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Exploiting of Green Synthesized Doped Metal Oxide Nanosensor for Electrochemical Determination of Aspirin and Ibuprofen in Biological and Pharmaceutical Samples

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Abstract

The aim of the present study was to develop electrochemical sensors based on pencil graphite electrode modified with green-caped ZnO, CdO nano particles and potassium tetra chloroplatinate (II), for a simple and fast simultaneous microextraction and determination of Aspirin (ASA) and Ibuprofen (IBU). The nanoparticles were initially synthesized by the use of four vegetable extracts including garlic, onion, green onion and cabbage. The fabricated nanoparticles and platinum were then deposited on the surface of a pencil graphite electrode and was used as a working electrode in a three electrodes system. The Taguchi experimental design was employed for investigating the effects different parameters. For this purpose, a Taguchi L16 orthogonal array (OA) design was applied and the results were confirmed by the ANOVA test. The electrochemical behavior of ASA and IBU at the modified electrodes, were studied. The calibration curves were linear in the range of 5.17to 134.0 µg.mL^{-1} and 3.13 to 231.0 µg.mL^{-1} for ASA and IBU respectively. The limits of detection for ASA and IBU was calculated to be 0.50 and 0.42 µg.mL^{-1} respectively. The modified sensor showed good performance for simultaneous analysis of ASA and IBU in biological and pharmaceutical samples.

Keywords

Green-Caped ZnO/ CdO Nano Particles; Voltammetry; Aspirin; Ibuprofen; Platinum.

1. INTRODUCTION

Acetyl salicylic acid (ASA) known as aspirin, and Ibuprofen with the chemical name of 2-[4-(2-methylpropyl) phenyl] propanoic acid, are two of the most important non-steroidal inflammatory drugs (NSAIDs) [1, 2]. They exhibit good performance for pain treatment such as headache, muscle aches, menstrual cramps, arthritis, backache, migraine, musculoskeletal disorders, fever and primary dysmenorrhea [3-5]. Aspirin given shortly after a heart attack decreases the risk of death. Lower doses of aspirin have also shown to reduce the risk of death from a heart attack or the risk of stroke in some circumstances [6, 7]. The effect of salicylates on cancer treatment has been studied, too. It may also decrease the risk of certain types of cancer, particularly colorectal cancer [8] although the mechanism of this effect is unclear [6]. One common adverse effect is stomach upset. More significant side effects include stomach ulcers, stomach bleeding, and worsening asthma. Bleeding risk is greater among elderlies and people who drink alcohol, take other NSAIDs, or are on other blood thinners.

As consumption of these drugs are increasing, the studies on their measurement and removal from biological samples and wastewaters with fast and sensitive analytical techniques is important. In this regards, a number of analytical approaches such as spectrophotometry, gas chromatography, mass spectroscopy, capillary electrophoresis, titrimetric, spectrofluorometric, UV-Vis spectrometry, flow injection analysis, Molecular imprinted technique (MIP) and high performance liquid chromatography (HPLC) coupled with different detectors and electrochemical methods have been applied for determination of ASA and IBU [3, 4, 9].

Each method has its advantages and limitations, some of the limitations of these methods include high solvent consumption, the need for expensive instruments, and the use of complex sample preparation methods [10].

Today, electrochemical methods have gained considerable attention in fundamental researches. The reason for such interest is its precision, simplicity, reasonable cost, high sensitivity, good selectivity, low detection limit and repeatability in identification and measurement of different drugs component [11, 12]. Electrochemical methods based on chemically modified electrodes are attractive alternatives for electroactive species detection, because of its inherent advantages of simplicity, high sensitivity and relatively low cost, quick response and selectivity for determination of trace level analytes [13].

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For increasing the sensitivity of voltammetry, pulse-based methods have been proposed. By application of differential pulse voltammetry, measurement of low amounts of electro-active drugs are possible, which has crucial importance in industry, pharmacology and the study of biologic mediums [14]. The substantial similarity between electrochemical biological interactions on the electrode surface with that of human body resulted in increasing interest in electrochemical methods for investigation of drug effects in ongoing procedures in human body [15, 16].

With these explanations, the present study was performed to create and develop a simple, fast and precise electrochemical sensors based on nano-CdO@PGE, nano-ZnO@PGE and Pt (II)@PGE for simultaneous determination of ASA and IBU. This modified electrode showed good performance for simultaneous determination of ASA and IBU with low detection limit and wide linear range. The proposed sensor was investigated for analytical applicability of the drugs in real and biological samples. Scheme 1S shows the chemical structure of Ibuprofen and Aspirin.

