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Full Paper

Square Wave Voltammetric and Ion Selective Potentiometric Strategies for Spiramycin Determination in Pharmaceutical Formulations

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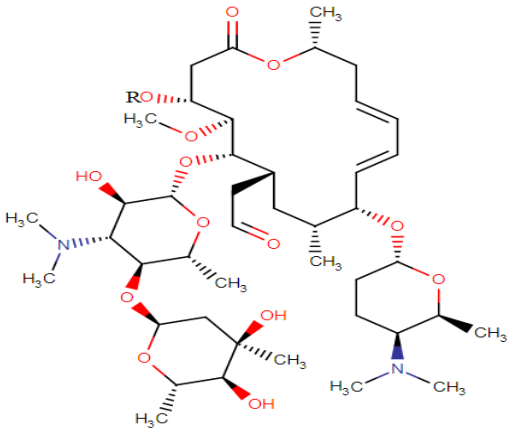
Abstract- Herein, two electrochemical methods are suggested for the determination of spiramycin (SPI) in pharmaceutical finished products. The first method is based on square wave voltammetric strategy (SWV) for the oxidation of SPI at a carbon paste electrode in a surfactant-containing electrolyte. Studying the cyclic voltammetry of SPI showed that the electrochemical oxidation process of SPI is irreversible with a peak current at 0.87 V in Britton-Robinson buffer (pH 9.0). Several important parameters including the influence of surfactants, the pH of the electrolyte and the rate of scan on the peak current were investigated. Under optimal experimental conditions, a linear response was obtained in the concentration range from 5 μM to 450 μM. The second method aims at the fabrication and characterization of a potentiometric homemade screen-printed electrode for the cost-effective determination of SPI. A Nernstian potentiometric response for SPI was achieved using potassium tetrakis (*p*-chlorophenyl) borate (KTpClPB) as a lipophilic ion exchanger in a polymeric PVC membrane over the concentration range from 1×10^{-6} to 1×10^{-2} M. However, the effect of membrane composition with respect to the ion exchanger and the plasticizers on the potentiometric response was remarked. The proposed voltammetric and potentiometric methods were successfully applied for the determination of SPI in bulk powder, in pharmaceutical formulations and monitoring SPI in natural water without extraction or sample pre-treatment.

Keywords- Spiramycin; Square wave voltammetry; Potentiometry; Screen printed electrode

1. INTRODUCTION

Macrolides are bacteriostatic or bactericidal antibiotics which could interfere with bacterial protein synthesis [1]. Besides their antibacterial effect, macrolides have been shown to have immune-modulatory and anti-inflammatory effect [2-4]. Furthermore, it has recently been predicted that macrolides would be an effective adjunctive therapy for Covid-19 pandemic disease which has been risen causing a great threat to both human and economy all over the world [5,6]. Spiramycin (Figure 1) is a 16-membered macrolide antibacterial produced by Streptomyces ambofaciens [7]. Like erythromycin, it is used for the treatment of susceptible bacterial infections. Also, it is used in the protozoal infections cryptosporidiosis and toxoplasmosis [1].



Spiramycin I R=H

Spiramycin II R=$COCH_3$

Spiramycin III R=$COCH_2CH_3$

Figure 1. Chemical structure of spiramycin (SPI)

Several analytical methods were proposed for the determination of SPI either alone or with other drugs. These methods include liquid chromatographic methods [8-13] and spectrophotometric [14]. However, the proposed methods are either use sophisticated techniques, which are not available in laboratories for routine analysis, or they use hazardous solvents. Even though spectrophotometric methods would provide a simple inexpensive tool, they depend on complex formation with several preparations and optimization steps that undermine the simplicity of the method.

Contrary to the reported methods, electroanalytical methods are simple and inexpensive tools with fast response and high sensitivity. To best of our knowledge only DPP and SWP on hanging dropping mercury electrodes were developed for studying the reduction process of (SPI) [15]. However, mercury has the disadvantage of being poisonous and difficult to handle.

Surfactants have the tendency to be adsorbed at the interface between electrode and solution. This phenomenon influences the electrochemical processes and the rate of electron transfer at the electrode solution interface [16,17]. Thus, surfactants can help improve the sensitivity and selectivity of electroanalytical methods [18-21].

Potentiometric ion selective electrodes (ISE) are simple and inexpensive tools with the capabilities of performing measurements in turbid samples [22,23]. A great attention has recently been focused on disposable screen printed ISEs owing to their simple planar design, production on a large scale as well as the small samples required for analysis [24]. These advantages made them desirable for rapid and in line-analysis [25,26].

In this work, we report for the first time SWV method for the determination of SPI at carbon paste electrode surface in a surfactant containing electrolyte. Furthermore, a home-made disposable screen-printed ISE was developed and fully characterized for the determination of (SPI) in the drug substance and finished pharmaceutical products; and in the environmental monitoring of SPI in natural water.

