La$_2$O$_3$/Co$_3$O$_4$ nanocomposite modified screen printed electrode for voltammetric determination of sertraline

SAYED ZIA MOHAMMADI$^{1*}$, HADI BEITOLLAHI$^2$, TAHEREH ROHANI$^1$, HOSSEIN ALLAHABADI$^1$ and SOMAYEH TAJIK$^3$

$^1$Department of Chemistry, Payame Noor University, Tehran, Iran, $^2$Environment Department, Institute of Science and High Technology and Environmental Sciences, Graduate University of Advanced Technology, Kerman, Iran and $^3$Research Center of Tropical and Infectious Diseases, Kerman University of Medical Sciences, Kerman, Iran

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Abstract: La$_2$O$_3$/Co$_3$O$_4$ nanocomposite was synthesized and then used for the modification of screen-printed electrode (SPE) prior to the electrochemical determination of sertraline. A significant increment in peak current response was observed and peak potential also shifted towards less positive potentials showing the facilitated oxidation procedure at surface of modified SPE (La$_2$O$_3$/Co$_3$O$_4$/SPE). The quantitative determination of sertraline was carried out by using different pulse voltammetry and the anodic peak current was found to increase with increasing sertraline concentration in the linear range of 5.0–400.0 µM with limit of detection as 1.0 μM. The prepared La$_2$O$_3$/Co$_3$O$_4$/SPE has been successfully used for detecting sertraline in sertraline tablet and urine samples with excellent recoveries.

Keywords: sertraline; electrochemical reaction; differential pulse voltammetry.

INTRODUCTION

Sertraline (cis-1S,45-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthalenaminehydrochloride), as a preferable drug for the treatment of premenstrual dysphoric disorder, social anxiety disorder, posttraumatic stress disorder, panic disorder, obsessive compulsive disorder and major depressive disorder.$^{1,2}$ Sertraline oral tablet is a prescription drug that’s available as the brand-name drug zoloft. It was first presented by Pfizer in 1991. Sertraline is an artificial selective inhibitor drug for reuptake of serotonin (5-hydroxytriptamine, 5-HT). This drug works by increasing the amount of serotonin, a natural substance in your brain, that helps maintain mental health balance.$^{3,4}$ Sertraline may cause loss of appetite, insomnia, increased sweating, sexual problems, shaking, fatigue and agitation. Furthermore, current researches have showed that selective

* Corresponding author. E-mail: szmohammadi@yahoo.com
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serotonin reuptake inhibitors such as sertraline interpenetrate the cell membrane are associated with a high risk of expanding cancer. Accordingly, the precise determination of component amounts of sertraline biological specimens, such as plasma, blood and urine is necessary. The development of robust analytical methods that can easily detect pharmaceutical contaminants is challenging. In the past years, many analytical methods including HPLC, voltammetry, capillary electrophoresis, gas chromatography-mass spectrometry, spectrofluorimetry and spectrophotometry have been reported for the measurement of sertraline in biological and pharmaceutical samples. Among all these techniques, electrochemical methods have advantages in relation to other techniques such as simplicity, short response time, good to excellent selectivity and inexpensive cost. However, because of the poor electrochemical behaviour of the most of electro-active analytes, low reducibility, sensitivity and high over potential at electrodes, the performance of the electrodes in electrochemical methods can be improved if they were modified by various nanomaterials and methodologies. Nanostructured materials are one of the most promising supporting materials for surface modification of electrodes, due to their unique properties, such as good biocompatibility, high surface-to-volume ratio, substantial mechanical power and electrical properties. Lanthanum (La) is one of the most important lanthanide elements. La ions have relatively low toxicity and extraordinary catalytic properties, thus, they can be used to construct environment-friendly sensors. Metal oxide nanoparticle that are used for modification of electrodes, have some distinct advantages such as low influence of the solution resistance, high mass transport rate, low detection limits and better signal-to-noise ratio compared to the conventional electrodes.