2. EXPERIMENTAL

2.1. Instruments and Materials

Ibuprofen, Aspirin, Potassium tetrachloroplatinate (II) and organic solvents and chemicals of analytical grade were provided from Merck (Darmstadt, Germany) and Sigma-Aldrich Company (USA). The stock solutions of drugs at 500 ppm concentrations were prepared in ethanol. Electrochemical studies were conducted by cyclic (CV) and differential pulse voltammetry (DPV) methods with the help of a Metrohm Model797Computrace (Switzerland). For pH measurements, a Metrohm pH meter 827 (Switzerland) was employed. A Hielscher ultrasonic bath processor (UTR200, Germany) with 60% amplitude and 0.5 Sec cycle was used for the nanoparticles dispersion. The functional groups of the nanocomposite were studied with a ShimadzuFTIR8400 Fourier transform infrared spectrophotometer (Japan). XRD studies were carried out by Philips D6792 (Netherlands) with cupper anode, and for recording the SEM imaging, a Hitachi SU3500 (Japan) was employed. The Minitab software was used for experimental design, based on a standard orthogonal array and statistical treatment of the results.

2.2. Green synthesis of nanoparticles

For the process of synthesis of nanoparticles, four vegetable including garlic (G), onion (O), green onion (GO), and cabbage (C), have been used. For this purpose, the plants were washed separately, dried, and divided into pieces. They were then crushed in an agate mortar, and the extracts were collected after filtering through a filter paper. Four separate dishes were taken in each of them with 0.02 mL of each extracts (garlic, onion, green onion or cabbage) followed by adding 10 mL of 0.02M zinc acetate solution and adjusted at pH of 12 with 0.4 M NaOH. These solutions were sonicated for 90 minutes until milky white solutions were obtained. The mixtures were then filtered and the obtained precipitates were washed with distilled water for three times and air dried. The white powders were then placed in a vacuum oven at 60 ^{0C} for 2 hours. These stages were repeated for synthesis of CdO nanoparticles as above using aqueous cadmium acetate employing four vegetable extracts [17]. The eight product powders: ZnO (G), ZnO (O), ZnO (GO), ZnO (C), CdO (G), CdO (O), CdO (GO), and CdO (C) were used for characterization of ZnO and CdO nanoparticles by FTIR, SEM and XRD methods. In this process, the metal acetate salts, were used as precursor and the vegetable extracts were employed as reducing and coating agents. The reason for adding the extracts was to make a cover around the metal oxide molecules in order to prevent the particles from sticking together and hence decreasing the nanoparticle size. Because ZnO (G) and CdO (C), showed the smallest particle size in FTIR, SEM and XRD studies, they were used in nano-CdO@PGE and nano-ZnO@PGE electrodes modification process.

2.3. Design of experiments; Taguchi's orthogonal array (OA)

In order to evaluate the effects of selected factors on the process, and reducing the number of experiments and also to describe the plan of experiments, Taguchi method can provide an accepted standard orthogonal array.

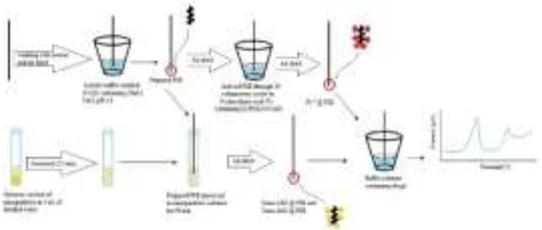
In this research, for identifying the optimal parameters and selecting the most effective ones, a Taguchi method was used as statistical experiment optimization method, to orthogonal array experimental design via Minitab (Ver. 16) software. Table 1S (in the supplementary data file) shows the assignments of the experimental factors and their levels.

2.4. Preparation of nano-CdO@PGE, nano-ZnO@PGE and Pt (II)@PGE

The construction of simple modified electrodes with the purpose of specific efficiency can be considered as a valuable step in the scientific progress. To improve sensing properties, the pencil graphite electrode, was modified with metal oxides. Zinc and cadmium oxides, were synthesized by an eco-friendly method at nano-scale, using vegetable extracts, to improve the performance of the electrodes.

Vegetable plants are favored reducing and/or capping agents and also stabilizers and may be a potential candidate for trapping drugs by means of suitable functional groups. The selected vegetables are found to be rich in flavonoids (polyphenolic compounds), alkaloids, terpenoids, glycosides, etc., which are responsible for enhancing the biogenic synthesis of ZnO, and CdO nanoparticles.

These green caped nano metal oxides can be linked to active drug sites, and therefore accelerate the extraction and simultaneous measurement of drugs in the reaction medium.



