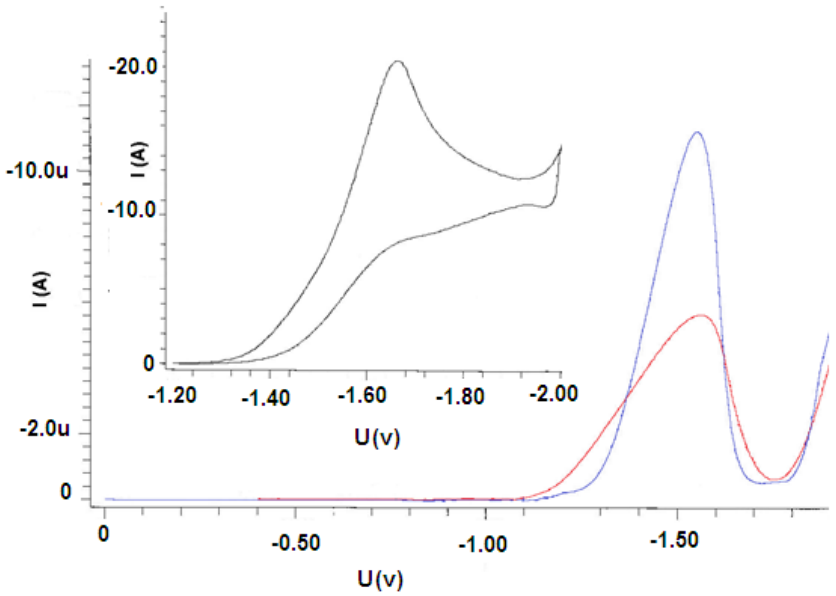


Figure 1. DPV, SWV, CV voltammograms for 0.079 µmolL^{-1} GFX at pH 5 acetate buffer, for (DPV——), pulse amplitude (E_{sw}) = 90 mV, pulse time 0.01s, voltage step ΔE_s = 8 mV and voltage step time 0.1s, for (SWV——) drop size = 4 mm^2, pulse amplitude (E_{sw}) = 80 mV, voltage step ΔE_s = 10 mV and *f* = 120 Hz, and for (CV ——) scan rate = 50 mV

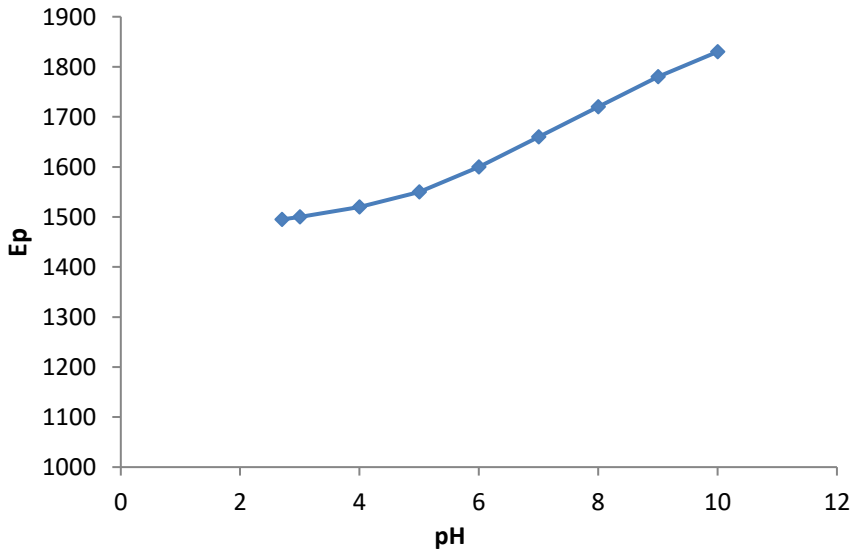


Figure 2. SWV electrode peak potential versus pH value of GFX (0.079 µmolL^{-1}), drop size = 4 mm^2, pulse amplitude (E_{sw}) = 80 mV, voltage step ΔE_s = 10 mV and *f* = 120 Hz

The experimental study clarified that the reduction of the investigated drug at the surface of HMDE is pH dependent. Upon increasing the pH, the peak potential of GFX was shifted to a more negative value in the three techniques due to the proton-transfer reaction [23] which facile excellent activity of the electrode. The peak potential of SWV (Figure 2) was plotted versus pH and two straight lines were recognized with a significant break at pH 5.5 which assigned to be corresponding to the pKa of GFX [24]. Furthermore, the cyclic voltammogram of 3.19 $\times 10^{-2}$ µmol L^{-1} GFX was recorded at pH 5 and the potential scanning is started from -1.2 V to the negative direction and reversed repeatedly at -2.0 V and -1.2 V.

