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Modification of Carbon Paste Electrode with MWCNTs and Benzethonium chloride and its Application as a Novel Sensor for Determination of Benzophenone-4 in Cosmetic Preparations

Hanan M. Elwy[1,*], *Rana S. Sherif*[1], *Sawsan M. Amer*[2], *G. A. Sedik*[2,**]

[1] Pharmaceutical Chemistry Department, National Organization of Drug Control and Research.Giza, Egypt.
[2] Analytical Chemistry Department, Faculty of Pharmacy, Cairo University, 11562
Cairo, Egypt.
[*]E-mail: hanan18s@yahoo.com
[**]E-mail: Ghada.sedik@pharma.cu.edu.eg

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A novel electrochemical sensor is designed for a quick and accurate voltammetric determination of Benzophenone-4 (BZ-4) using a multiwalled carbon nanotube (MWCNTs) electrode in the presence of emulsifying agents. The amounts of surfactant added had a great influence on the voltammetric behavior of the modified carbon paste electrode. The developed voltammetric response of the designed electrode is studied in the existence and absence of Benzethonium chloride (BC) and interesting electrocatalytic effects are found. The increase of the current signal during the oxidation process of BZ-4 is related to the concentration of BZ-4, pH of the medium, concentration, kind of surfactant and accumulation time at the surface of the electrode. By the aid of scanning electron microscope as well as cyclic voltammetry, the electrochemical inspection in addition to the characterization of the modified electrode were conducted. Benzethonium chloride (BC) is used in the quantification of BZ-4 in cyclic and square-wave voltammetry at multiwalled carbon nanotubes (MWCNTs) modified electrode. It was found to enhance the peak current from 46.4µA in deprivation of surfactant to 60.4µA when present. Peak current response obtained for BZ-4 under optimum experimental conditions is linear within a range of 6.0×10^{-9} to 1.09×10^{-4} mol L^{-1} with correlation coefficients of 0.9995. The limit of detection is 3.3×10^{-9} mol L^{-1}. The modified electrode displays high sensitivity and reproducibility which enables its utilization for quantification of BZ-4 in its pharmaceutical formulations.

Keywords: Square wave voltammetry, Benzethonium chloride, Benzophenone-4.

1. INTRODUCTION

Massive injurious effects in the skin, together with precocious photoaging and besides the induction of immunosuppression and skin carcinogenesis [1-3] can be caused by Ultraviolet (UV) radiation, as a consequence of excessive exposure to sunlight and also due to the reduction of the ozone layer.

The boosting of skin cancer and photoaging becomes more noticeable. Thus, the prominent usage of sunscreen products became a necessity [2, 3], and provided agreed key protection against the detrimental effects of harmful radiation.

Chemical sunscreens tend to be conjugated aromatic compounds having in ‘ortho’ or ‘para-position an electron-donating group as well as an electron acceptor group. Energies of UVA and UVB radiations are the energy required for this transition [4, 5]. Due to short wavelength and considerably high energy of UVB; it can damage the human skin, thus making the protection against radiation a pressing issue. Benzophenone-4 (BZ-4) is one of the numerous organic compounds entitled to UVA/UVB safety in sunscreen preparations [1-4].

BZ-4, (2-Hydroxy-4-methoxybenzophenone-5-sulfonic acid, Fig.1), is a water-soluble UVA/UVB filter used up to 5.0 % (as free acid) in cosmetic preparations. It is therefore recommended that BZ-4 be neutralized with sodium hydroxide or triethanolamine before being applied to a cosmetic formulation because of its high acidic nature. As it is soluble in both water and alcohol; it posses great effect in the protection of cosmetic formulas from photodegradation in aqueous preparations (shampoos, oil-free sunscreen sprays) [1].

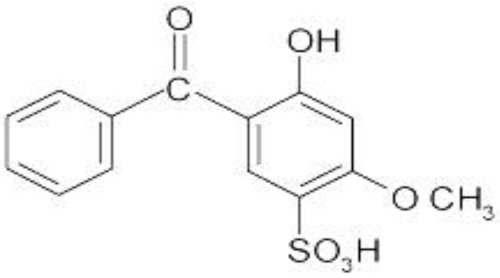


Figure 1. Structure of BZ-4

To date, RP-HPLC was the most used technique for the determination of BZ-4 [5-13], (sequential injection) analysis [14] and CE (capillary electrophoresis) [15-16] were less frequently used. Liquid chromatography was also used in BZ-4 analysis in environmental samples [17-18] or in skin permeation studies [19] as well as mass spectroscopy [20]. However, electrochemical procedures are extensively used in the pharmaceutical analysis as alternative methods. Our research group has successfully developed a new electroanalytical method for the quantification of the UV filter BZ-4. Electroanalytical methods are sensitive and provide low detection limits, ease of operation, inexpensive instruments and analysis procedures. So, voltammetric procedures were an important alternative to more sophisticated chromatographic methods [21].

Surface active agents have great importance in electrode reactions, as well as electrochemical determination of drugs and biological agents. These are widely used in electrochemical procedures due to their ability to solubilize organic compounds, thereby creating a particular pattern of the molecules at the electrode surface. [22-26].

Electrode surfaces such as carbon paste electrodes with hydrophobic characters interact with surfactants, via surface adsorption. Thus, the ability and efficiency of the modified carbon paste electrode in combination with surfactants permitted its usage in the determination of both inorganic [27] and biological molecules [28]. Multi-walled carbon nanotubes (MWCNTs) proved to be as modifiers to encourage electron transfer in electrochemical reactions, by enhancing sensitivity and chemical inactivity [29-36].

The main goal of the present study was based on the establishment of a modified carbon paste electrode (BC/MWCNTs/CPE), which was used for the first time for BZ-4 determination in cosmetic preparations.

2. EXPERIMENTAL

2.1. Materials and reagents

Analytical grade chemicals were used without further purification. Benzophenone-4 standard was kindly provided by Eva cosmetics (Egypt). Its purity was checked to be 99.90%. Sodium lauryl sulfate (SLS) (Lobal chemie, India). Benzethonium chloride (BC) and Cocamidopropyl betaine (Betain) were supplied from Aldrich Chem.Co.(USA). Britton Robinson buffer (B-R buffer) was prepared by mixing 0.04 mol L^{-1} of H_3PO_4, acetic acid and boric acid and the appropriate amount of 0.2 mol L^{-1}NaOH to acquire a concentration of 4.0 x 10^{-2} mol L^{-1}. A series of pH values from 2.0–11.0 were used as supporting electrolyte. Graphite powder (particle dimension 20 μm) and MWCNTs (purified to more than 95.0 % with a diameter of 6.0 – 9.0 nm and length of 5.0 μm) were supplied from Sigma Aldrich (Germany). Aqueous solutions were prepared using sterilized Milli-Q deionized water.

Commercial cosmetic preparations including hair conditioner claimed to contain 0.01% (w:w) BZ-4, shampoo claimed to contain 0.05% (w:w) BZ-4 and body scrub claimed to contain 0.1% (w:w) BZ-4 were supplied from the local market.