Based on our previous reports that La₂O₃/Co₃O₄/SPE used for determination of carvacrol and cabergoline, in this work, a simple and low cost electrochemical sensor based on modification of screen printed electrode using La₂O₃/Co₃O₄ nanocomposite was proposed and used for determination of sertraline within real samples.

**EXPERIMENTAL**

**Reagents and apparatus**

Sertraline hydrochloride and all other reagents were of analytical grade, and were purchased from Merck (Darmstadt, Germany). Stock solutions of sertraline were prepared by dissolving its appropriate amount of its powder in double distilled water and preserved in the dark inside a refrigerator at 4 °C. Double-distilled water was used entirely. Working solutions were prepared by accurate dilution from stock solution using double distilled water. For the preparation of phosphate buffer solutions, the ortho-phosphoric acid and its salts were used. Phosphate buffer solutions (PBS) with different pH values were used as the supporting electrolyte.

The morphology of the nanocomposites was analyzed with KYKY EM 3200 scanning electron microscopy (SEM). Powder X-ray diffraction (XRD) studies were performed on a Rigaku D/max 2500 V instrument with a graphite monochromator and a Cu target. Chemical
characterizations La<sub>2</sub>O<sub>3</sub>/Co<sub>3</sub>O<sub>4</sub> nanocomposite was studied by Fourier transform infrared (FT-IR) spectroscopy in order to identify the functional groups at the surface of nanocomposite. FT-IR spectra was recorded with a Brucker Tensor 27 spectrometer, from 400 to 4000 cm<sup>-1</sup>, using the KBr wafer technique. Wafers were prepared from the mixture of 1 mg of the sample and 100 mg of KBr. The SPE (DropSens, DRP-110, Spain) consists of three conventional electrodes: a graphite working electrode, a silver pseudo-reference electrode, and a graphite counter electrode. An Autolab potentiostat/galvanostat (PGSTAT 302N, Eco Chemie, the Netherlands) was employed to perform the electrochemical experiments and the system was controlled using the software GPES, version 4.9. A Metrohm 710 pH meter equipped with the glass electrode was used for pH adjustment.

La<sub>2</sub>O<sub>3</sub>/Co<sub>3</sub>O<sub>4</sub> nanocomposite synthesis

All the chemicals used for the preparation of the La<sub>2</sub>O<sub>3</sub>/Co<sub>3</sub>O<sub>4</sub> nanocomposite, including cobalt acetate (Co(CH<sub>3</sub>COO)<sub>2</sub> 2H<sub>2</sub>O), thiourea ((NH<sub>2</sub>)<sub>2</sub>CS) and ammonia (25 % NH<sub>3</sub>) were analytical grade. All the precursors were dissolved in double distilled water. The ammonia was considered as complexing agent during the preparation of the nanocomposite. At first, 0.46 mol of cobalt acetate, 0.18 mol of thiourea and 19.76 mL of ammonia was dissolved in 3 beaker contain 80 mL double distilled water, separately. Then, the beaker containing cobalt acetate was transferred to a water bath (40 °C) and thiourea solution was added to it and stirred for a few seconds. At last, ammonia solution was added slowly into the mixture, while stirring was continued for 5 min. Then, the temperature of the bath was increased up to 80 °C. The resulting precipitation was left overnight, finally filtered and washed with ethanol. The drying process of the resulting powder was carried out for several days at the room temperature. La<sub>2</sub>O<sub>3</sub>/Co<sub>3</sub>O<sub>4</sub> nanocomposites were prepared by the impregnation of La<sub>2</sub>O<sub>3</sub> nanoparticles onto the surface of Co<sub>3</sub>O<sub>4</sub> hexagonal nanosheets. For this purpose, 0.2 mol lanthanium nitrate was dissolved in 50 mL double distilled water and mixed with 0.1 g Co<sub>3</sub>O<sub>4</sub> hexagonal nanosheets. After this, the appropriate amount of NaOH solution (1.5 M) was added dropwise into the mixture until the pH of the mixture reached to 10. The obtained precipitation was heated up to 80 °C and was stirred for 1 h. After the reaction was completed and cooled to room temperature, the resulting product was centrifuged for 15 min at 3000 rpm. Finally, the precipitate was washed several times with double distilled water and vacuum-dried at 60 °C overnight.