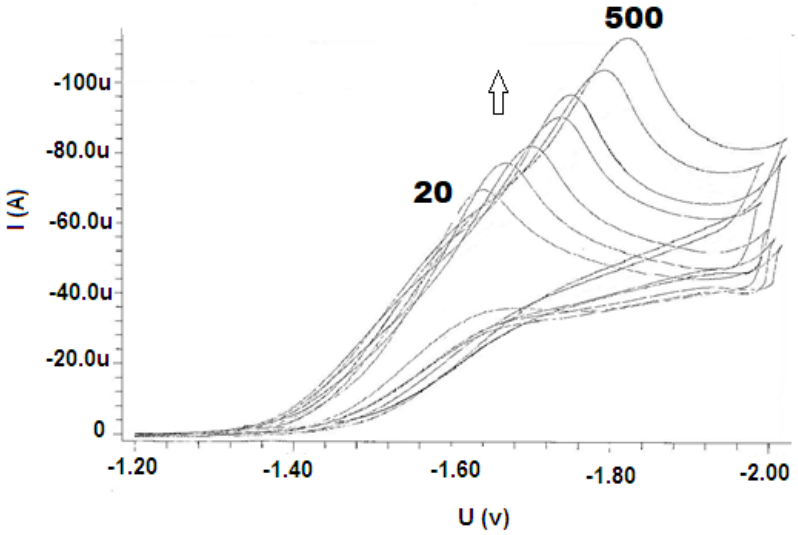


Figure 3. Cyclic voltammograms of 0.319 µmolL^{-1} GFX at pH 5, with scan rate (20-500) mV s^{-1}

The reduction peak was observed at -1.65 V due to the reduction of the C=O group in the GFX molecule (Scheme 1). The absence of oxidation peak in the positive scanning half cell proved the irreversible nature of the electrode. The cyclic voltammograms of GFX were carried out at different scan rate values over the range 20-500 mV s^{-1} and the peak current (i_p) increased with increasing in ν (Figure 3). It was observed that the peak potentials displayed a cathodic shift by elevating the scan rate, indicating the irreversible feature of the reduction process [25].

3.1 Optimization of experimental parameters

To evaluate the supporting electrolyte effect on the peak height, different types of buffers, such as Britton-Robinson, acetate, phosphate and borate buffer were investigated. The recorded results showed maximum peak currents in acetate buffer of pH 5. The cathodic peaks of drug reduction were found to be at 1.55, 1.55 and 1.65 for DPV, SWV and CV, respectively (Figure 4). It was noticed that the peak current increased by increasing the concentration of the supporting electrolyte. The high and sharp peak was recorded when 25 mL of acetate buffer was used. Therefore, 25 mL is the selected value for further experimental studies.