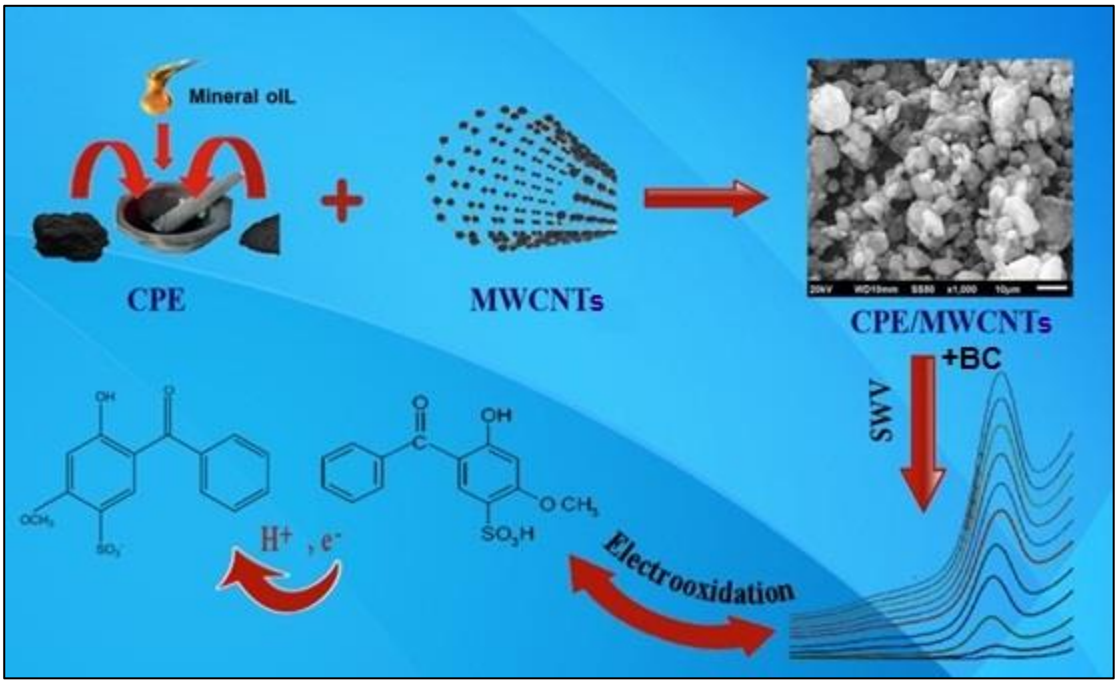
A stock solution of 1.0×10^{-2} mol L^{-1} BZ-4 was prepared in deionized water and stored in a refrigerator. Working solutions were daily prepared with deionized water just prior to use. A stock solution of 1.0×10^{-2} mol L^{-1} of SLS, BC and Betain were prepared in deionized water.

2.2. Instrumental conditions

Metrohm 797VA Computrace electro analyzers were used for all electrochemical measurements. VA Computrace version 1.3.1 was used to record data. A one-compartment cell contains the electrodes, (MWCNTs/CPE) working electrode, a platinum wire was used as an auxiliary electrode. All the cell potentials were measured with respect to Ag/AgCl (3.0 mol L^{-1} KCl) reference electrode. Scanning electron microscopy (SEM) measurements were made using A JSM-6700F scanning electron microscope (Japan Electro Company). For pH measurement, Cyberscan 500 digital (EUTECH Instruments, USA) pH-meter was utilized. All the electrochemical investigations were performed at 25°C.

2.3. Preparation of bare and MWCNTs modified carbon paste electrodes

For the preparation of the carbon paste electrode, in a mortar, 0.225 g of graphite powder was mixed with 0.2 mL paraffin oil. The carbon paste was loaded inside the electrode body and smoothed untill it got a shiny appearance. MWCNTs/CPE was prepared by mixing graphite powder equivalent to (0.5 g) and a varying amount of MWCNTs was mixed well for 10.0 min with paraffin oil as pasting liquid (0.2 ml) to get a wetted paste, the modified carbon paste was then filled in a Teflon holder. To get a fresh surface polish the electrode with a clean paper until it became smooth [37]. The corresponding fabrication of MWCNTs/CPE was shown in (Scheme 1).



Scheme 1. Schematic illustration of electrochemical sensor based on MWCNTs/CPE

2.4. Recommended experimental procedure

The modified electrode MWCNTs/CPE was cycled between 900–1400 mV with the scan rate of 100.0 mV s^{-1} in 4.0×10^{-2} mol L^{-1} B–R buffer (pH 2.0), several times until a reproducible response was attained before any voltammetric measurement. Then, the electrode was transferred into another cell containing B–R buffer (pH 2.0) and BZ-4, where 0.8 mL of 1.0×10^{-2} mol L^{-1} BC was added to the solution. After accumulating of BC for 120.0 s, cyclic voltammograms (CV) at a scan rate of 100.0 mV s^{-1} were done between 900–1400 mV. For SWV procedure, aliquots equivalent to 6.5×10^{-9} to 5.5×10^{-5} mol L^{-1} BZ-4 were transferred in 10 mL volumetric flasks, then 0.8 mL of 1.0×10^{-2} mol L^{-1} BC solution was added and completed with B–R buffer pH 2.0 to the mark. For the quantitative analysis, 5.0 mL of the prepared solution was moved to the cell and SWV was recorded. Using SWV method, measurement of the anodic peak current was carried out at a scan rate of 100.0 mV s^{-1}at BC/MWCNTs/CPE electrodes.

2.5. Sample preparation

To examine the validity of the suggested method, commercial cosmetic preparations of BZ-4 were analyzed. A one-step dilution procedure was used for sample preparation. An appropriate amount of each product was weighed, diluted, and then transferred accurately into a calibrated flask to get a concentration of 1.0×10^{-4} mol $L^{-1}$of BZ-4. Then, the sample was dissolved for 15.0 min in 20.0 mL of deionized water under agitation and sonication. The supernatant was transmitted into a 25-mL volumetric flask and completed to volume with deionized water, after centrifuging for 10.0 min at 4500.0 rpm. A voltammogram was performed after the appropriate amount of the resulting solution was applied to the voltammetric container. The standard addition technique was employed to determine the total content of BZ-4 in the matrix.

3. RESULTS AND DISCUSSION

3.1. Surface characterization of the MWCNTs/CPE

A scanning electron microscope (SEM) was applied to study the morphological response of the electrochemical sensor. Fig.2 shows the morphological property of (a) CPE and (b) MWCNTs/ CPE.