2. EXPERIMENTAL SECTION

2.1. Materials and reagents

Spiramycin adipate was obtained from Lide pharmaceuticals, China (Purity= 96.10%). Britton–Robinson (BR) buffer was prepared by mixing equal volumes of 0.04 M phosphoric acid (Piochem Co., Egypt), 0.04 M acetic acid (Adwic Co., Egypt) and 0.04 M in boric acid (Adwic Co., Egypt). Buffer solutions with variable pH values (pH 2-11) were obtained by adjusted the pH with sodium hydroxide solution. Graphite powder, cetyltrimethylammonium bromide (CTAB) as well as paraffin oil were purchased from Sigma–Aldrich; sodium dodecyl sulfate (SDS) was supplied by Adwic Co., Egypt. Tween 20 was obtained from Loba Chemie Co., India. Membrane matrix components including high molecular weight Poly (vinyl chloride) and di-butyl phthalate (DBP) were purchased from Sigma-Aldrich, St. Louis, USA. Different plasticizers including 2-nitrophenyl octylether (*o*-NPOE), sodium tetraphenylborate (Na-TPB) and tricresyl phosphate (TCP) were obtained from Fluka co., Switzerland. Potassium tetrakis(4-chlorophenyl)borate, a lipophilic ion exchanger, was purchased from Alfa Aesar. Volatile organic solvent such as tetrahydrofuran (THF) was purchased from Sigma-Aldrich, Germany. All measurements were carried out using double distilled water unless otherwise stated.

2.2. Standard solution

The standard stock solution of SPI (10.0 mM) was prepared into 10-mL volumetric flask by dissolving 98.8 mg of SPI in 10.0 mL water.

2.3. Pharmaceutical formulations

Spyratech® oral solution (batch number: SPY-001) containing 234.67 mg spiramycin adipate per 1.0 gram was obtained from Infinity Company, Cairo, Egypt. Spirex® 1.5 M.I.U film film-coatedets containing 468.75 mg spiramycin per tablet (3200 unites of SPI are contained in 1 mg) [27], was obtained from MUP Company, Cairo, Egypt.

2.4. Apparatus

Bio-logic SP 150 electrochemical workstation with a three-electrode configured stand (model C-3). The working electrode was a carbon paste electrode (CPE, BAS model). Ag/AgCl (3 M KCl) reference electrode and Platinum wire counter electrode was from BAS, USA. All electrochemical measurements were conducted using Ag/AgCl as a reference electrode, the potentiometric ion-selectiveectrode measurements were carried out using a Jenway 3510 pH/mV meter. The cell used for the potentiometric measurements is represented as Ag/AgCl / 3 M KCl // sample /ion-selectivectrode.

2.5. Procedures

2.5.1. Voltammetric method

2.5.1.1. Preparation of working electrode

The CPE was prepared by mixing 0.5 g of graphite powder with 0.3 mL paraffin oil in a mortar; the mixture was well homogenized using a pestle. The paste was pressed into the hole of the electrode and smoothed using a filter paper until the surface was shiny**.**

2.5.1.2. Analytical procedure

The CPE was immersed in the electrolyte solution, BR (pH 9.0), and the CV was recorded between 0 and 1.4 V and repeated several times until a stable CV was obtained. The electrode was subsequently transferred into another cell containing BR pH 9.0 and 0.05 mM SDS and the concentration of SPI was increased from 0.005-0.45 mM. The electrode remains 30 s under stirring at open circuit potential, then, the CV was recorded**.**

2.5.1.3. Construction of calibration curve

Different aliquots of SPI standard solution were accurately transferred to the electrolytic cell. BR buffer pH 9.0 containing 0.05 mM SDS was added. The calibration curve was constructed in the concentration range from 0.005 - 0.45 mM by recording the SWV for each concentration and plotting the anodic peak current versus the concentration of the drug in µM**.**

2.5.2. Potentiometric method

2.5.2.1. Preparation of ion associate

Spiramycin-tetraphenyl borate (SPI-TPB) ion associate was prepared by dropwise addition of 50 mL of 0.01 M of Na-TPB to an equal volume of 0.01 M of the drug solution. The mixture was stirred for 5 min, then, the precipitate was filtered on a filter paper and washed with distilled water several times. The collected precipitate was dried at room temperature for 48 h.

2.5.2.2. Construction of screen-printed electrodes

All electrodes were printed on a flexible PVC plastic sheet using a custom-mesh stainless steel template [24]. The electrodes (3×28 mm each) were printed in an array of four electrodes as follows: The ink was prepared by mixing graphite powder with PVC as a binder in 1:1 cyclohexanone:acetone; then, the ink was printed using a squeegee. The printed electrodes were put in an oven at 60 °C for 2 h for curing. Afterward, the ion-selective membrane with the composition of 66.0% oNPOE and 34% PVC (in THF) was printed over the graphite track by drop casting. The dried electrodes were covered with an insulating tape except and areas of 3×3 mm were left uncovered at both ends.

2.5.2.3. Construction of calibration curve

Potentiometric calibration curves were constructed by plotting the electrode potential against the drug concentration. The concentration of the drug was increased in the potentiometric cell by the addition of small aliquots of 0.01 M drug substance to 50 mL double-distilled such as to cover the concentration range from 1×10^{-6}-1×10^{-3} M. The potential readings of 3×10^{-3} and 1×10^{-2} M were recorded by dipping the working and reference electrodes in each solution separately. All measurements were carried out under constant stirring and calibration graphs were constructed by plotting the cell potential vs. -log [conc., M].

2.5.2.4. Interference effect

The separate solution method was used in this study to evaluate the selectivity of the electrode [28]. Alongside, calibration curves were constructed using the interfering ions, typically over the concentration range from 1×10^{-6} to 1×10^{-2} M**.**

2.5.3. Analytical application

4.2 ml Spyratech® oral solution (containing 989.0 mg of Spiramycin adipate) was transferred into a 100 mL volumetric flask containing 60 mL water and sonicated for 15 min, followed by adjusting the flask to the mark with water to obtain final concentration 10.0 mM. Five tablets of Spirex® were weighed accurately and grounded to fine powder. An accurate amount equivalent to 494.5 mg SPI was weighed and transferred to 50 mL volumetric flask containing 10 mL water. The flask was sonicated for 15 min and completed to the volume with water to obtain final concentration 10.0 mM. For environmental monitoring of SPI in tap water, we prepared 10.0 mM SPI in tap water by dissolving 98.8 mg of SPI standard in 10 mL. An aliquot of these solutions was then analyzed according to the proposed voltammetric and potentiometric procedures based on standard addition method.