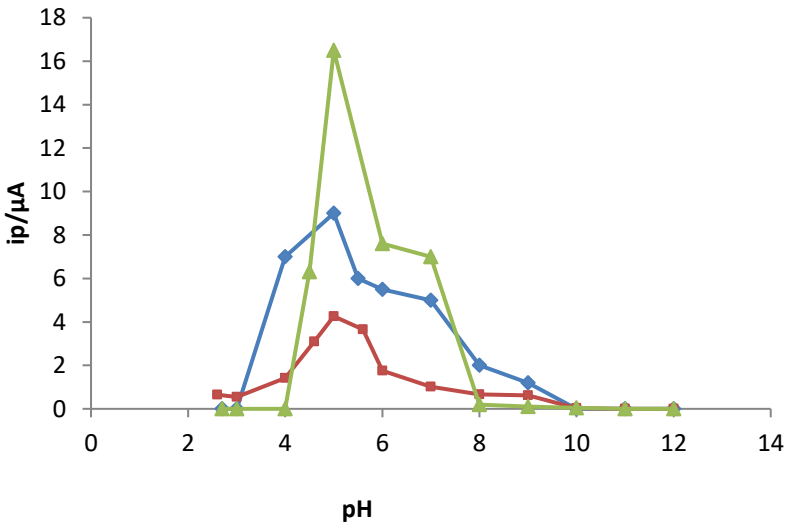


Figure 4. Effect of pH on DPV, SWV and CV peak current of GFX (0.079 µmolL^{-1}), for DPV (-♦-♦-) pulse amplitude (E_{sw}) = 90 mV, pulse time 0.01 s, voltage step ΔE_s = 8 mV and voltage step time 0.1 s, for (SWV-■-■-) drop size = 4 mm^2, pulse amplitude (E_{sw}) = 80 mV, voltage step ΔE_s = 10 mV and f = 120 Hz, and for CV (-▲-▲-) scan rate = 50 mV

3.2 Effect of instrumental parameters

Several instrumental parameters, such as drop size (1-9 mm^2), pulse amplitude (-90-90 V), pulse time (0.01-0.1 s), voltage step (1-10 V), voltage time (0.05-2 s), frequency (30-120) and scan rate was optimized. It was found that for DPV higher peak currents were observed with: pulse amplitude (E_{sw}) = 90 mV, pulse time 0.01 s, voltage step ΔE_s = 8 mV and voltage step time 0.1 s. The optimal instrumental variables for SWV were: drop size = 4 mm^2, pulse amplitude (E_{sw}) = 80 mV, voltage step ΔE_s = 10 mV and frequency (f) = 120 Hz. For CV the optimal conditions were: the initial potential was -1.2V, the final potential was about -2.0 and scan rate = 50 mV, (Figures 5-7).

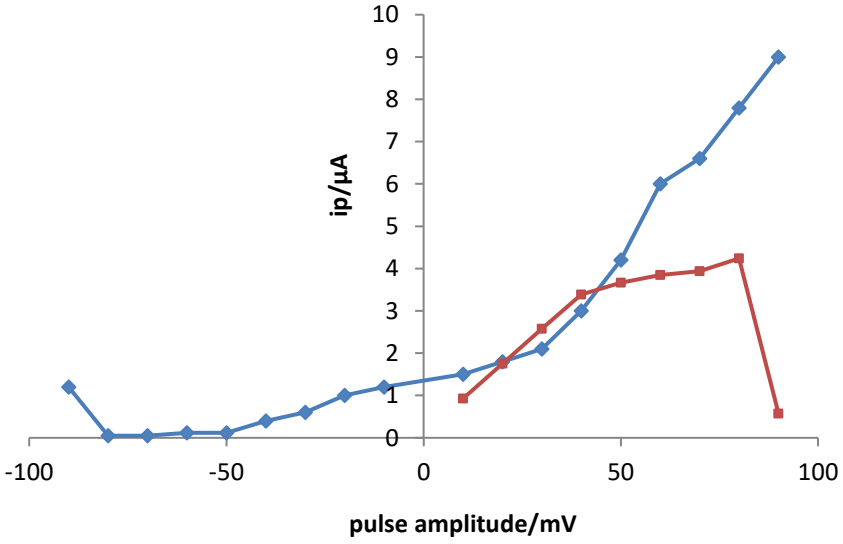


Figure 5. Effect of pulse amplitude on DPV, SWV peak current of GFX (0.079 µmolL^{-1}), for DPV (-♦-♦-) pulse time 0.01 s, voltage step ΔE_s = 8 mV and voltage step time 0.1 s, for (SWV-■-■-) drop size = 4 mm^2, voltage step ΔE_s = 10 mV and f = 120 Hz