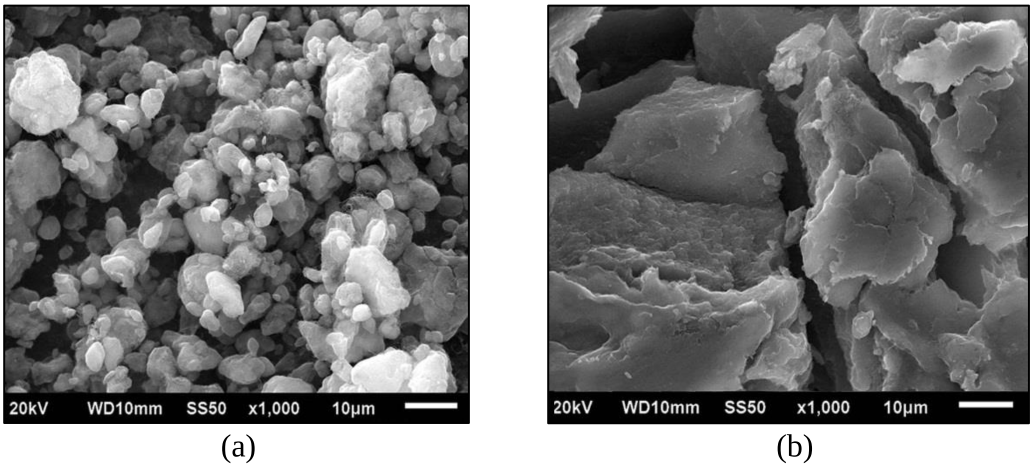


Figure 2. SEM micrographs of (a) CPE and (b) MWCNTs/CPE

SEM images showed remarkable differences in the electrodes' surface morphologies. The SEM of the bare CPE was characterized by soft irregular graphite flakes and homogeneously separated layers (Fig. 2a). While the SEM image of MWCNTs modified electrode displayed flowery shaped SEM with a physical appearance and surface characteristics of dispersed particles homogeneously on the electrode's surface. This flowery like structure exhibited a high surface area (Fig.2b).

3.2. Cyclic Voltammetric Behavior of Benzophenone-4

In the present study, the voltammetric response of BZ-4was studied from 900 to 1400 mV. Fig.3 demonstrates the electrochemical response of BZ-4 in B-R buffer pH 2.0, at a scan rate of 100.0

mV s^{-1} using three different electrodes bare CPE, MWCNTs/CPE and BC/MWCNTs/CPE in the absence and existence of surfactant. For the bare CPE, the voltammetric behavior displayed a distinct irreversible oxidation peak. The anodic peak current showed electrochemical oxidation of BZ-4 at 1.23 V and 40.0 µA. The incorporation of MWCNTs in the matrix of CPE caused intensification in the current peak. The intensification in peak current was related to the significant surface area of the studied electrode that ameliorates the kinetics of the electrode. Adding BC to the drug solution increased the polarity on the modified surface electrode, expediting the electron transfer process; thus producing a noticeable change in the cyclic voltammograms. The rise in anodic peak current was noticed by a significant intensification of the peak current of (60.4 µA) in comparison to the bare CPE, and MWCNTs/CPE. The addition of BC as a cationic surfactant enhanced the peak current by about 2 times more than CPE and about 1.3 times more than MWCNTs/CPE used in absence of surfactant due to the increase of the electron transfer rate [38] as shown in Fig. 3. Thus, the optimal reaction condition was found upon using the BC/MWCNTs/CPE electrode.

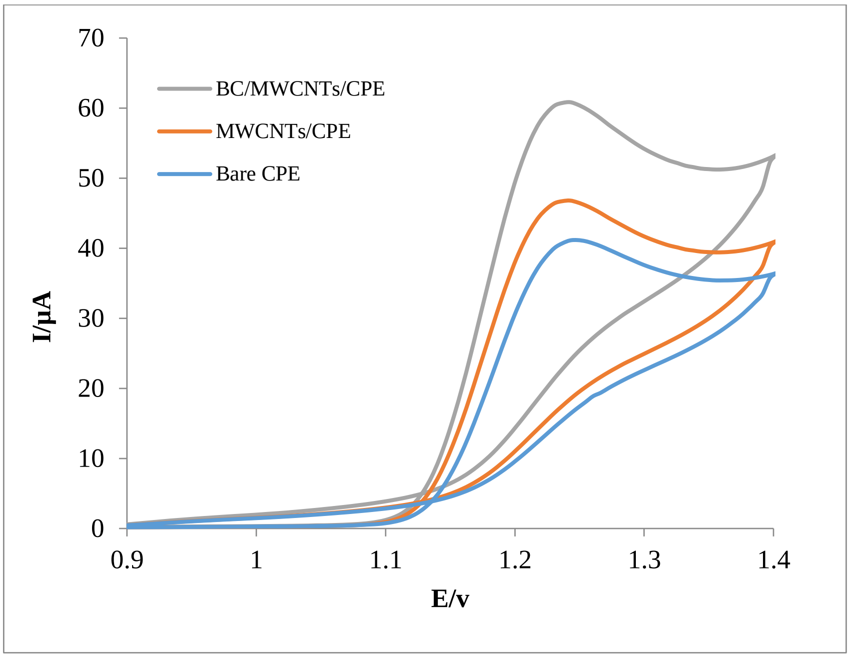


Figure 3. Cyclic voltammograms of 1.0 x10^{-3} mol L^{-1} BZ-4 in B–R buffer (pH 2.0), scan rate 100.0 mV s^{-1} recorded at three different working electrodes: bare CPE, MWCNTs/CPE and BC/MWCNTs/CPE.

3.3 Effect of surfactant

Surfactants are known as surface-active agent, they are amphiphilic molecules that have polar hydrophobic head and a hydrophobic tail. Surfactant molecules robustly influence the electro-oxidation process, even at trace levels [39]. The pivotal function of surfactants is to lower the interfacial tensions and permit the expansion of the molecules. The reversibility of the electro-oxidation process depends on the type and amount of surfactant used. The electrochemical behavior of BZ-4 upon additions of different surfactants, anionic surfactant; sodium lauryl sulfate (SLS), cationic surfactant; benzethonium chloride (BC) and amphoteric surfactant; cocamidopropyl betaine (Betain) of the same concentration was presented in Fig.4. It was clear that the presence of BC ameliorates the polarity on the MWCNTs/CPE surface, which promoted the electron transfer for the oxidation of BZ-4 as observed by a significant enhancement of the peak current (60.4 µA) [40] in comparison to the bare CPE, and MWCNTs/CPE; as shown in Fig 4. Electrochemical data for the drug oxidation in the existence of surfactants are summarized in Table 1. The highest peak current is observed for BC; accordingly, it was used for all the subsequent measurements. Different concentrations of BC were tested in the concentration range (1.0 x 10^{-5} to 96.0 x 10^{-5} mol L^{-1}) and it was noticed that the increase of concentration above 74.0 x 10^{-5} mol L^{-1} had no effect on the electrode response. Thus, it revealed that the anodic peak current is greatly affected by the surfactant concentration. Therefore, the concentration 74.0 x 10^{-5} mol L^{-1} of BC was chosen to be used for further investigations as shown in Fig 5.

Table 1. Electrochemical data for the oxidation of BZ-4 in the presence of different surfactants.