3. RESULTS AND DISCUSSION

3.1. Voltammetric method

3.1.1. Electrochemical oxidation of SPI

The electrochemical oxidation/reduction of SPI was studied at a carbon paste electrode in a micellar medium using cyclic voltammetry (CV). The CV displayed one anodic peak of 3.0 µA at 0.87 V; no cathodic peak was observed in the reverse scan which means that the electrochemical oxidation process of SPI is irreversible (Figure 2).

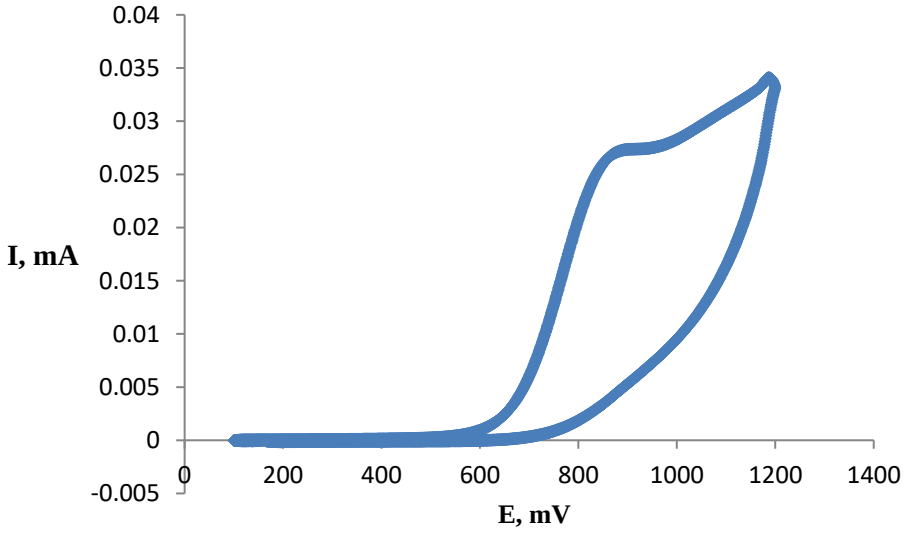


Figure 2. Cyclic voltammogram of 1.0 mM SPI in BR buffer of pH 9.0 at CPE

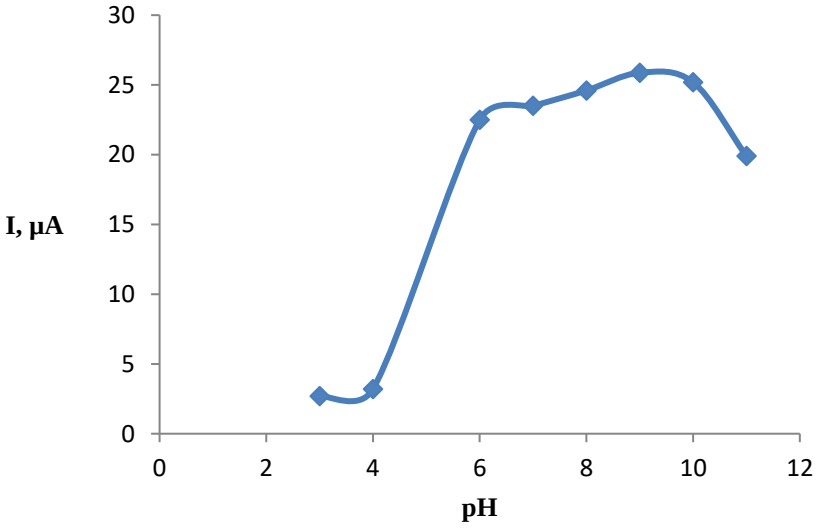


Figure 3. Anodic peak current of 1.0 mM SPI in different pH (2.0-11.0) at CPE, at scan rate 100 mV s^{-1}

3.1.2. Optimization of experimental conditions

3.1.2.1. Effect of pH

The effect of pH variation of the electrolyte on the oxidation peak of SPI was investigated using CV from 0.5-1.2 V at a scan rate of 100 mV s^{-1}. To define the optimum pH for electrochemical oxidation of SPI, the effect of pH was studied using BR buffer of variable pH (2-11) and 1.0×10^{-3} M SPI. Figure 3 shows the influence of variation of the pH on the height of the peak current. The current intensity was found to increase with increasing the pH of the medium (from 5 to 10). The maximum peak current was recorded at pH 9.0. So that, BR buffer of pH 9.0 was chosen as the optimal pH in this study.

3.1.2.2. Effect of surfactant

The anionic surfactant (SDS) was found to enhance the oxidation current of SPI. The effect of SDS was studied by changing its concentration in the electrolyte. This was carried out by the addition of different volumes from SDS solution of 10.0 mM. Plotting the peak current against the SDS concentration in the electrolyte is shown in Figure 4; the highest current signal was achieved when 0.05 mM of SDS was added to the electrochemical cell. Additionally, the effect of the cationic surfactant (CTAB) and nonionic surfactant Tween 20 on the peak current of SPI was tested at the same concentration of SDS (0.05 mM). The peak current values were 2.6 and 4.2 µA for Tween 20 and CTAB, respectively, which is below the peak current obtained using SDS (6.5 µA). Figure 5 shows the effect of surfactant on the oxidation peak current of SPI.