Scheme 1. Preparation steps of the nano-CdO@PGE, nano-ZnO@PGE and Pt(II)@PGE green-caped composites for modifying platinum modified pencil graphite electrode

As the Follow up steps of electrodes preparation shown in scheme 1, the modified nano-CdO@PGE and nano-ZnO@PGE electrodes were made in three steps: initially, for activation of carboxyl and hydroxyl groups on the PGE surface, the electrochemical procedure was used. For this purpose, the PGE electrodes were placed in 10 mL of the acetate buffer solution (0.1 M) containing 20 mM NaCl (pH 4.8) for 30seconds at the potential of +1.40 V [18]. Second, the required amounts of each nano metal oxide (obtained from the Taguchi design method) in 1 mL of distilled water, was sonicated for 15 minutes for complete dispersion.
Third, the activated PGE was immersed in the dispersed solution of each nanometal oxides for 90 minutes and then dried at room temperature. The nano metal oxides particles were physically adsorbed into the PGE surface by permeation and penetration into graphite micropores [18, 19].
For preparation of Pt(II)@PGE, the activated PGE, was placed in 10 mL hydrochloric acid 5% containing 0.02 mM Pt(II) (In the form of K_2PtCl_6), and the Pt(II) was uniformly deposited on the activated PGE through 10 cycles of voltammetry [20]. The CV curves are depicted in Fig. 1. The cathodic peak produced during this process, is attributed to the reduction of Platinum (IV) to Platinum (II).

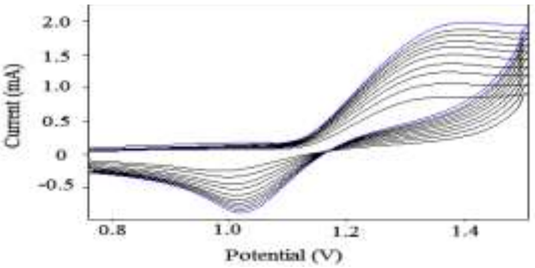


Fig. 1. The cyclic voltammograms of preparation of Pt(II)@PGE, through 10 voltammetry cycles in the presence of 10 mL hydrochloric acid 5% containing 0.02 mM Pt(II) (In the form of K_2PtCl_6).

3. RESULT AND DISCUSSION

3.1 characterization of nanoparticles

The Structure and morphology of synthesized nanoparticles were investigated by Furrier Transform Infrared spectroscopy (FTIR), X-Ray Diffraction patterns (XRD) and Scanning Electron Microscopy (SEM). As can be seen in Fig. 2, the CdO nanoparticle was analyzed by FTIR spectrum and the functional groups were recorded in the range of 400-4000 cm^{-1}. The characteristic bands at 1660.71 and 650.01 cm^{-1} is correlated to Cd-O. The peak corresponding to the wagging vibration of pure CdO is observed at 1345 cm^{-1}. FTIR peaks at 800, 1103, 1480, 1623, 2360, 2862 and 3140 cm^{-1} represent the diverse functional groups of the adsorbed biomolecules on the surface of the CdO nanoparticles. The variations in the peak positions indicate, presumably, some metabolites such as tannins, flavonoids alkaloids, and carotenoids which are abundant in flower extracts and produce the CdO nanoparticles [21, 22].