Surfactant	Concentration of surfactants/mol.L^{-1}	Peak Potential/V	Peak current/µA
Betain	1.7E^{-07}	1.24	38.5
SLS	1.7E^{-07}	1.23	37.5
BC	1.7E^{-07}	1.23	60.4

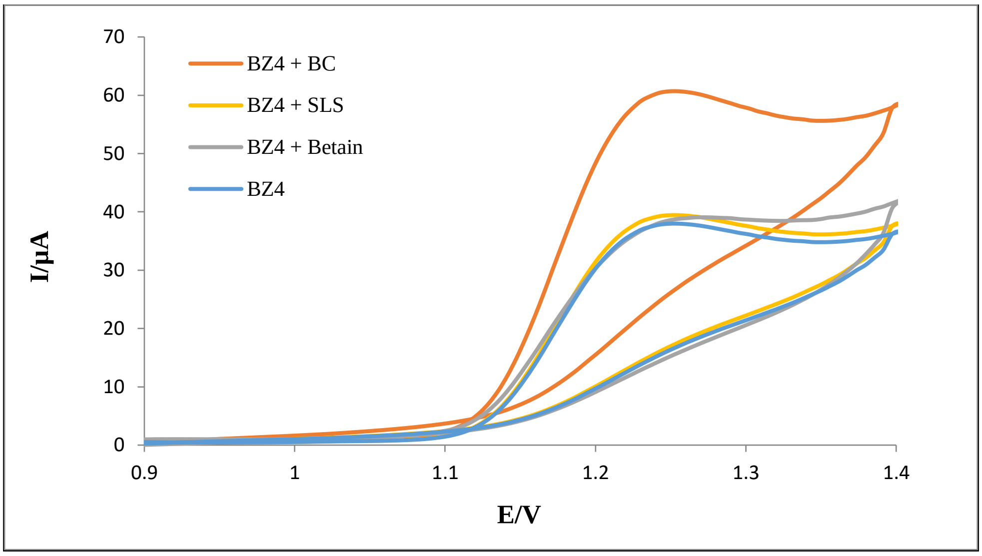


Figure 4. Effects of different surfactants; Betain, SLS, BC on voltammetric behavior of 1.0 x 10^{-3} mol L^{-1} BZ-4 in B–R buffer (pH 2.0), at scan rate 100.0 mV s^{-1}.

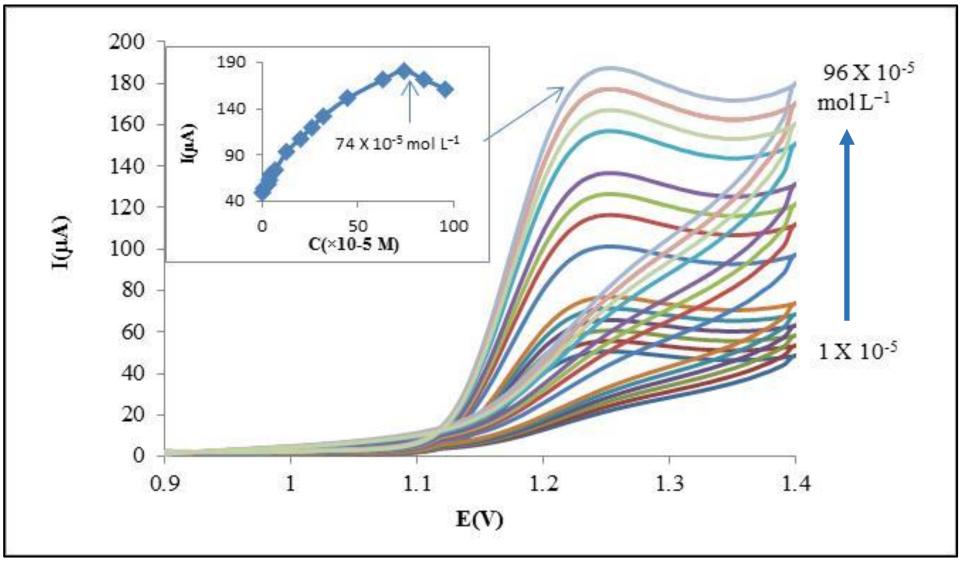


Figure 5. Variation of anodic peak current (Ipa) of BZ-4 at MWCNTs/CPE with the corresponding cationic surfactant (BC) concentrations.

3.4 Effect of varying amounts of MWCNTs

The influence of adding various amounts of MWCNTs from 0.1–1.0% to the carbon paste was examined. We noticed that BZ-4 oxidation peak current increases on the addition of MWCNTs until 0.5% and then decreases as demonstrated in Fig 6. Results showed that MWCNTs amount equivalent to 0.5% enhanced the sensitivity of the electrode, increasing the amount had a reverse impact on the anodic peak current. Hence, 0.5% of MWCNTs was chosen as the optimum amount to use in the coming experiments

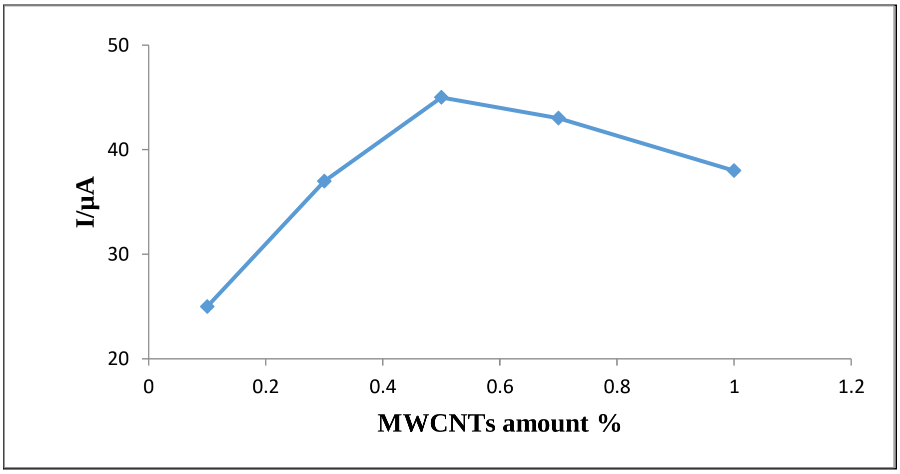


Figure 6. Effect of varying amounts of MWCNTs on peak current response of 1.0 x10^{-3} mol L^{-1} BZ-4 in B–R buffer (pH 2.0), at scan rate 100.0 mV s^{-1}

3.5. Effect of pH

Cyclic voltammetry procedures were performed to examine the influence of solution pH on the electrocatalytic oxidation of BZ-4 at MWCNTs in the pH range of 2.0 – 11.0.