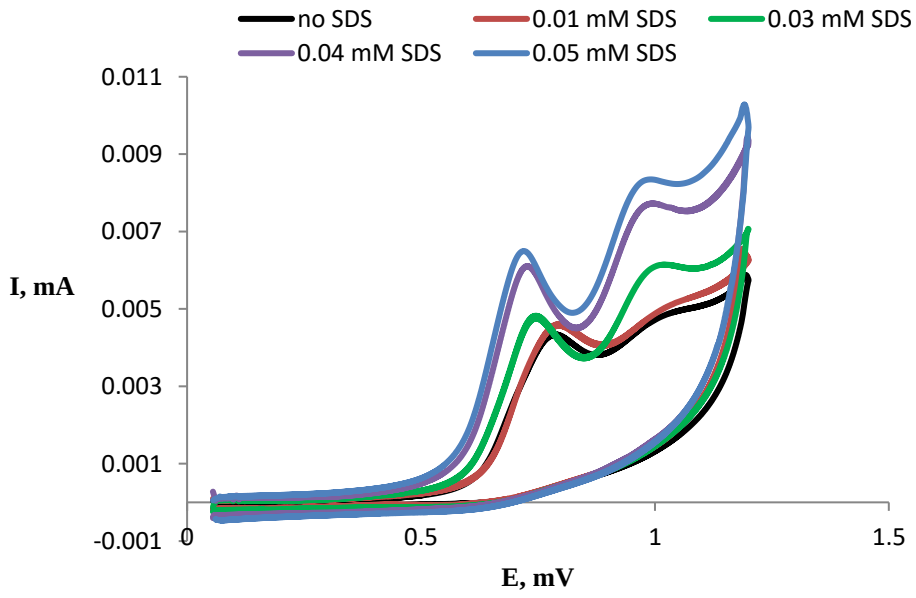


Figure 4. Cyclic voltammograms of 0.1 mM SPI in at CPE in BR buffer (pH 9.0) using different volumes (10-50 µl) SDS (10.0 mM)

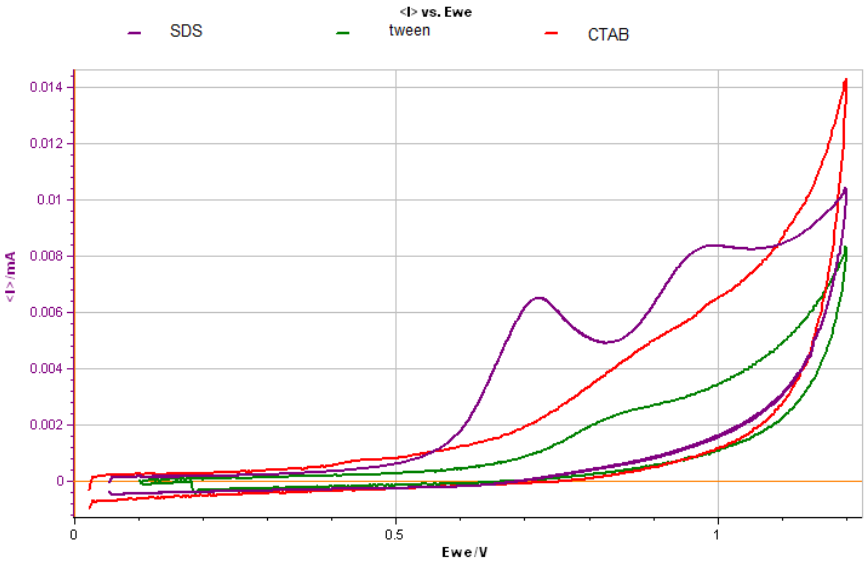


Figure 5. Cyclic voltammograms of 0.1 mM SPI at CPE in BR buffer (pH 9.0) using 0.05 mM of three different surfactants

3.1.2.3. Effect of scan rate

The effect of the speed of the CV on the electrochemical behavior of SPI in BR buffer pH 9.0 containing 0.05 mM of SDS was studied by increasing the scan rate from 50 to 300 mV s^{-1}. The current intensity increased significantly as the scan rate is raised as shown in Figure 6a.

Plotting log anodic peak current against log the scan rate in the range from 50-300 mV s^{-1} gave a straight line as shown in Figure 6b, indicating that the SPI oxidation is a diffusion-controlled process [29]. Figure 6c shows a linear relationship between the peak potential and log scan rate. According to Laviron′s equation [30]:

$$E_p = E^{o'} + (\frac{2.303RT}{\alpha nF})\log(\frac{RTk^{\circ}}{\alpha nF}) + (\frac{2.303RT}{\alpha nF})\log \upsilon \qquad (1)$$

where α is the electron transfer coefficient, k^o is the standard heterogeneous rate constant of the reaction, υ is the scan rate, and E^o refers to the formal potential, n is designated to the number of electrons involved in the electrochemical process. The value of αn was obtained from the slope of the relationship of Ep vs log υ. The slope was found to be 0.065 and αn was calculated and found to be 0.902, According to Bard and Faulkner [31] α can be calculated from the following equation:

$$\alpha = \frac{47.7}{Ep - Ep/2}\,mV \qquad (2)$$

$E^{o'}$ in Eq. (1) is the intercept of Ep versus υ curve, it is obtained by extrapolating to the vertical axis at υ = 0 [32]. αn, α, n and $E^{o'}$ calculated values are summarized in Table 1.