Real samples

Urine samples were stored in a refrigerator immediately after collection. 10 mL of the sample was centrifuged for 15 min at 3000 rpm. The supernatant was filtered out using a 0.45 μm filter. Then, 1 mL of filtrate was transferred into a 10 mL volumetric flask and diluted with 9 mL of PBS pH 7). Then various volumes of sertraline hydrochloride standard solution were added to it and the measurements were done.

To prepare the tablet samples, five 50 mg sertraline tablets (Kern Pharma, Spain) were completely ground and homogenized, 50 mg of this powder was accurately weighed and dissolved with ultra-sonication in 15 mL of water. Finally, the mixture was filtered, and the clear filtrate was transferred into a 25 mL volumetric flask and diluted to the mark using 0.1 M PBS with pH 7.0. Then, 5 mL of the resultant solution was transferred into a 25 mL volumetric flask and various volumes of sertraline hydrochloride standard solution were added to it, diluted to the mark with PBS (pH 7.0) and vortexed for 1 min.

Preparation of modified electrode

The bare SPE was coated with La<sub>2</sub>O<sub>3</sub>/Co<sub>3</sub>O<sub>4</sub> nanocomposite according to the following simple procedure: 1 mg La<sub>2</sub>O<sub>3</sub>/Co<sub>3</sub>O<sub>4</sub> nanocomposite was dispersed in 1 mL double distilled

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water, during 45 min ultra-sonication. Then, 5 µl of the prepared suspension was dropped on the surface of the working electrode. It remained at room temperature until becomes dry.

RESULTS AND DISCUSSION

Morphology and structure of La$_2$O$_3$/Co$_3$O$_4$ nanocomposite

The FT-IR spectra of La$_2$O$_3$/Co$_3$O$_4$ nanocomposite sample are shown in Fig. 1a in the frequency range of 400–4000 cm$^{-1}$. The FT-IR spectrum of La$_2$O$_3$/Co$_3$O$_4$ nanocomposite showed strong vibrational bands in the lower frequency regions (at around 520 and 449 cm$^{-1}$), related to the vibration of metal–O. The absorption seen at ~3417 cm$^{-1}$ is thought to be due to the symmetric vibration of the –OH groups of the absorbed H$_2$O molecules.$^{31}$

![Fig. 1. FT-IR image of La$_2$O$_3$/Co$_3$O$_4$ nanocomposite (a), XRD pattern of La$_2$O$_3$/Co$_3$O$_4$ nanocomposite (b) and SEM image of La$_2$O$_3$/Co$_3$O$_4$ nanocomposite (c).](image-url)

The X-ray diffraction (XRD) pattern of La$_2$O$_3$/Co$_3$O$_4$ nanocomposite is shown in Fig. 1b. It can be seen that all major diffraction peaks in the spectrum indicate a pure phase for the La$_2$O$_3$/Co$_3$O$_4$ nanocomposite and match with the standard peaks of this sample. For La$_2$O$_3$/Co$_3$O$_4$ nanocomposite, the diffraction peaks at 31.7, 36.1, 44.5, 59.9 and 64.9° (JCPDS 74-2120) can be indexed to (220), (311), (400), (511) and (400) planes of Co$_3$O$_4$, the diffraction peaks at 15.1, 28.5, 29.1, 39.8, 49.1 and 55.2° (JCPDS 41-4019) can be indexed to (100), (002), (101), (102), (211) and (201) plane of La$_2$O$_3$, respectively.$^{32,33}$

The surface morphology of La$_2$O$_3$/Co$_3$O$_4$ nanocomposite was examined via SEM image (Fig. 1c) and shown that Co$_3$O$_4$ nanosheets and La$_2$O$_3$ nanoparticles construct La$_2$O$_3$/Co$_3$O$_4$ nanocomposite.
Electrochemical behaviour of fabricated sensor