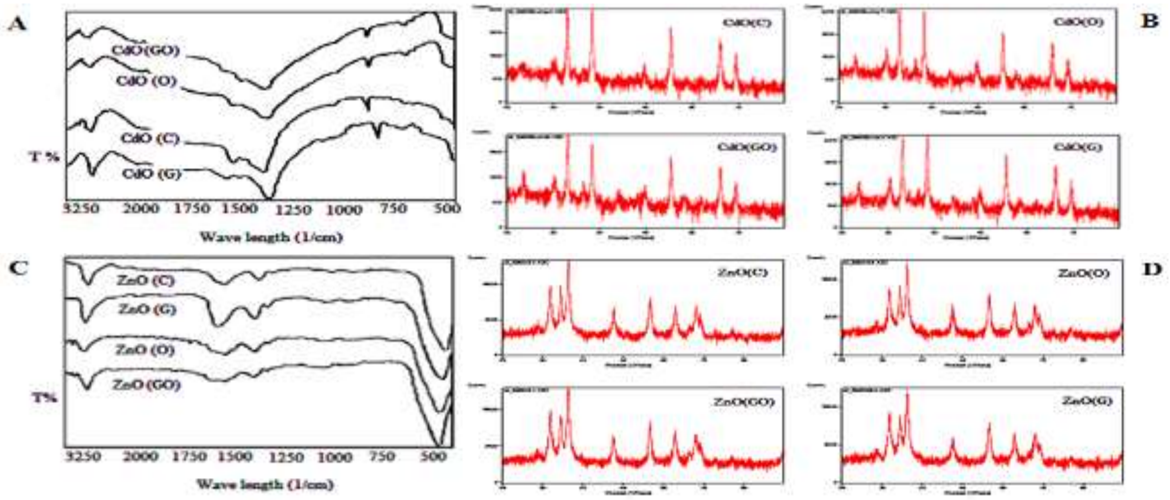


Fig. 2. A) FTIR spectrum and B) XRD patterns of CdO nanoparicles, synthesized by four vegetable extracts including garlic (G), onion (O), green onion (GO), and cabbage (K). C) FTIR spectrum and D) XRD patterns of ZnO nanoparicles, synthesized by four vegetable extracts including garlic (G), onion (O), green onion (GO), and cabbage (K).

FTIR spectra of ZnO nanoparticles have been carried out in the range of 4000-400 cm^{-1} is shown in figure 2. The FTIR spectrum shows, bands at 1400-1600 cm^{-1} due to C=O stretching mode and the absorption stretching band at 481 cm^{-1} is the stretching mode of ZnO [23, 24].

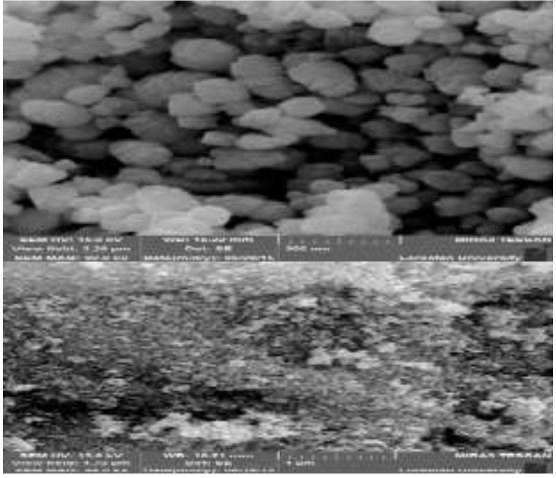


Fig. 3. SEM images of nanoparicles, synthesized by vegetable extracts: A) CdO (Synthesized with the help of extract of Cabbage) at the scale of 500 nm, B) ZnO (Synthesized with the help of extract of Garlic) at the scale of 1 µm.

As can be seen in the SEM image (Fie. 3 and Fig. 1S and 2S in the supplementary data file), the Metal oxide nanoparticles was obtained with regular arrangement. With the help of XRD pattern (figure 2), its data and Scherrer equation (equation 1), the size of nanoparticles, were calculated (Table2). A comparison between synthesized nanoparticles by different vegetable extracts and the obtained size by SEM and XRD techniques is shown in Table3. The method of nanoparticle size calculation, can be performed by the use of the following equation.

$$\tau = \frac{K\lambda}{\beta \ Cos\theta} \qquad (1)$$

where:

τ: nanoparticle size (nm)

λ: wave length of $K_{\alpha1}$of anode (for Cu:1.540)

K: Shape Factor (usually is 0.9)

β: Full width at half maximum (FWHM)

θ: diffraction angle

For example, the size of ZnO (G) in Rel. Int 1.27%, is calculated as follows:(β and 2θ come fromthe Table 2S).

The conversion of the unit of β from degree to length unit is performed using:

$$\beta(nm)=\beta(^{0}2\theta)\times \frac{2\times3.1416}{360}$$

$$\beta(nm)=0.8502\times \frac{2\times3.1416}{360}=0.1483$$

2θ=72.66, therefore θ=36.33 and Cos θ= 0.8056

K=0.9 and λ for Cu=1.54 (because the XRD patterns given by an instrument with Cu anode)

$$\tau = \frac{K\lambda}{\beta \ Cos\theta}= \frac{0.9\times1.54}{0.0148\times0.8056}=11.62 \text{ nm}$$

A comparison of synthesis method of nano metal oxides in the present work and the previously reported one in terms of nanoparticle size and reagents, is shown in Table 1.

Table 1. A comparison between the synthesis method of nano metal oxides in the present work and the previously reported methods in terms of nanoparticle size and reagents.