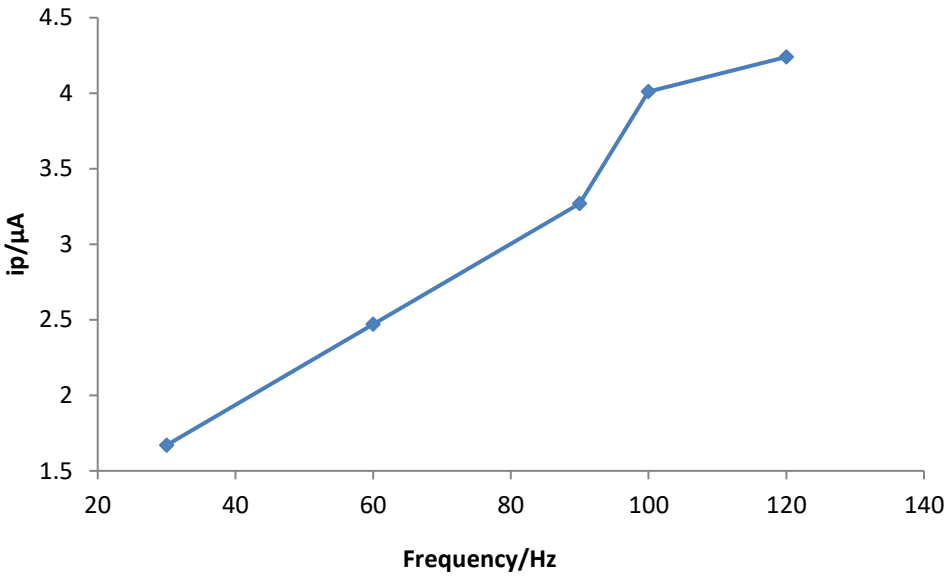


Figure 6. Effect of frequency (*f*) on SWV peak current of GFX (0.079 µmol L^{-1}), drop size = 4 mm^2, pulse amplitude (E_{sw}) = 80 mV and voltage step ΔE_s = 10 mV

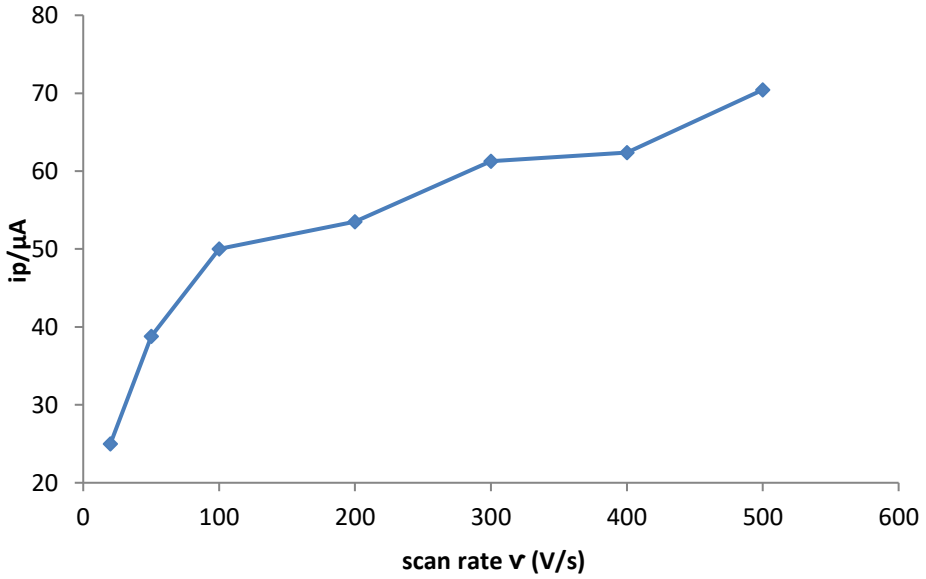


Figure 7. Effect of scan rate on CV peak current of GFX (0.32 µmol L^{-1})

3.3 Method Validation

The proposed DPV, SWV and CV methods for determination of GFX displayed linear relationships were obtained over the ranges (23.9 – 398, 11.90 - 270 and 16 – 557) × 10^{-3} µmol L^{-1} for DPV, SWV and CV, respectively. Table 1 showed the characteristic data for the three proposed methods. The limits of detection (LOD) and quantification (LOQ) were determined using 3.3 S_a/b and 10 S_a/b respectively, where S_a is the standard deviation of the intercept, and b is the slope. The values of LOD and LOQ are listed in Table 1.