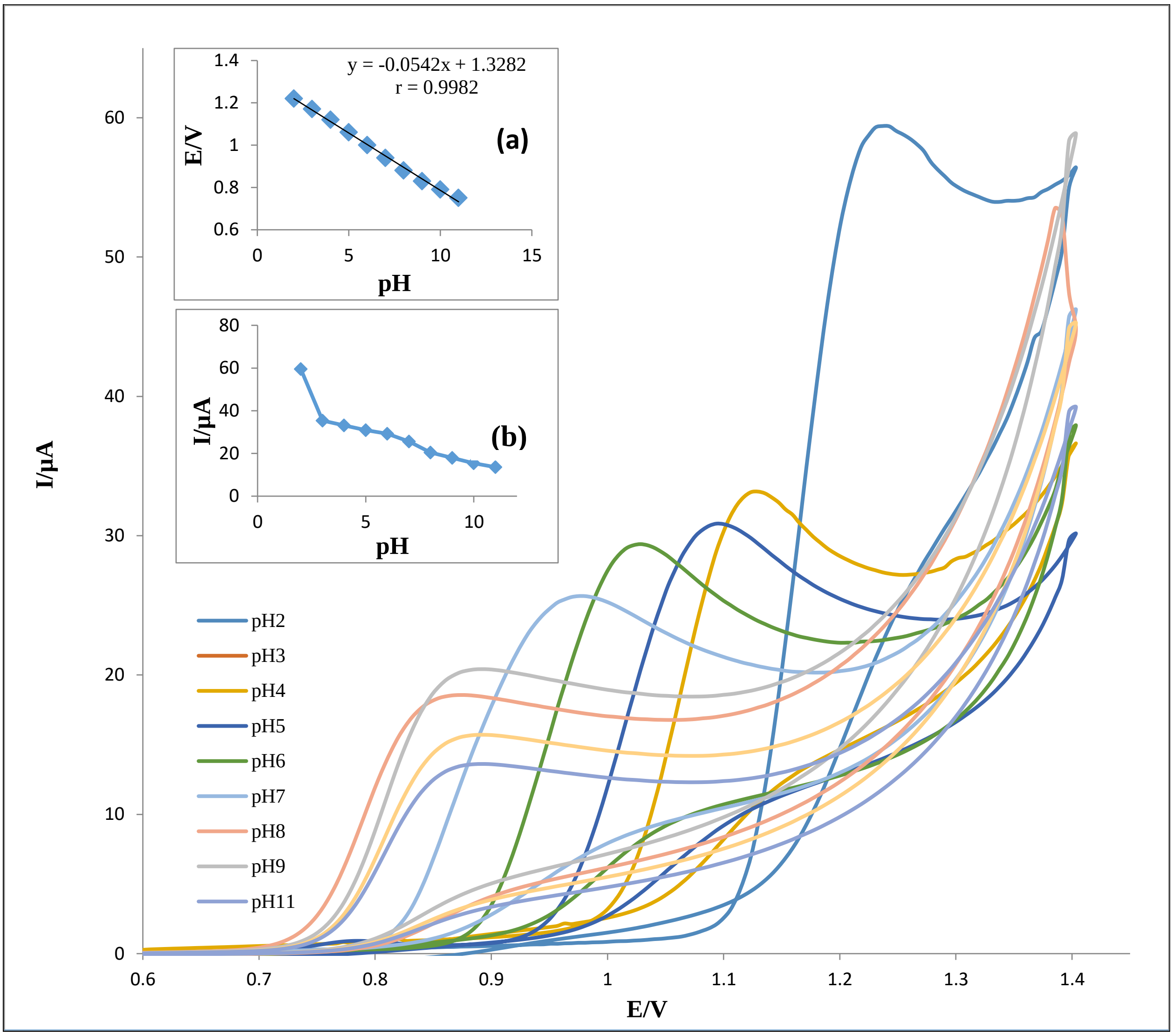
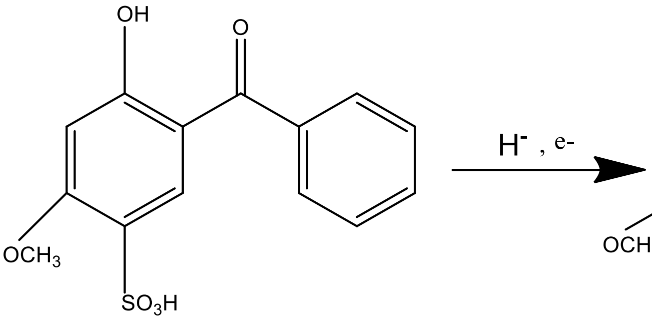


Figure 7. Cyclic voltammograms of 1.0 x10^{-3} mol L^{-1} BZ-4 at different pH values using BC/MWCNTs/CPE. Inset: Plot of peak potential (a) and anodic peak current (b) of 1.0 x10^{-3} mol L^{-1} BZ-4 versus pH values.



Scheme 2. Proposed oxidation mechanisms for BZ-4 at BC/MWCNTs/CPE.

From the obtained data, we showed that proton plays an important role in electrode reaction processes. We observed that the oxidation peak potentials were changed negatively with pH increased, showing that the electrocatalytic oxidation process at the electrode surface is highly influenced by pH.

It has been noticed that at pH 2.0, the higher oxidation peak current was observed; so pH 2.0 was the selected pH for this study. The dependence of oxidation peak potential on the pH can be demonstrated by the linear equation Ep (V) = 1.3282 - 0.0542pH, with a correlation coefficient of 0.9982. The slope was 54.2mV / pH at 25 ºC, is close to the theoretical value 59 mV, and obeys Nernst equation. These results showed that an equal number of protons and transferred electrons were involved in the oxidation cycle (one electron and one proton). The proposed mechanism was the loss of one proton for the sulphonic group, as illustrated in scheme 2.

3.6. Effect of accumulation time

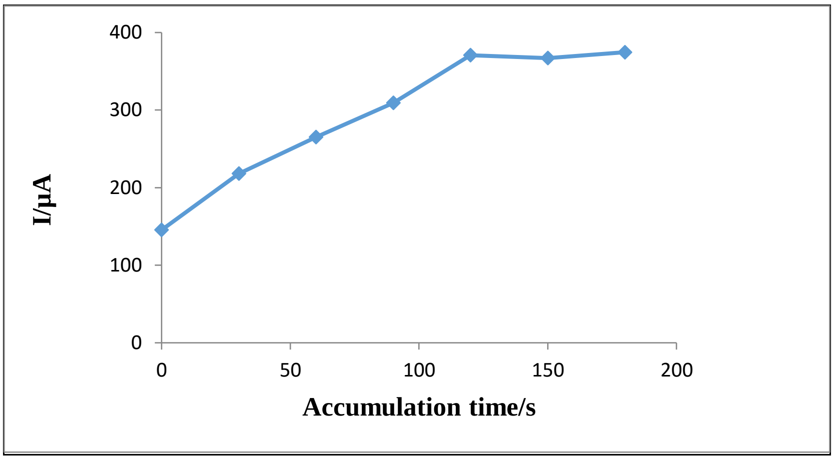


Figure 8. Effect of accumulation time on the oxidation peak current of 1.0 x10^{-3} mol L^{-1} BZ-4.

Accumulation time was an effective parameter; it could influence the mass transport process. The impact of accumulation time on the anodic peak current was investigated to describe the sensitivity of a working electrode. In this study, an open-circuit was utilized to study the correlation between the BZ-4's oxidation peak current at the BC/MWCNTs/CPE electrode and accumulation times. Fig. 8 showed that the oxidation peak current depended on accumulation time. Increasing the accumulation time from 0.0 s to 120.0 s, the oxidation peak current of BZ-4 at the BC/MWCNTs/CPE electrode increased sharply and attained the maximum after120s noticeably enhanced. Above 120.0 s the peak current became steady, due to the saturation of the surface with BZ-4 which could be due to blocking of the active sites at the electrode surface, so the accumulation time was fixed at 120.0s. Therefore, the accumulation time of 120.0 s was selected for the subsequent experiment.