Nanoparticle	Precursor agent	Reagent agent	Coverage agent	Smallest synthesized nanopartinle size (nm)	Reference
Cdo	$Cd(NO_3)_2$	NaOH	Cannabis sativa	84	25
	Cd(CH3COO)$_2$	-	Penicillium oxalicum	23	26
	Cd(CH3COO)$_2$	-	*Penicillium oxalicum*	40-80	27
	$CdCl_2$	NaOH	Ethylene glycol	39	28
	$Cd(NO_3)_2$	-	Polyethylene glycol	15	28
	Dmphen-CdI2 complex	-	-	50	29
	$Cd(NO_3)_2$	NaOH	Cabbage	18	This work
	$Cd(NO_3)_2$	NaOH	Onion	31	This work
	$Cd(NO_3)_2$	NaOH	Green onion	18	This work
	$Cd(NO_3)_2$	NaOH	Garlic	29	This work
ZnO	$Zn(CH_3COO)_2$	NaOH	-	81	30
	$Zn(NO_3)_2$	-	Nelumbo nucifera	20-40	31
	$Zn(NO_3)_2$	NaOH	*Lippia adoensis*	18-27	32
	$ZnSO_4$	NH_4OH	-	24	33
	$Zn(CH_3COO)_2$	NaOH	*Mikaniamicrantha*	20-30	34
	$Zn(NO_3)_2$	NaOH	Catharanthus roseus	24	17
	$Zn(NO_3)_2$	KOH	-	20	35
	$Zn(NO_3)_2$	NaOH	Cabbage	11	This work
	$Zn(NO_3)_2$	NaOH	Onion	13	This work
	$Zn(NO_3)_2$	NaOH	Green onion	17	This work
	$Zn(NO_3)_2$	NaOH	Garlic	11	This work

3.2. Study of the method variables and statistical analysis

As mentioned earlier, the Taguchi method is a powerful tool for obtaining data in a controlled manner and to analyze the effects of important process parameters. The critical stage in planning the experiments is the selection of effective factors in the process.

In this research the main factors were found; the type and amount of metal oxide in the electrode modification process and pH, are important factors. So, in order to optimize the effective parameters on the trace measurement of ASA and IBU by the modified electrodes, the evaluation was conducted in terms of a mixed Taguchi L16 orthogonal array design. The level of factors in each experiment, and the results are given in Table 3S.

As can be seen in Table 2, as regards with the response for signal to noise ratios is given, the investigated factors can be ranked according to their influence on the response by comparing the calculated Δ(max-min) value. ANOVA test was applied to the data in order to organize the systematic analysis of the relative importance of factors.

As can be seen in Table 2, the parameters affecting the method efficiency, including the electrolyte buffer pH, type and amounts of metal oxides in the modified electrodes were investigated.

Table 2. Response Table for Signal to Noise Ratios (Larger is better)

Level	A	B	C
1	41.37	38.28	32.11
2	44.70	41.17	41.08
3	46.29	45.99	49.47
4	40.08	46.99	49.77
Delta	6.22	8.71	17.67
Rank	3	2	1

The ANOVA Table gives the sum of squares of the main factors and their interactions with the corresponding contribution to the total variance and the values of P.

According to these results, P values for all the main parameters, is less than 0.05, which means the effect of these factors on the extraction of ASA and IBU are statistically significant. The importance of the factors can be found out better, in the main effects plot (Fig. 3S in the supplementary data file). In this plot, the average response for each level of affective factors, is connected by a line. As shown in graphs for the buffer pH, type and amount of used metal oxides (Zn, Cd or Pt) in electrode modification process, the greater magnitude of the main effect, showed by the steeper slope of the line. The significance rate of the process parameters on the response of the electrode (The percentage contribution PC %) is calculated by dividing SS_d (the sum of squared deviations for each factor) to SST. Also, to check the parameters with significant effects on the quality characteristics, the F-value (a ratio of the mean square error to the residual error) was used as a statistical tool [36].

The percent numbers explain that the buffer pH in the electrolyte, type and amount of used metal oxides (Zn, Cd or Pt) in electrode modification process, have significant effects on the current amounts. As the result of the Table 4S, the (A) buffer pH in the electrolyte, (B) type and, (C) amount of metal in the modified electrodes, affect the electrode response by 8.42%, 17.07%, 71.14% in the electrochemical sensor performance, respectively.

3.3 Electrochemical studies on modified electrodes

The experimental design results show that the type of nanoparticle has a greatest influence on the sensor response. In order to evaluate the effects of type of nanoparticles on sensor efficiency, the nanoparticles containing of nano ZnO, nano CdO, and Pt(II) were used. Among them, the Pt(II) offered the highest current. The increase in atomic number increases the electron-positive property, and so the platinum with a higher atomic number 78 has a more suitable function for drugs binding than cadmium and zinc with lower atomic numbers of 48 and 30 respectively. Fig. 4 shows a comparison between bare and nano-CdO@PGE, nano-ZnO@PGE, nano-(ZnO+CdO)@PGE, and Pt(II)@PGE in the extraction and determination of drugs process. The peaks at about -0.7 and 1.0 (V) are related to Ibuprofen (IBU) and Aspirin (ASA) respectively.