Table 1. Performance data of the determined GFX by the proposed DPV, SWV and CV methods

Parameter	DPV	SWV		CV
		Low	High	
Concentration range (µg mL^{-1})	0.01-0.19	0.006-0.023	0.023-0.130	0.008-0.27
Concentration range (µmol L^{-1})	0.02-0.40	0.01-0.06	0.06-0.27	0.016-0.557
Regression equation	Y= 75.48x + 3.008	Y= 50.50x + 1.123	Y= 6.846x + 3.660	Y= 91.03x + 9.519
SD of slope (S_b)	0.351	1.859	0.157	0.445
SD of intercept (S_a)	0.070	0.065	0.028	0.133
Number of points (n)	9	7	7	10
Coefficient of correlation	---	0.997	0.999	0.999
LOD (nmol L^{-1})	3.06×10^{-3}	4.25×10^{-3}	-	4.82×10^{-3}
LOQ (nmol L^{-1})	9.27×10^{-3}	0.01	-	0.015

Table 2. Intra-day and inter-day precision of GFX using the proposed DPV, SWV and CV methods

		Intra-day				Inter-day			
	*Taken	*Found	Mean±SD	RSD %	Error %	*Found	Mean±SD	RSD %	Error %
DPV	3.19×10^{-2}	3.17×10^{-2}	99.48±0.18	0.19	0.11	3.18×10^{-2}	99.69±0.32	0.32	0.18
	16.00×10^{-2}	15.93×10^{-2}	99.59±0.96	0.96	0.55	16.03×10^{-2}	100.21±1.30	1.3	0.75
	39.80×10^{-2}	39.83×10^{-2}	100.08±0.14	0.14	0.08	39.90×10^{-2}	100.25±0.25	0.25	0.14
SWV	2.4×10^{-2}	2.38×10^{-2}	99.30±0.48	0.48	0.28	2.39×10^{-2}	99.72±0.64	0.64	0.37
	7.94×10^{-2}	7.92×10^{-2}	99.71±0.19	0.19	0.11	7.91×10^{-2}	99.58±0.32	0.32	0.18
	23.4×10^{-2}	23.32×10^{-2}	99.64±0.30	0.3	0.17	23.2×10^{-2}	99.15±0.43	0.43	0.25
CV	7.99×10^{-2}	7.97×10^{-2}	99.75±0.25	0.25	0.14	7.94×10^{-2}	99.41±0.62	0.63	0.36
	23.90×10^{-2}	23.7×10^{-2}	99.02±0.64	0.64	0.37	23.80×10^{-2}	99.58±0.42	0.42	0.24
	31.90×10^{-2}	31.83×10^{-2}	99.79±0.79	0.79	0.46	31.63×10^{-2}	99.17±0.48	0.48	0.28

*****Taken and Found (µmol L^{-1})

Table 3. Analytical results of GFX analysis in pure and dosage forms using DPV, SWV, CV and reference methods

Formulation	Proposed methods									Reference method
	DPV			SWV			CV			
	*Taken	*Found	Recovery %	*Taken	*Found	Recovery %	*Taken	*Found	Recovery %	Recovery %
Pure form	3.2×10^{-2}	3.17×10^{-2}	99.37	1.19×10^{-2}	1.19×10^{-2}	100	1.60×10^{-2}	1.61×10^{-2}	100.63	98.00
	3.9×10^{-2}	3.95×10^{-2}	99.25	3.19×10^{-2}	3.16×10^{-2}	99.06	3.98×10^{-2}	3.97×10^{-2}	99.75	99.94
	4.8×10^{-2}	4.79×10^{-2}	100.21	4.00×10^{-2}	3.99×10^{-2}	99.75	7.99×10^{-2}	7.98×10^{-2}	99.87	99.75
	16.0×10^{-2}	15.8×10^{-2}	98.75	7.94×10^{-2}	7.93×10^{-2}	99.87	23.9×10^{-2}	23.7×10^{-2}	99.16	99.91
	23.9×10^{-2}	23.7×10^{-2}	99.16	15.7×10^{-2}	15.5×10^{-2}	98.73	31.9×10^{-2}	31.6×10^{-2}	99.06	99.60
	31.9×10^{-2}	31.8×10^{-2}	99.69	27.0×10^{-2}	26.8×10^{-2}	99.22	47.8×10^{-2}	47.5×10^{-2}	99.37	99.82
Mean±SD	99.41±0.5			99.44±0.5			99.64±0.6			99.50±0.8
F-test	2.24 (5.05)**			2.15 (5.05)**			1.65 (5.05)**			
t-test	0.25(2.23)**			0.16 (2.23)**			0.36 (2.23)**			
Factive® 320 mg/tablet	3.2×10^{-2}	3.18×10^{-2}	99.69	1.19×10^{-2}	1.18×10^{-2}	99.16	1.60×10^{-2}	1.59×10^{-2}	99.38	99.33
	3.9×10^{-2}	3.97×10^{-2}	99.75	3.19×10^{-2}	3.17×10^{-2}	99.37	3.98×10^{-2}	3.96×10^{-2}	99.50	99.71
	4.8×10^{-2}	4.76×10^{-2}	99.58	4.00×10^{-2}	3.98×10^{-2}	99.50	7.9×10^{-2}	7.98×10^{-2}	99.75	98.75
	16.0×10^{-2}	15.9×10^{-2}	99.38	7.94×10^{-2}	7.95×10^{-2}	100.13	23.9×10^{-2}	23.8×10^{-2}	99.58	99.11
	23.9×10^{-2}	23.9×10^{-2}	100.00	15.7×10^{-2}	15.6×10^{-2}	99.36	31.9×10^{-2}	31.6×10^{-2}	99.75	99.6
	31.9×10^{-2}	31.7×10^{-2}	99.37	27.0×10^{-2}	26.8×10^{-2}	99.37	47.8×10^{-2}	47.5×10^{-2}	99.16	99.82
Mean±SD	99.41±0.5			99.48±0.3			99.35±0.4			99.38±0.4
F-test	2.24			0.37 (5.05)**			1.15(5.05)**			
t-test	0.25			0.47 (2.24)**			0.14 (2.24)**			