3.7 Effect of scan rate on the electrochemical oxidation of BZ-4

The influence of the scan rate on the cyclic voltammetric response BC/MWCNTs/CPE electrode of 1.0 x10^{-3} mol L^{-1} BZ-4 in B–R buffer a (pH 2.0) was shown in Fig. 9. Scan rate is an experimental parameter for studying the electrochemical response and kinetic characteristics. Also, it can aid in giving an overview of the relationship between peak current and scan rate. Using a scan rate of 10.0-200.0 mVs^{-1} the oxidation peak current increased with a positive peak potential shift. The positive shift in peak potential with elevating the scan rate suggested that the oxidation process was irreversible. The inset (a) describes the correlation between the anodic peak currents with elevating the scan rate. We found that the anodic peak currents increased with a linear equation as log i_{pa}(10^{-6}A) = 0.2732log υ (v/s) -1.1407 (n = 5, r = 0.9964 suggesting that the reaction was diffusion-controlled electrode reaction [41].The relationship between anodic peak current and scan rate was utilized to assess the diffusion coefficient of the cited drug by using Randels-Sevcik equation; cyclic voltammetric technique and $K_4Fe\ (CN)_6$1.0 mM as a test solution at different scan rates in 0.1 M KCl as supporting electrolyte was used to calculate the surface area. For a reversible process, Randels-Sevcik equation is

$$Ipa = (2.69X10^5)n^{\frac{3}{2}}AD_\circ^{1/2}V^{1/2}C_\circ^*$$

I_{pa} is the peak current, A is denoted as the area of the electrode surface and $D_\circ$ is the diffusion coefficient 7.6 × 10^{-6} cm^2 s^{-1}, ν as scan rate and $C_\circ$ is the concentration of $K_4Fe\ (CN)_6$. From the slope of the plot of Ip vs. $\nu^{1/2}$, the surface area of the bare electrode was found to be 0.086 cm^2 and for the modified electrode, the calculated surface area was 0.346 cm^2. The electro-active area of the modified electrode was found to be greater than that of the bare electrode, then a significant response of peak current was noticed for the modified electrode. The apparent diffusion coefficient, D app, for the cited drugs were found to be 1.35 × 10^{-6} cm^2 s^{-1}, 2.561 × 10^{-7} cm^2 s^{-1} for the bare and modified electrodes respectively.

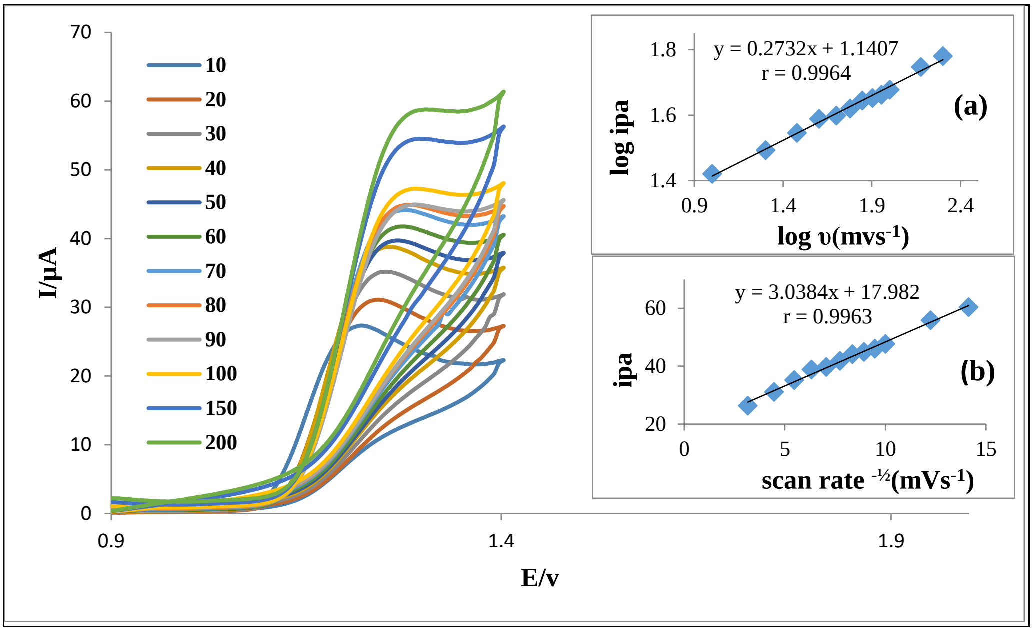


Figure 9. Cyclic voltammograms 1.0 x10^{-3} mol L^{-1} BZ-4 at different scan rates (from 10.0 to 200.0 mVs^{-1}) using BC/MWCNTs/CPE in B-R buffer (pH 2.0) and accumulation time 120.0 s. Inset (a) represented a plot of log the anodic peak current versus log the scan rate. Inset (b) represented a plot of the anodic peak current values versus the square root of the scan rate.

3.8 Method Validation

The International Conference on Harmonization (ICH) [42] provides guidelines for method validation that were used for the validation of the proposed method. Under the optimized condition, it was obvious that there was a positive linear relationship between anodic peak current (Ip) and the concentration of the drug. To show the sensitivity of BC/MWCNTs/CPE towards the electrochemical measurement of BZ-4 in pH (2.0), the square wave voltammetry was chosen for this study; the following are the experimental parameters for the square wave voltammetry experiments: Ei = 0.6 V, Ef = 1.4 V, scan rate = 100.0 mV s^{-1}. The corresponding calibration plots were described in the insets Fig 10. The plot was linear over the concentration ranges 6.5×10^{-9} to 5.5×10^{-5} mol L^{-1} with a regression equation of I_{pa} (μA) = 0.483+ 0.9029 C (μmol L^{-1}) and a correlation coefficient of 0.9995 and the second concentration ranges 5.5×10^{-5}- 3.9×10^{-4} mol L^{-1} with a regression equation of I_{pa} (μA) = 44.293+ 0.1263 C (μmol L^{-1}) and a correlation coefficient of 0.9991, respectively. The limits of detection (LOD) and the limits of quantification (LOQ) were calculated and found to be 3.6 $\times10^{-9}$ mol L^{-1} and 11.0 $\times10^{-9}$mol L^{-1}, respectively, for the first linear range, and the second linear range was found to be 2.3 $\times10^{-8}$ mol L^{-1} and 7.9×10^{-8} mol L^{-1}, respectively, according to the following equations:

$$LOD = 3.3sm^{-1}$$
$$LOQ = 10sm^{-1}$$

Where s is the standard deviation of the current peak and m is the slope of the calibration curves.