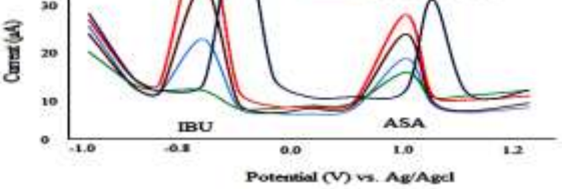


Fig. 4. A comparison between bare, nano-CdO@PGE, nano-ZnO@PGE, nano-(ZnO+CdO)@PGE, and Pt(II)@PGE modified electrodes out at pH 8.0 by DP voltagrams in the range of -1.0 to 1.2 V, for extraction and determination of ASA and IBU.

It is obvious that, pH of the buffer solution is an important factor for studying of drugs, because the oxidation of drugs is pH-dependent. Since the best electrode response was observed with Pt(II) @PGE at a concentration of 1.0 mg / mL(optimum value obtained by Taguchi method); the electrochemical studies by CV method were performed with Pt(II)@PGE electrode, and the electron transfer process was investigated. For this purpose, the pH optimization was performed in the range of 2.0 to 9.0 using Pt(II)@PGE, and the number of electrons and electron transfer coefficient were calculated. Also, by investigation of the effect of scan rate, the electrode reactions were studied.

3.3.1. Effect of pH solution

Because the studied processes are irreversible; first, by repeating the cycles, the cathodic peak potential shifted to more negative values and the anodic peaks tended to more positive values, about 30/αn by a 10-fold increase in scanning rate (in which α is the charge transfer coefficient and n is the number of electrons in velocity determining step) [37]. Second, in low scanning rates, the return-peak was not observed. Hence, by application of Laviron equation, the value of electron transport coefficient (α) is equal to 0.603 and 0.558 and the number of transferring electrons is 1.03 and 1.44 for ASA and IBU respectively. It shows one electron transfer process in ASA and IBU reactions [4, 38].

Due to peak shift as a result of the pH change, the proton has an important role in this process. In this regard, the peak potential was plotted versus pH of the buffer solution (Fig. 4S). For ASA, it showed a linear relation with a suitable slope. The plot of potential vs pH for IBU was linear up to pH 5.0 and then levelled off at higher pHs. This pH was near to the pKa for IBU which is 4.43±0.03. It can be concluded that the acid-base balance in an electroactive group of IBU-Metal is responsible for potential variations at different pH [47].

3.3.2. Effect of Scan rate

Investigation of the relation between peak current and scan rate of an electrochemical reaction could give useful information on the type of reaction and whether it is controlled by adsorption or diffusion process. Therefore, the scan rate is one of the other basic and effective factors in electrochemical reactions that should be studied by cyclic voltammetry method. This study was carried out over the range of 0.01-1.3 V/s. At very small scanning rates, any anodic or cathodic peaks were observed. By increasing of the scanning rate to 0.07 V/s, the reactions were started. A very small anodic peak (pre-wave) can be observed in the negative potential which is probably associated with the reduction of the impurities of the drugs.

The curves of peak current versus the square of scanning rate were plotted for ASA and IBU. In both curves, the correlation coefficients are close to the theoretical values of 0.9089 and 0.9311 respectively. It can be concluded that the electrode processes are governed under the control of diffusion process [4, 37, 38].

3.3.3. Calibration curves and method validation

Using Taguchi experimental design and under the optimized conditions, the calibration equations were obtained using standard concentrations of the analytes. As Pt(II)@PGE showed the best response, the individual and simultaneous voltammetric determination of ASA and IBU by using the Pt(II)@PGE modified electrode was carried out at pH 8.0 by DPV, so that when concentration of one analyte is changed, the concentration of another analyte was constant. Fig. 5A, shows the DP voltagrams of ASA at different concentrations in the presence of 1×10^{-4} M IBU. The peak current for ASA increased linearly with the increase of concentration with the correlation coefficient 0.9881. Fig. 5B, also shows that the peak current of IBU also increases linearly with increasing the concentration with the correlation coefficient 0.9850while the concentration of ASA was kept constant equal to 1×10^{-4} M.