*****Taken and Found (µmol L^{-1}), **Theoretical values for t-student's and F-test at 95% confidence limit (n=6) were 2.23 and 5.05 respectively

The repeatability was conducted through the analysis of three concentrations of GFX in pure form adopting the three voltammetric modes (DPV, SWV and CV) on three successive times (Table 2). The validity of the suggested electrochemical methods [26] was evaluated as summarized in Table 3. The results obtained from the previously reported spectrophotometric method [12] were used for a comparative study. Using Student's t-test and Variance ratio F-test, [27] revealed an excellent agreement between the two methods regarding accuracy and precision, respectively.

The selectivity of the optimized procedures was tested by analyzing the investigated drug in the presence of additives such as polyethylene glycol, microcrystalline cellulose, crospovidone, hydroxypropyl methylcellulose, titanium dioxide, magnesium stearate, and povidone) in FACTIVE® tablets. In the presence of these additives, no significant interfering were observed, indicating high selectivity of the suggested methods.

3.4 Analytical applications

3.4.1 Analysis of Factive® tablets

The validity of developed DPV, SWV and CV procedures were tested by determining GFX in its pharmaceutical formulations. Recoveries of GFX in its dosage forms, based on the average of three replicate measurements, are illustrated in Table 3. Due to the calculated t-value and Variance ratio less than those of the theoretical one, no significant difference between both proposed and previously published methods with respect to accuracy and precision.

3.4.2 Analysis of spiked bio-fluids

Table 4. Results of analysis of GFX in biological fluids by the proposed DPV, SWV and CV methods

Proposed methods		Serum		Urine	
	*Taken	*Found	Recovery %	*Found	Recovery %
DPV	2.39×10^{-2}	2.38×10^{-2}	99.58	2.39×10^{-2}	100.00
	7.99×10^{-2}	8.00×10^{-2}	100.13	7.98×10^{-2}	99.87
	16.00×10^{-2}	15.90×10^{-2}	99.38	15.80×10^{-2}	98.75
	23.90×10^{-2}	24.00×10^{-2}	100.41	23.80×10^{-2}	99.58
	31.90×10^{-2}	31.80×10^{-2}	99.69	31.70×10^{-2}	99.37
	39.80×10^{-2}	39.70×10^{-2}	99.75	39.90×10^{-2}	100.25
		Mean ±SD	99.82±0.38	Mean ± SD	99.64±0.53
	*Taken	*Found	Recovery %	*Found	Recovery %
SWV	1.60×10^{-2}	1.59×10^{-2}	99.38	1.58×10^{-2}	98.75
	2.40×10^{-2}	2.38×10^{-2}	99.17	2.39×10^{-2}	99.58
	3.59×10^{-2}	3.60×10^{-2}	100.28	3.58×10^{-2}	99.72
	5.96×10^{-2}	5.95×10^{-2}	99.83	5.94×10^{-2}	99.66
	12.00×10^{-2}	11.92×10^{-2}	99.33	11.92×10^{-2}	99.17
	23.40×10^{-2}	23.30×10^{-2}	99.57	23.25×10^{-2}	99.36
		Mean ±SD	99.59±0.41	Mean ±SD	99.37±0.37
	*Taken	*Found	Recovery %	*Found	Recovery %
	3.98×10^{-2}	3.97×10^{-2}	99.75	3.94×10^{-2}	98.99
	7.99×10^{-2}	7.95×10^{-2}	99.5	7.98×10^{-2}	99.87
	23.9×10^{-2}	23.8×10^{-2}	99.58	2.4×10^{-2}	100.42