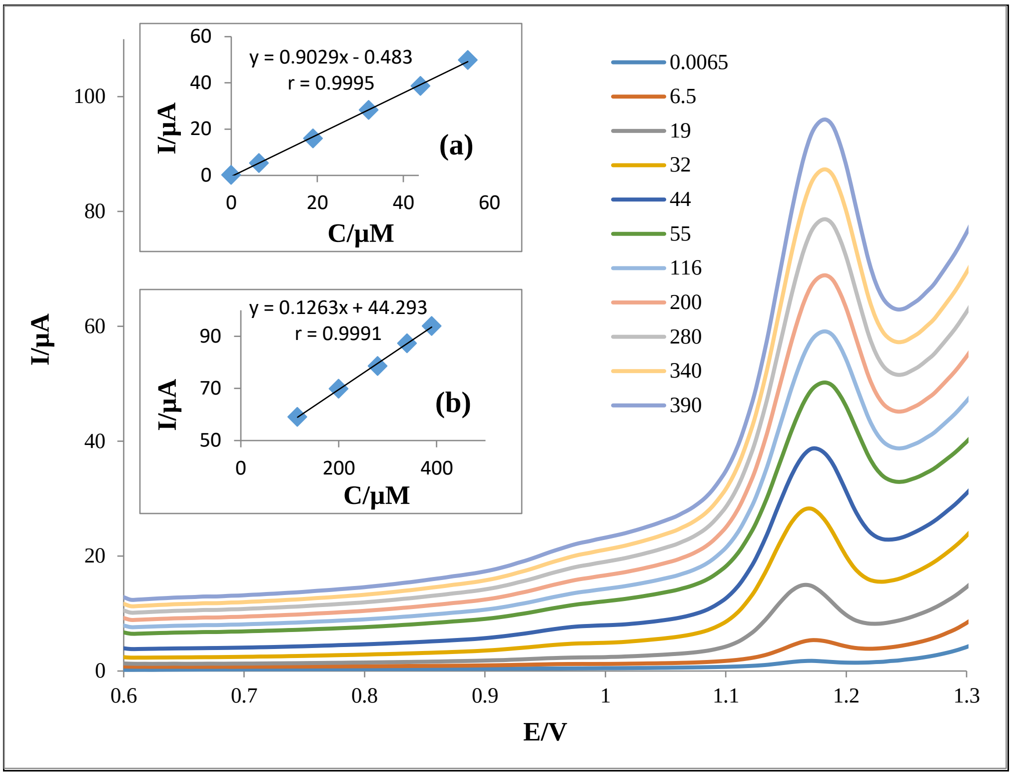


Figure 10. The effect of changing the concentration of BZ-4, using square wave mode at BC/MWCNTs/CPE, in B–R buffer (pH 2.0) and 100.0 mV s^{-1}. The inset (a): represented the SWV of the smaller concentration range. The inset (b): represented the SWV of the larger concentration range.

3.8.1 Accuracy and precision

Accuracy of the suggested method was established by using five different concentrations levels of BZ-4, each was repeated in triplicate. The results obtained, including % recovery ± standard deviation, were calculated as well and found to be 100.3 ± 0.77, which were displayed in Table 2. Intraday and interday precision using three different concentrations on the same day and for three separate days of BZ-4 denoted that the reproducibility of the results obtained by the suggested procedure was precise. The percentage of the relative standard deviations for Intra- and inter-day were found to be less than 2.0 % are displayed in Table 2

Table 2. Parameters of linear calibration equation for BZ-4

Parameter	BZ-4
Linear range (mol L^{-1})	6.0×10^{-9} - 5.5×10^{-5}
Intercept (a)	0.483
SE of intercept (Sa)	0.000577
Slope	0.9029
SE of slope	0.000348
Correlation Coefficient (r)	0.9995

LOD (mol L^{-1})	3.6×10^{-9}
LOQ (mol L^{-1})	11.0×10^{-9}
Accuracy	100.3± 0.77
Inter-day assay RSD(a) %	0.931
Intra-day assay RSD(b) %	0.853

[a] intraday (n=3) average of three responses of three different concentrations repeated three times on the same day.

[b] interday (n=3) average of three responses of three different concentrations repeated three times on three successive days.

3.8.2. Robustness.

To assess the robustness of the method, small changes in the experimental conditions were carried out such as the electrolyte pH (2.0 ± 0.2) and the surfactant concentration. Each of the previous parameters was changed while keeping all other parameters constant. These small variations did not change the current intensity; as shown in Table 3.

Table 3. Robustness results for the simultaneous determination of BZ-4 using the proposed voltammetric method**.**

Robustness parameter		Peak current /µA	% Assay*
pH of buffer	2.0 + 0.2 mL/min	60.5	100.71
	2.0 – 0.2 mL/min	60.7	99.52
Concentration of BC	72.0×10^{-5} mol L^{-1}	60.3	101.83
	76.0×10^{-5} mol L^{-1}	60.8	100.44
% RSD		0.366	0.945

** Assay was calculated from the regression equation*

3.9. Comparison between different methods for the determination of BZ-4

Surveying the literature in hand, BZ-4 could be quantified using many spectrophotometric and different chromatographic methods, but no voltammetric assay has been described in the literature for BZ-4 determination its cosmetic preparations. Upon comparing the data obtained for BZ-4 quantification by different assays and the proposed electrochemical one, the BC/MWCNTs/CPE sensor appeared to have some benefits. The sensor was highly sensitive and the detection limit was very low with adequate reproducibility and low cost by using safe and economic reagents. The proposed method did not need pre-treatment, on the contrary, HPLC, TLC densitometry, SPE and spectrophotometry are much complicated with a higher cost than that of the BC/MWCNTs/CPE sensor, as shown in Table 4 [6, 9, 43].

Table 4. Comparison of the BC/MWCNTs/CPE sensor with other reported methods for the determination of BZ-4

Method	Calibration range mol L^{-1}	Detection limit mol L^{-1}
HPLC using CD [6]	0.137-1.371	$1.15x10^{-5}$
HPLC [9]	$5.48x10^{-4}$-$2.7x10^{-6}$	$2.6x10^{-6}$
TLC Densitometry [43]	$1.09x10^{-2}$-$5.4x10^{-4}$	$1.64x10^{-4}$
Derivative UV spectrophotometry [43]	$2.19x10^{-2}$-$2.19x10^{-1}$	$5.4x10^{-5}$
The proposed electroanalytical method	1.09×10^{-4}-$6.\times10^{-9}$	3.6×10^{-9}

Statistical analysis of the results revealed that no considerable difference between the proposed assay and the reported method [6]. The calculated t- and F- values are less than the tabulated ones, at 95% confidence limit [40]; as illustrated in Table 5.

Table 5. Statistical analysis of the results obtained using the proposed electrochemical method compared with the reported method for the determination of BZ-4 in its cosmetic preparation.

Parameters	Proposed method	Reported method (6)**
Linearity range(molL^{-1})	6×10^{-9} - 5.5×10^{-5}	0.137-1.371
Mean%	100.54	100.45
N	5	5
SD	0.99	1.15
Variance	0.98	1.32
t-test*	0.13	---
F-test*	1.35	---

**The theoretical t- and F- values at P=0.05 (2.31) and (6.39); respectively.*

***HPLC method where the column used was* C_{18} *with a mobile phase consisting of ethanol-water-acetic acid (70:29.5:0.5) containing 65.4 mM of hydroxypropyl-b-cyclodextrin, with flow rate of 0.6 mL/min and UV detection at 313.0 nm.*

3.10. Determination of BZ-4 in cosmetic preparations

The suggested method was effective for the quantification of BZ-4 in three cosmetic formulations, as shown in Table 6. The specificity of the SWV method was confirmed by the capacity to analyze BZ-4 without interference from common excipients in cosmetic preparations. The % recovery was ranging from 98.5% to 102.9% and the standard deviations (SD) were less than 2.0 showed that the common interfering compounds had no effect on the present procedure. Therefore, the voltammetric method has excellent precision, due to the minimum RSD values. The agreement between labeled and found BZ-4 contents showed that the sample preparation process was not only simple and rapid but very effective. All the oncoming results indicated that the developed method was reliable in quality control in pharmaceutical industry as an electroanalytical method for the quantification of BZ-4 in cosmetic formulas.