It was concluded that, the selective determination of each analyte is possible in the presence of another. As the electrochemical signals of ASA and IBU were independent of each other using the Pt(II)@PGE. The correlation coefficient (R^2), experimental limit of detection (LOD) and quantification (LOQ), and the linear dynamic range (LDR) were studied under the optimum conditions to evaluate the practical applicability of the sensor. The LOD and LOQ were calculated to be 0.50, 1.48 for ASA and 0.42, 1.37 for IBU respectively. The linear dynamic range were found to be in the range of 5.17-134.0 $\mu g.mL^{-1}$ for ASA and 3.13-231.0 $\mu g.mL^{-1}$ for IBU respectively. Table 3 shows a comparison between previously reported methods for ASA and IBU determination, and proposed method.

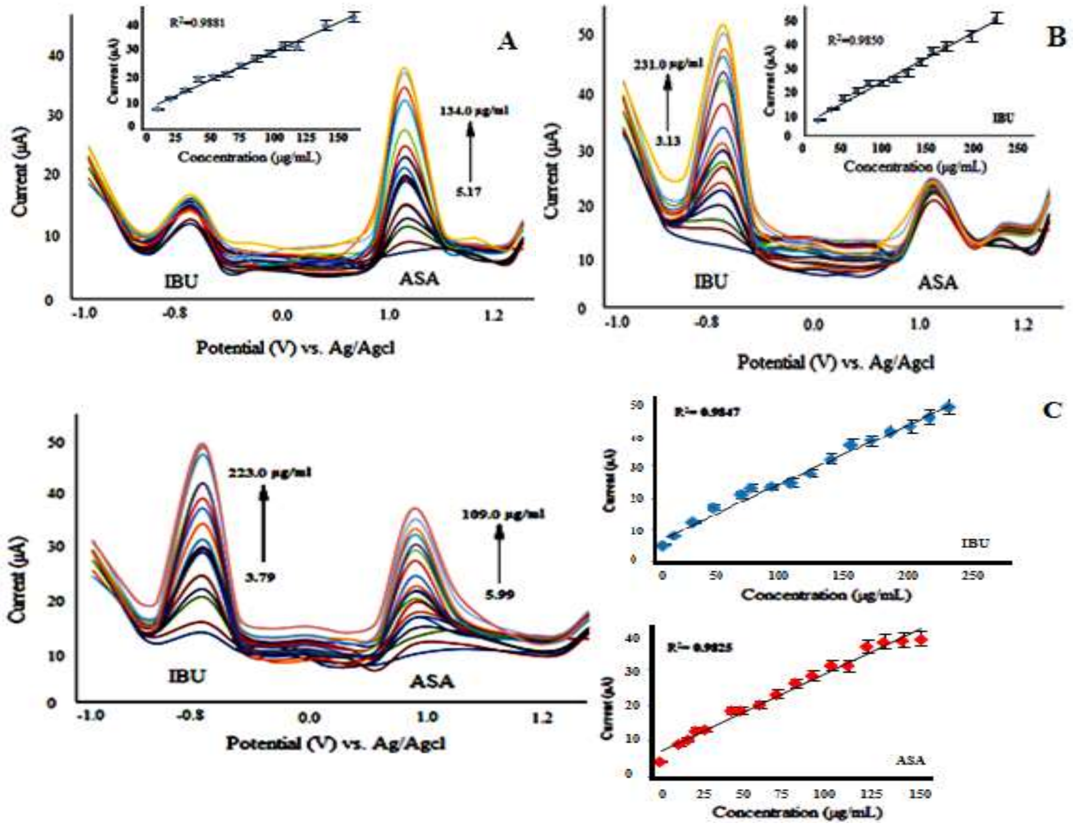


Fig. 5. Calibration curves by using the Pt(II)@PGE modified electrode out at pH 8.0 by DP voltagrams of A) ASA in the presence of 1×10 $^{-4}$ M IBU B) IBU in the presence of 1×10 $^{-4}$ M ASA and C) Simultaneous determination of ASA and IBU (when concentration of one analyte is changed, the concentration of another analyte was constant).

Table 3. The comparison between methods of determination of ibuprofen (The previously reported methods and proposed method).

Analyte	Technique	Linear range (μg/ml)	LOD (μg/ml)	Reference
ASA	DLSVA	0.88-2.8	0.26 mM	39
	CTAB-PGE	50-300μM	-	40
	DPV	0.04-350	1.19 nM	41
	SWV	0.139-27.8	411 nM	42
	UV/VIS	0.5-100	0.5	43
	Colorimetric Detection	0.4-28 μM	0.26 μM	44
	Differential Pulse and Cyclic Voltammetry	5.17-134	0.50	This work
IBU	Spectrophotometric Determination	6-54	76ng/ml	3
	GC and Spectrophotometriy	2-10μg/L	0.4μg/L	45
	Chromatography	50-500	-	46
	RP-HPLC	-	0.03	47
	UV/VIS	0.4-40	0.4	43
	Differential Pulse and Cyclic Voltammetry	3.13-231	0.42	This work

Table 4. Results of investigation of drugs determination method on real samples.