CV	31.9×10^{-2} 39.8×10^{-2} 47.8×10^{-2}	32.0×10^{-2} 39.9×10^{-2} 47.3×10^{-2}	100.31 100.25 98.95	31.7×10^{-2} 4.0×10^{-2} 47.7×10^{-2}	99.37 100.5 99.79
		Mean ±SD	99.73±0.50	Mean ±SD	99.82±0.59

*****Taken and Found (µmol L^{-1})

GFX is rapidly absorbed after oral administration [28]. C_{max} was achieved after 1 h dosing and the mean C_{max} value was found as 1.48 ± 0.39 µg mL^{-1} following a single oral dose of 320 mg GFX. This concentration is much higher than the LOQ of the proposed method (4.50, 6.26 and 7.09 ng mL^{-1}) for DPV, SWV and CV, respectively.

Figures 8a, 8b and 8c, illustrated the DPV, SWV and CV voltammetric response of different concentrations of spiked serum and urine. The bio-fluids outcome results were summarized in Table 4. A comparative study was carried out between the current electrochemical approaches and other reported analytical methods. The proposed electrochemical methods using different voltammetric modes DPV, SWV and CV displayed more sensitivity, and simplicity rather than other methods (Table 5).

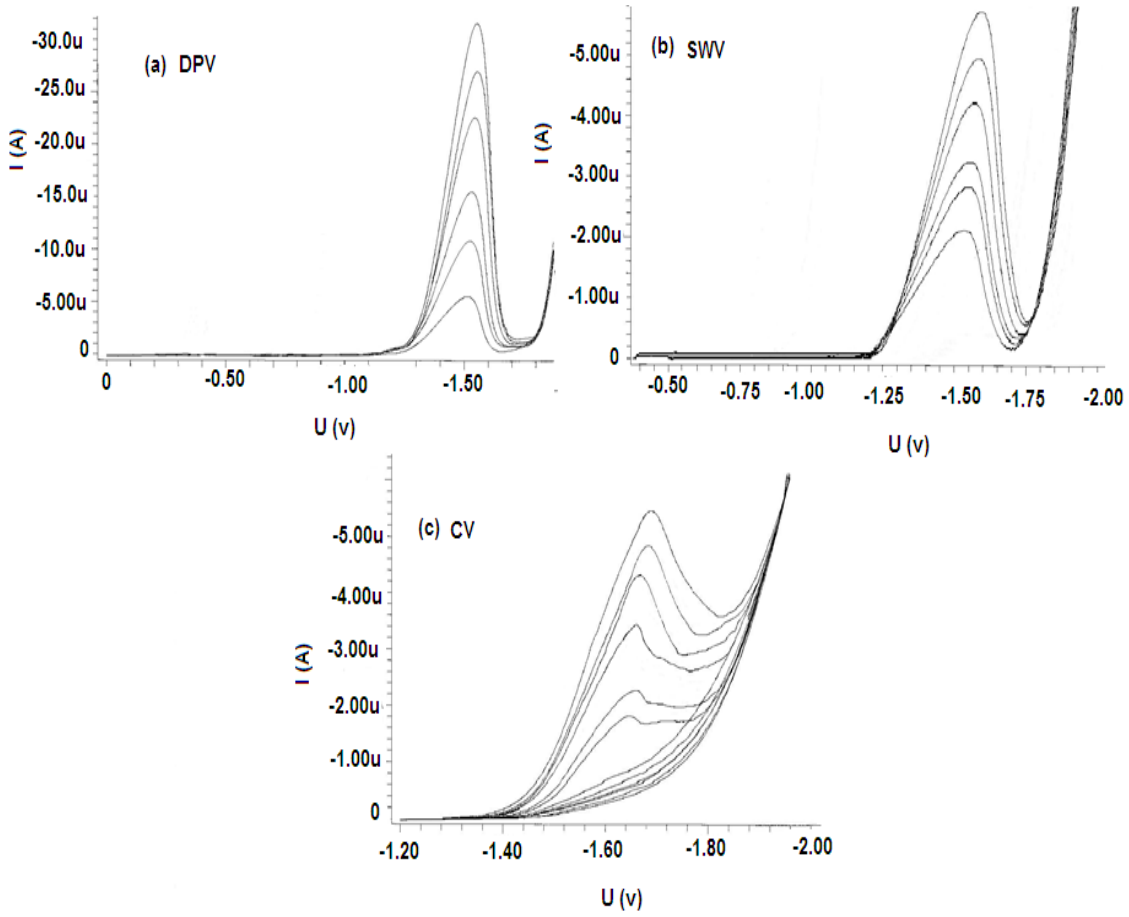


Figure 8. (a) DPV voltammograms for different concentrations of GFX in serum samples, pulse amplitude (E_{sw}) = 90 mV, pulse time 0.01 s, voltage step ΔE_s = 8 mV and voltage step time 0.1 s, (b) SWV voltammograms for different concentrations of GFX in serum samples, drop size = 4 mm^2, pulse amplitude (E_{sw}) = 80 mV, voltage step ΔE_s = 10 mV and f = 120 Hz and (c) CV voltammograms for different concentrations of GFX in serum samples, scan rate = 50 mV

Table 5. Comparative study of the suggested electrochemical methods and the previously reported analytical methods

Methods	Linear range	**LOD**	**LOQ**	Reference
The proposed:				-
DPV	0.01-0.19 µg mL^{-1}			-
SWV	0.006-0.13 µgmL^{-1}			-
CV	0.008-0.27 µgmL^{-1}			-