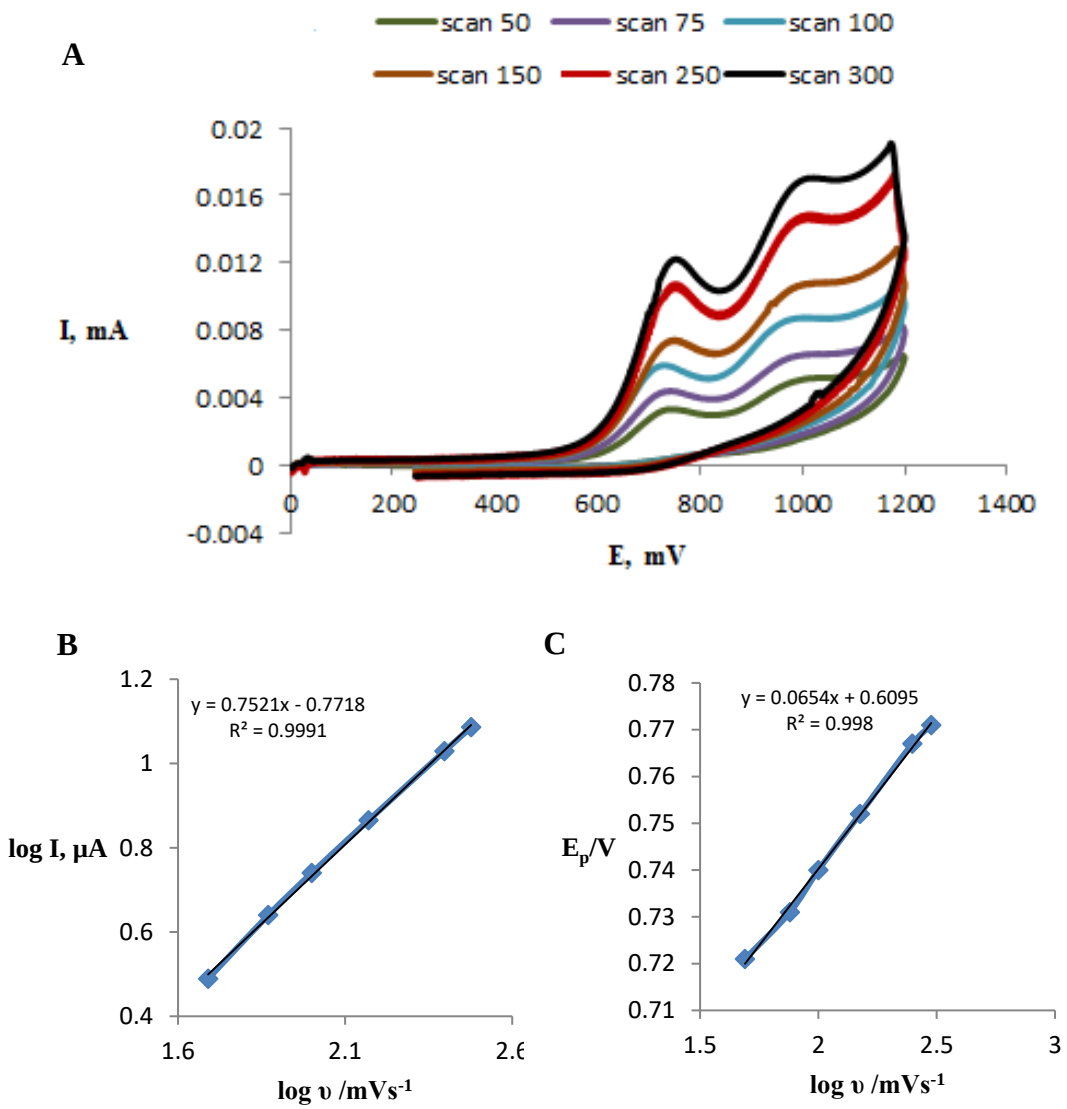


Figure 6. a) Cyclic voltammograms of 0.1 mM SPI at CPE in BR buffer (pH 9.0) using 0.05 mM SDS at different scan rates; b) Plot of log anodic peak current as a function of log scan rate on 0.1 mM SPI; c) Plot of anodic peak potential as a function of log scan rate on 0.1 mM SPI

Table 1. The calculated values of αn, α, n and $E^{0\prime}$ for the electro-oxidation of SPI by cyclic voltammetry (CV) at CPE

Parameters	**CPE**
αn	0.902
α	0.5
n	1.8
$E^{0\prime}$	0.61

3.1.2.4. Square wave voltammetry (SWV)

Figure 7 shows the SWV as a result of the addition of different concentrations of SPI to the electrolyte. Prior to measurements, the analyte solution was stirred in presence of the electrode for 30 s at 400 rpm at open circuit potential. The SWV were carried out using the following parameters: pulse height 50 mV, pulse width 50 ms and step height 10 mV. A calibration curve was constructed and a linear relationship between anodic peak current and the corresponding concentration was obtained in the range from 4.97 µM-450 µM with correlation coefficients close to unity, the LOD was found to be 0.49 µM (Table 2).