Sample	Analyte	RR%*	RSD
Tablet	ASA	97.13	0.042
	IBU	101.94	0.001
Nail	ASA	31.02	0.071
	IBU	29.18	0.021
Laboratory waste	ASA	74.13	0.037
	IBU	73.23	0.041

* Relative Recovery %

3.4 Real samples

For validating the method, analysis of drugs in real samples such as Tablet, nail and lab wastewater were conducted.

The tablets were prepared as follows: to prepare the sample, 5 tablets were first weighed and then mixed and thoroughly ground. First, a weighted amount of tablets was dissolved in a certain amount of ethanol, and the resulting mixture was filtered to separate insoluble substances. Then an ethanol-water solution (10%, v/v) of them was prepared.

Nail samples were obtained by cutting the the nails using a nail clipper. Nails from all fingers were collected, and stored in separate bags. To prepare the nail sample, 0.1 g of the nail was washed with acetone, dried and dissolved in 5 ml of sulfuric acid 1.0 M.

Wastewater samples were filtered a few times and finally centrifuged before testing. Specified amounts of analyte were spiked to nail, drug tablet samples and laboratory wastewater and the extraction process were performed. The results are shown in Table 4.

4. CONCLUSION

The electrochemical study of drugs and drug compounds would lead to investigate the mechanism in order to improve the effectiveness of drugs in different illnesses. In this research nano-CdO@PGE, nano-ZnO@PGE and Pt(II)@PGE sensors were successfully fabricated based on nanoparticles synthesized by vegetable extracts. In these sensors, ASA and IBU were extracted to the pores of the activated PGE and further detected in biological samples through nano-CdO@PGE, nano-ZnO@PGE and Pt(II)@PGE with good selectivity. To achieve optimal conditions a Taguchi method was used. The results showed that the fabricated Pt(II)@PGE was successfully applied for one-step extraction and DPV analysis of ASA and IBU in biological samples. The method presents a wide linear range and low limit of detection. Good selectivity, easy preparation and simple operation, high sensitivity, and low cost make the method suitable for the study of ASA and IBU levels in real samples and pharmaceutical formulations with satisfactory results.

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بهره برداری از یک نانوحسگر دوپه شده ی اکسید فلزی سنتز شده سبز برای تعیین الکتروشیمیایی آسپرین و ایبوپروفن در نمونه های بیولوژیکی و دارویی

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چکیده

هدف از مطالعه حاضر، توسعه حسگرهای الکتروشیمیایی مبتنی بر الکترود گرافیتی اصلاح شده با ذرات اکسید روی، نانو ذرات CdO و پتاسیم تترا کلروپلاتینات (II)، برای یک میکرواستخراج همزمان ساده و سریع و تعیین آسپرین و ایبوپروفن بود. این نانوذرات در ابتدا با استفاده از چهار عصاره گیاهی شامل سیر، پیاز، پیاز سبز و کلم سنتز شدند. سپس نانوذرات و پلاتین ساخته شده بر روی سطح یک الکترود گرافیتی مدادی رسوب کردند و به عنوان یک الکترود کار در یک سیستم سه الکترودی مورد استفاده قرار گرفتند. برای بررسی اثرات پارامترهای مختلف از طرح آزمایشی تاگوچی استفاده شد. برای این منظور از طرح آرایه متعامد تاگوچی L16 (OA) استفاده شد و نتایج با آزمون ANOVA تایید شد. رفتار الکتروشیمیایی آسپرین و ایبوپروفن در الکترودهای اصلاح شده مورد بررسی قرار گرفت. منحنی های کالیبراسیون به ترتیب برای آسپرین و ایبوپروفن در محدوده ۵٫۱۷ تا ۱۳۴٫۰ میکروگرم بر میلی لیتر و ۳٫۱۳ تا ۲۳۱٫۰ میکروگرم بر میلی لیتر در لیتر خطی بودند. حدود تشخیص برای آسپرین و ایبوپروفن به ترتیب ۰٫۵۰ و ۰٫۴۲ میکروگرم بر میلی لیتر در لیتر محاسبه شد. حسگر اصلاح شده عملکرد خوبی برای آنالیز همزمان آسپرین و ایبوپروفن در نمونه های بیولوژیکی و دارویی نشان داد.

واژه‌های کلیدی

نانوذرات ZnO/CdO با کلاه سبز؛ ولتامتری؛ آسپرین؛ ایبوپروفن؛ یون پلاتین.