The pH of aqueous solution is effective on the sertraline’s electrochemical behaviour. Therefore, the pH of the solution was optimized to approach high accurate results for sertraline electro-oxidation. Accordingly, the electrochemical activity of sertraline was examined in 0.1 M PBS with different pH (3.0–9.0) onto surface of La$_2$O$_3$/Co$_3$O$_4$/SPE, via differential pulse voltammetry (DPV) (Fig. 2). The obtained results showed that neither acidic nor basic medium was appropriate for the electro-oxidation of sertraline onto surface of La$_2$O$_3$/Co$_3$O$_4$/SPE and best results obtained at neutral conditions. Accordingly, the pH 7.0 was selected as the optimal pH for electro-oxidation of sertraline onto surface of La$_2$O$_3$/Co$_3$O$_4$/SPE.

![Fig. 2. DPVs of the La$_2$O$_3$/Co$_3$O$_4$/SPE in the presence of 100.0 µM sertraline at various buffered pHs (at 50 mV s$^{-1}$). The inset shows the $I_p$ vs. pH of PBS (3.0, 4.0, 5.0, 6.0, 7.0, 8.0 and 9.0).](image)

The cyclic voltammetric responses for electro-oxidation of 400.0 µM sertraline at the La$_2$O$_3$/Co$_3$O$_4$/SPE and unmodified SPE are shown in Fig. 3. The peak potential on the surface of La$_2$O$_3$/Co$_3$O$_4$/SPE (modified electrode) was observed at 860 mV corresponding to the sertraline oxidation, which is about 320 mV more negative than the unmodified SPE. Moreover, the anodic peak current for the sertraline oxidation at La$_2$O$_3$/Co$_3$O$_4$/SPE was much higher in comparison with the unmodified SPE, indicating to the effectiveness of SPE modification with La$_2$O$_3$/Co$_3$O$_4$ nanocomposite in the sertraline oxidation process.

The effect of potential scan rates on the oxidation current of sertraline has been studied. The results showed that increasing in the scan rate leads to the increase of oxidation peak current. In addition, there is a linear relationship between $I_p$ and the square root of the potential scan rate ($\nu^{1/2}$) that demonstrates that the oxidation procedure of sertraline is diffusion control.\(^{34}\)
Fig. 3. CVs of: a) La$_2$O$_3$/Co$_3$O$_4$/SPE and b) unmodified SPE in 0.1 M PBS (pH 7.0) in the presence of 400.0 μM sertraline at the scan rate 50 mV s$^{-1}$.

The Tafel curve of analyte was plotted by using the data from the rising section (i.e., the Tafel region) of the current–voltage curve obtained at 10 mV s$^{-1}$ (Fig. 4). The kinetics of electron transfer in the electrode response has effect on the Tafel region of the current-potential curve. In this case, a Tafel slope of 0.1918 V was obtained, which agrees with the involvement of one electron in the

Fig. 4. CV (at 10 mV s$^{-1}$) of electrode in 0.1 M PBS (pH 7.0) containing 30.0 μM sertraline. The points are the data used in the Tafel plot. The inset shows the Tafel plot derived from the CV.
rate determining step of the electrode process, assuming a charge transfer coefficient of $\alpha = 0.69$.\textsuperscript{34}

**Chronoamperometric analysis**

Chronoamperometric measurements of sertraline at surface of $\text{La}_2\text{O}_3/\text{Co}_3\text{O}_4$/SPE were carried out by setting the working electrode potential at 900 mV, vs. Ag/AgCl/KCl (3.0 M) for the various concentrations of sertraline (Fig. 5) and in PBS (pH 7.0). After this, the experimental plots of $I$ vs. $t^{-1/2}$ were drawn in Fig. 5A. Then, the slopes of the resulting straight lines were plotted vs. sertraline concentrations (Fig. 5B). From the resulting slope and Cottrell equation, the mean value of the $D$ was found to be $1.1 \times 10^{-6}$ cm$^2$ s$^{-1}$ for sertraline.\textsuperscript{34}