Table 2. Performance data of the proposed SWV method for determination of SPI

Parameters	**SPI**
Linearity range (µM)	4.97- 450
Slope	54.39
intercept	2.48
Correlation coefficient (r)	0.9997
LOD (µM)	0.49
LOQ (µM)	0.99
Accuracy (mean ± S.D.)	99.27 ± 1.14
Precision (RSD %)	
Inter-day	1.47
Intraday	1.03

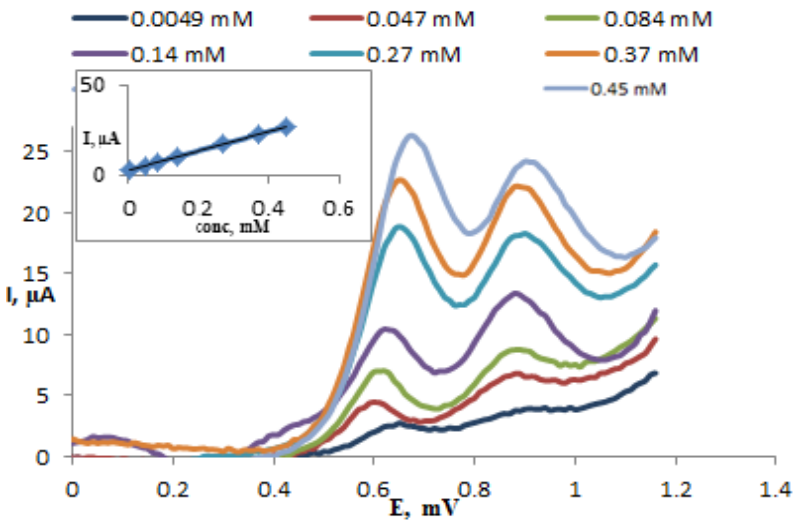


Figure 7. Square wave voltammograms of different concentrations of SPI, at CPE in BR buffer (pH 9.0) using 0.05 mM SDS

3.2. Potentiometric method

As a matter of fact, the ion exchanger and the type of the plasticizer have a great impact on the potentiometric response of an ion selective electrode. In the present study, a set of SPI selective electrodes were constructed using two different cation exchangers namely SPI-TPB and *K*(TpClPB). For each electrode, a calibration curve (E versus -log conc.) was constructed and the potentiometric characteristics comprising the value of the Nernstian slope, linearity and the limit of detection were evaluated. The potentiometric characteristics of these electrodes are summarized in Table 3. SPI-TPB based electrodes showed a non Nernstian response (≤f23.5 mV/decade) in presence of DBP, TCP or *o*-NPOE. This would be leaching the ion exchanger from the membrane into solution. In contrast, the response was dramatically improved when *K*(TpClPB), as a lipophilic cation exchanger, was incorporated into the membrane (Figure 8). A membrane containing 6 mg *K*(TpClPB) in presence of *o*-NPOE exhibited a near Nernstian response equal to 28.36±0.80 mV/decade (n=3), over range from 1×10^{-6} to 1×10^{-2} M. Whereas, sub-Nernstian responses with slopes of 26.38 and 25.38 mV/decade were obtained when oNPOE was replaced by DBP or TCP, respectively, indicating that *o*-NPOE is the best plasticizer. Thus, all subsequent measurements were carried out using an electrode containing 6 mg KTpClPB, 100 mg *o*-NPOE and 200 mg PVC. The potentiometric characteristics [33] of the sensors were calculated and summarized in Table 4.

Table 3. Composition and analytical performance of SPI-SPEs

Sensor	PVC	Plasticizer	IP	Slope	Linearity	LOD	R^2
	mg	mg	mg	mV/Conc.	M	M	
SPI-SPEs			**SPI-TPB**				
Sensor 1	100	200.0 DBP	7.5	19.68	4×10^{-5}-1×10^{-3}	2×10^{-5}	0.998
Sensor 2	100	200.0 DBP	15	23.098	1×10^{-5}-1×10^{-3}	6×10^{-6}	0.999
Sensor 3	100	200.0 DBP	22	19.95	6×10^{-5}-1×10^{-3}	8×10^{-6}	0.999
Sensor 4	100	200.0 DBP	30	21.04	6×10^{-5}-1×10^{-3}	8×10^{-6}	0.998
Sensor 5	100	200.0 TCP	15	23.56	1×10^{-5}-1×10^{-3}	8×10^{-6}	0.995
			in situ KTpClPB				
Sensor 6	100	200.0 *o*-NPOE	3	26.2	1×10^{-5}-1×10^{-2}	6×10^{-6}	0.998
Sensor 7	100	200.0 *o*-NPOE	6	28.36	1×10^{-6}-1×10^{-2}	1×10^{-6}	0.999
Sensor 8	100	200.0 *o*-NPOE	9	23.89	1×10^{-5}-1×10^{-2}	8×10^{-6}	0.999
Sensor 9	100	200.0 DBP	3	26.38	5×10^{-5}-3×10^{-3}	5×10^{-6}	0.999
Sensor10	100	200.0 TCP	3	25.38	1×10^{-6}-1×10^{-2}	1×10^{-6}	0.995

Table 4. Analytical performance of SPI-SPE

Parameters	**SPI-SPE**
Slope* (mVdecade^{-1})	28.36
Correlation coefficients (r)	0.9995
Working pH range	5 – 8.5
Lower detection limit (M)	1 x 10^{-6}
Life time (days)	15
Response time (s)	10
Concentration rang (M)	1×10^{-6} – 1×10^{-2}
Accuracy (%)	99.41
Precision (RSD %)	
Intraday	1.15
Inter-day	1.82