Table 6. Recovery data obtained by the standard addition method for BZ-4 in three cosmetic preparations:

		Standard addition technique		
Cosmetic preparation	%Found * ±SD	Taken (mol $L^{-1}\times10^{-5}$)	Standard added (mol $L^{-1}\times10^{-5}$)	%Recovery of standard added
Hair conditioner	100.32 ±1.02	2.00	1.00	100.51
		2.00	2.00	102.3
		2.00	4.00	98.5
		Mean ±SD		100.44±1.90
Shampoo	101.80 ±1.61	2.00	1.00	98.90
		2.00	2.00	100.00
		2.00	4.00	100.60
		Mean ±SD		99.83±0.86
Body scrub	100.94 ±0.87	2.00	1.00	100.00
		2.00	2.00	99.70
		2.00	4.00	102.90
		Mean ±SD		100.87±1.77

**Mean of three determinations.*

3.11. Storage and Stability

Standard solutions of BZ-4 were refrigerated during experiments and kept in dark place except for the time needed for the experiment. Under the recommended condition, solutions were stable for at least two weeks.

4. CONCLUSIONS

Our study discloses that the modified carbon paste electrode along with the surfactant were used to demonstrate the enhancement of sensitivity to the electrochemical response of UV filter BZ-4. The effect of changing the experimental parameters, the solution pH, scan rate, the type of surfactant on the electrochemical response of the developed electrode showed that electrochemical assay of BZ-4 can be used to determine this sun screening agent in cosmetic preparations without pretreatment of the sample with acceptable results. The key benefits of the modified sensor which render it beneficial for accurate and sensitive for quantification of BZ-4 were the low detection and quantification limit, comparable with methods formerly reported in the literature. It had a renewal surface made it an economic sensor, although it can replace costly and sophisticated HPLC methods by low-cost instrumentation.

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References

1. G.M. Halliday, *Mutat. Res. Fundam. Mol. Mech. Mutagen.,* 571 (2005) 107.
2. K.M. Hanson, E. Gratton, C.J. Bardeen, *Free Radical Biol. Med.,* 41 (2006) 1205.
3. E. Touitou, B. Godin, *Clin. Dermatol.*, 26 (2008) 375.
4. C. Couteau, A. Faure, J. Fortin, E. Paparis, L.J. Coiffard, *J. Pharm. Biomed. Anal.*, 44 (2007) 270.
5. A. Salvador, A. Chisvert, *Anal. Chim. Acta*., 537 (2005) 15.
6. A. Chisvert, M. Pascual-Martı, A. Salvador, J. *Chromatogr. A.,* 921 (2001) 207.
7. A. Chisvert, A. Salvador, . *Chromatogr. A.,* 977 (2002) 277.
8. A. Chisvert, M. Vidal, A. Salvador, *Anal. Chim. Acta.*, 464 (2002) 295.
9. D. De Orsi, G. Giannini, L. Gagliardi, R. Porrà, S. Berri, A. Bolasco, I. Carpani, D. Tonelli, *Chromatographia.,* 64 (2006) 509.
10. L. Gagliardi, A. Amato, A. Basili, G. Cavazzutti, D. Tonelli, *J, Chromatogr. A.,* 408 (1987) 409.
11. T. Liu, D. Wu, *Int J Cosmet Sci.*, 33 (2011) 408.
12. S. Rastogi, G. Jensen, *J. Chromatogr. A.,* 828 (1998) 311.
13. P. A. Segura, M. Racine, A. Gravel, E. Eysseric, A. M. Grégoire, D. Rawach,F. X. Teysseire, *Can. J. Chem.*, 97(2019) 197.
14. P. Pietta, A. Bruno, P. Mauri, C. Gardana, R. Maffei-Facino, M. Carini, *J. Pharmaceut. Biomed. Anal.,* 13 (1995) 229.
15. S. P. Wang, W. T. Lee, *J. Chromatogr. A.,* 987 (2003) 269.
16. A. Zenker, H. Schmutz, K. Fent *J. Chromatogr. A.,* 1202 (2008) 64.
17. R. Rodil, J.B. Quintana, P. López-Mahía, S. Muniategui-Lorenzo, D. Prada-Rodríguez, *Anal.Chem.*, 80 (2008) 1307.
18. M.S. Díaz-Cruz, D. Barceló, *TrAC, Trends Anal. Chem*, 28 (2009) 708.
19. G. Potard, C. Laugel, A. Baillet, H. Schaefer, J.-P. Marty, *Int J. Pharm.*, 189 (1999) 249.
20. L. Lopardo, A. Rydevik, B. K. Hordern, *Anal. Bioanal.Chem*., 411 (2019) 689.
21. D. De Souza, R.A. de Toledo, H.B. Suffredini, L.H. Mazo, S.A. Machado, *Electroanalysis.,* 18 (2006) 605.
22. P.G. Westmoreland, R. Day, A. Underwood, *Anal Chem.*, 44 (1972) 737.
23. A. Levent, Y. Yardim, Z. Senturk, *Electrochim Acta.*, 55 (2009) 190.
24. R. Jain, R. Mishra, A. Dwivedi, *J Sci Ind Res India.,* 68 (2009) 540.
25. G. Ziyatdinova, E. Giniyatova, H. Budnikov, *Electroanalysis.,* 22 (2010) 2708.
26. R. Jain, A. Dwivedi, R. Mishra, *Langmuir,* 25 (2009) 10364.
27. M. Galík, M. Cholota, I. Švancara, A. Bobrowski, K. Vytřas, *Electroanalysis.,* 18 (2006) 2218.
28. C. Hu, Q. He, Q. Li, S. HU, *Anal Sci.,* 20 (2004) 1049.
29. H.R. Zare, N. Nasirizadeh, *Sens. Actuators, B.*, 143 (2010) 666.
30. P.A. Sundari, S. Palaniappan, P. Manisankar, *Anal Lett., 43* (2010) 1457.
31. X. Liu, L. Wang, S. Zhang, X. Deng, X. Tang, X. Huang, *Electroanalysis.,* 18 (2006) 2385.
32. R.T. Kachoosangi, G.G. Wildgoose, R.G. Compton, *Electroanalysis.,* 20 (2008) 1714.
33. G.R. Xu, S. Kim, *Electroanalysis.,* 18 (2006) 1786.
34. Y.-h. Zhu, Z.-l. Zhang, W. Zhao, D.-w. Pang, *Sens.. Actuators. B.,* 119 (2006) 308.
35. R.N. Goyal, V.K. Gupta, S. Chatterjee, *Sens. Actuators B,* 149 (2010) 252.
36. S. Majdi, A. Jabbari, H. Heli, H. Yadegari, A. Moosavi-Movahedi, S. Haghgoo, *J. Solid. State. Electrchem.,* 13 (2009) 407.
37. H.A.M. Hendawy, H.M. Elwy, A.M. Fekry, *Int. J. Pharm.*Sc., 9 (2017) 43.
38. N. Yang,, Q. Wan, J. Yu, *Sens.. Actuators. B,*110 (2005) 246.
39. M.P. Char, E. Niranjana, B.K. Swamy, B. Sherigara, K.V. Pai, *Int. J. Electrochem. Sci.,* 3 (2008) 588.
40. D.S. Nayak, N.P. Shetti, *J. Surfactants. Deterg.*, 19 (2016) 1071.
41. A.J. Bard, L.R. Faulkner, *Electrochemical Methods Fundamentals and Applications,* 2nd ed. John

Wiley and Sons, New York, (2001).
42. ICH, Q2 (R1): *Validation of analytical procedures: text and methodology*, predented in International Conference on Harmonization, Geneva, (2005).
43. A.W. Sobańska, K. Kałębasiak, J. Pyzowski, E. Brzezińska, *J. Anal. Methods. Chem.*, 2015 (2015) 1.