RP-HPLC/UV	1-6 µgmL^{-1}	0.57 µgmL^{-1}	1.72 µgmL^{-1}	[17]
Capillary electrophoresis	5-50 µg/mL	2.93 µgmL^{-1}	4.91 µgmL^{-1}	[20]
Fluorimetry	1-20 *n*g mL^{-1}	0.18 *n*g mL^{-1}	0.54 *n*g mL^{-1}	[10]
UV-visible spectrophotometry	1-30 µg mL^{-1}	0.23 µg mL^{-1}	0.77 µg mL^{-1}	[14]
Chemiluminescence	0.001- 0.3 µg/mL^{-1}	7.3×10^{-4} µg mL^{-1}	…	[15]
Ion Selective electrodes	1.0×10^{-5}- 1.0×10^{-2} mol L^{-1}	0.02 µgmL^{-1}	…	[6]
Voltammetry	0.5-10.0 µmol L^{-1}	0.15 µmol L^{-1}	5.0 µ mol L^{-1}	[7]

4. CONCLUSION

This study concerned with the development of simple, rapid, and sensitive electrochemical methods for determination of GFX in the bulk form, pharmaceuticals and biological fluids. The suggested electrochemical methods depended on employing three different voltammetric modes DPV, SWV and CV for quantifying the selected drug. The suggested methods exhibited an excellent sensitivity and a high selectivity proving their suitability for determination of study compound in dosage forms and biological fluids. The suggested electrochemical methods revealed clear impact advantages such as the short time of analysis, no required pre-treatment of samples, no high technical skills are needed and no extraction or large amount of solvents are necessary. The outcome results encourage the quantify of the investigated drug in bio-samples such as human serum and urine. Furthermore, the comparative study which was carried out between the suggested electrochemical methods and the previously described spectroscopic and chromatography techniques proved the simplicity and reproducibility of the suggested methods for the determination of GFX in different forms and media.

CONFLICT OF INTEREST

The authors of this study clarified that no any conflict of interest associated with it.

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