* Average of three different calibrations

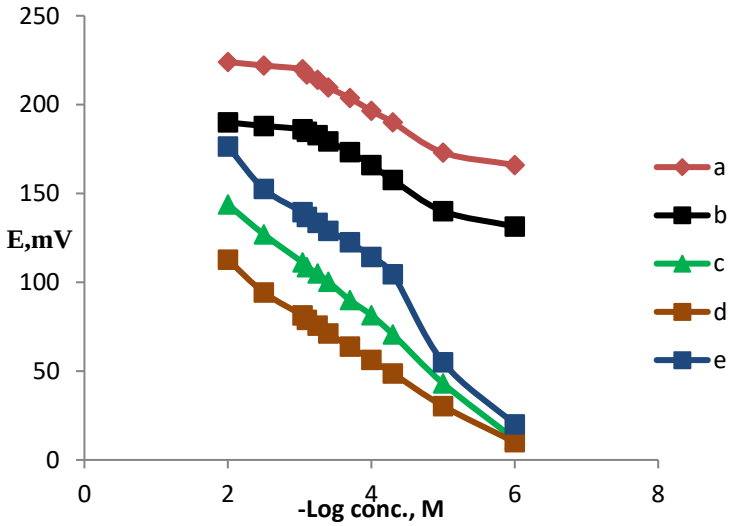


Figure 8. Calibration graphs (*E vs. log Conc.*) of different types of spiramycin screen printed electrodes. Curves (a) and (b) are for screen printed electrodes composed of SPI-TPB as ion exchanger in presence of DPB (a) and TCP (b) plasticizers. Curves (c), (d) and (e) are for screen printed electrodes composed of *K*(TpClPB) as libophilic cation exchanger in presence of (c) *o*-NPE, (d) TCP and (e) DBP plasticizers

3.2.1. Response time

The dynamic response time was measured by immersing the electrode in a series of the corresponding drug solutions of 1.0×10^{-4}, 1.0×10^{-3} and 1.0×10^{-2} M. The electrodes exhibited

fast response time (≤10 s) in 1.0×10^{-2} M and 1.0×10^{-3} M concentration. Nevertheless, the response time reached 30 s at lower concentrations and. The potential versus time is displayed in (Figure 9). The potential of each electrode remained constant for approximately 8 min. The potentiometric response of the membrane electrode was fond to be independent on the direction of the measurements, i.e., from low to high concentrations or vice versa (Figure 10). The electrodes proved to be efficient over 2 weeks of measurements without deterioration of the working concentration range, slope or response time.

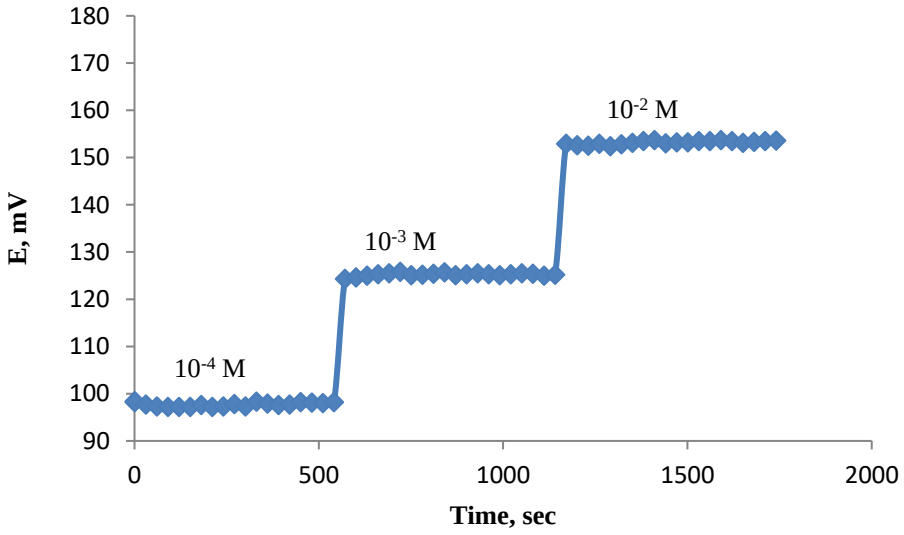


Figure 9. Dynamic response time of SPI screen printed electrode

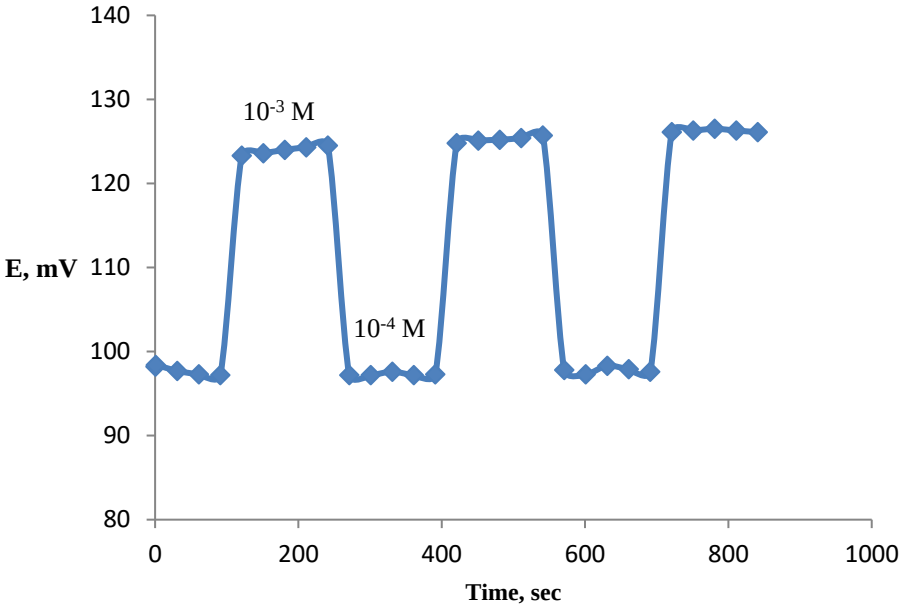


Figure 10. Reproducibility of the proposed electrode recorded in 1×10^{-4} and 1×10^{-3} M of SPI, the solutions were changed alternately.

3.2.2. pH effect

The pH effect on the potentiometric response was studied by changing the pH of drug solution while monitoring potentiometric reading of the electrode. The pH of the drug solution was controlled using small volumes of HCl and/or NaOH solution (0.1-1.0 M of each). Plotting the relationship between E in mV and the pH indicated that the effect of changing the pH from 5-8.5 on the potentiometric response is negligible (Figure 11).

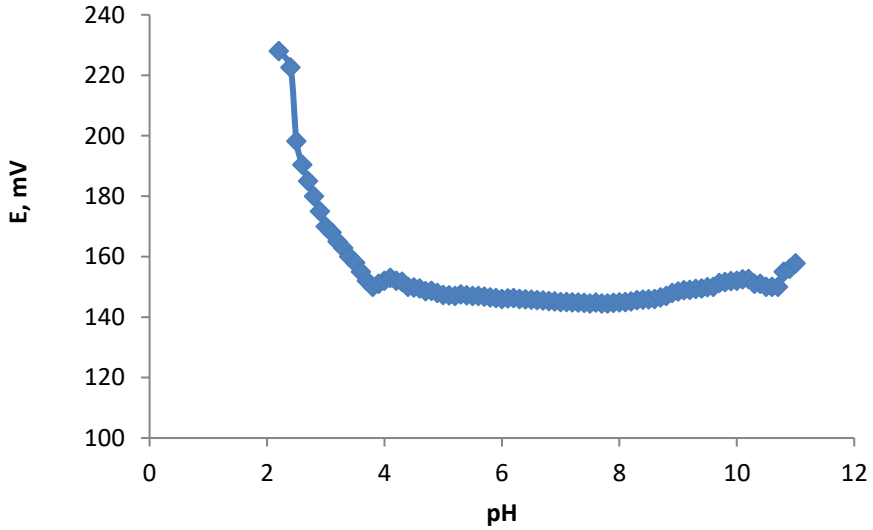


Figure 11. Effect of changing the pH of the SPI solution (1×10^{-3} M) on the electrode response

3.2.3. Interference

The effect of interference caused by different substances was evaluated. The contribution from these compounds has been evaluated by calculating the selectivity coefficient $K^{pot}_{drug,\,j}$ according the IUPAC using the separate solutions method [28]. The selectivity coefficients of the proposed electrodes are summarized in Table 5. The SPI-SPE exhibited a high selectivity for SPI over inorganic cations and amino acids.

Table 5. Selectivity coefficient values (- log $K^{pot}_{drug,\,j}$) for SPI-SPE

Effect of interferents	**SPI-SPE**
Ca^{++}	4.72
Zn^{++}	2.75
Na^{+}	5.08
K^{+}	4.94
Lactose monohydrate	5.87
glycine	4.09
Leucine	3.88

3.3. Application to pharmaceutical formulations and environmental water

The proposed methods have been used successfully for the quantitative analysis of SPI in pharmaceutical finished products. Also, due to the high selectivity of SPI-SPE, it can be used for SPI determination in natural water without prior extraction or purification steps. The proposed methods showed a high accuracy (±2%) and precision (RSD≤1%) Table 6. The results of the proposed methods were compared with that obtained using a SWP published method [15]. The calculated student t-test and F-ratio values confirmed that the two methods are alike with respect to accuracy and precision Table 7. However, the proposed SWV method is more save than the published SWP method and the proposed SPE has the merits of measurements in turbid sample solutions without any purification steps.

Table 6. Determination of SPI using the proposed SWV method and SPE

Sample	**Taken (μg mL^{-1})**		**Found (μg mL^{-1})**		**Recovery (%)**		**RSD***	
	SWV	**SPE**	**SWV**	**SPE**	**SWV**	**SPE**	**SWV**	**SPE**
Spyratech®	51.43	98.90	50.76	96.81	98.71	97.89	0.71	0.68
	108.09	197.33	106.54	199.08	98.57	100.89	0.52	0.62
	265.84	393.72	262.36	391.91	98.69	99.54	0.37	0.48
Spirex®	51.43	98.90	51.18	96.95	99.52	98.03	0.51	0.94
	108.09	197.33	108.54	199.84	100.42	101.27	0.89	0.73
	265.84	393.72	259.36	396.71	100.98	100.76	0.64	0.99
Tap water	–	9.89	–	9.73	–	98.38	–	0.49
	–	98.90	–	99.83	–	100.94	–	0.63
	–	556.15	–	554.43	–	99.69	–	0.57

* Average of three determination

Table 7. Statistical comparison between the proposed methods and published method

Parameters	**proposed methods**		**reference method [14]**
	SWV	**SPE**	
Mean%	99.27	99.41	98.30
S.D.	1.14	1.15	1.77
n		5	
Variance	1.29	1.32	3.13
t-value (2.77)*	0.29	0.53	–
F-value(6.39)*	2.43	1.54	–

* The values in parenthesis are the corresponding theoretical values of *t* and *F* at (P = 0.05).

4. CONCLUSION

Two simple electrochemical methods SWV and potentiometric screen-printed electrode are proposed for the determination of spiramycin in pharmaceutical formulations and in natural water. The electrochemical oxidation of SPI was studied at a carbon paste electrode in the presence of sodium dodecyl sulfate surfactant. The SPE was optimized with respect to the sensing element and type of plasticizer. Optimal potentiometric response was obtained with KTpClPB and *o*-NPOE as a plasticizer. The SPE has the merits of being highly selective for SPI, portable and disposable. The SWV and SPE were found to be linear in the concentration range from 5 μM to 450 μM and from 1 μM to 10 mM, respectively.

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