![Fig. 5. Chronoamperograms obtained at $\text{La}_2\text{O}_3/\text{Co}_3\text{O}_4$/SPE in 0.1 M PBS (pH 7.0) for different concentration of sertraline. Numbers 1–4 correspond to 0.1, 0.3, 0.8, and 1.5 mM. Insets: A) plots of $I$ vs. $t^{-1/2}$ obtained from chronoamperograms 1–4. B) plot of the slope of the straight lines against sertraline concentration.](image)

*The working curve and detection limit*

The electro-oxidation peak current of sertraline at the surface of $\text{La}_2\text{O}_3/\text{Co}_3\text{O}_4$/SPE can be used for determination of sertraline in the solution. Due to higher sensitivity and the enhanced performance of DPV in analytical applications, the DPV experiments were carried out using $\text{La}_2\text{O}_3/\text{Co}_3\text{O}_4$/SPE in 0.1 M PBS containing different concentrations of sertraline. The calibration curve exhi-
bited linearity over the range of 5.0 to 400.0 μM, with a correlation coefficient of 0.9997 \( (Y = 0.003C + 0.34) \), where \( Y \) is the peak current, μA and \( C \) is the concentration of sertraline, μM). Limit of detection based on three times the standard deviation of the blank (3σ) and limit of quantification based on ten times the standard deviation of the blank (10σ) were \( 10^{-6} \) and \( 3.3 \times 10^{-6} \) M, respectively. These values were compared with values reported by other research groups for electrochemical determination of sertraline (Table I). With respect to Table I, the linear dynamic range (LDR) and the detection limit of (LOD) present work are comparable to values acquired by other research groups.

TABLE I. Comparison of the efficiency of electrochemical methods used in detection of sertraline

<table>
<thead>
<tr>
<th>Method</th>
<th>Electrode</th>
<th>Modifier</th>
<th>LOD μM</th>
<th>LDR μM</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differential pulse</td>
<td>Glassy carbon</td>
<td>Rutin</td>
<td>1.0</td>
<td>3.0–90.0</td>
<td>7</td>
</tr>
<tr>
<td>voltammetry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potentiometry</td>
<td>Carbon paste</td>
<td>Sertraline tetraphenylborate</td>
<td>9.95</td>
<td>10–10000</td>
<td>17</td>
</tr>
<tr>
<td>Potentiometry</td>
<td>Ion selective</td>
<td>Molecularly imprinted polymers</td>
<td>0.8</td>
<td>1–10000</td>
<td>18</td>
</tr>
<tr>
<td>sensor</td>
<td>Mercury</td>
<td></td>
<td>0.15</td>
<td>0.2–1.2</td>
<td>19</td>
</tr>
<tr>
<td>Voltammetry</td>
<td>Screen printed</td>
<td>( \text{La}_2\text{O}_3/\text{Co}_3\text{O}_4 )</td>
<td>1.0</td>
<td>5.0–400.0</td>
<td>This work</td>
</tr>
</tbody>
</table>

**Analysis of real samples**

The applicability of the present modified electrode in determination of real samples was assessed through the determination of sertraline in urine and tablet samples by the standard addition method. The obtained results are presented in Table II and showed that acceptable recoveries for sertraline were obtained. Also, the reproducibility of present electrode was investigated via the relative standard deviation (RSD) percentage.

TABLE II. The application of \( \text{La}_2\text{O}_3/\text{Co}_3\text{O}_4/\text{SPE} \) for determination of sertraline in real samples \((n = 5)\)

<table>
<thead>
<tr>
<th>Sample</th>
<th>Amount of added sertraline, μM</th>
<th>Amount of founded sertraline, μM</th>
<th>Recovery, %</th>
<th>RSD / %</th>
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<tr>
<td>Sertraline tablet</td>
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<td>3.2</td>
<td>–</td>
<td>1.8</td>
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<tr>
<td></td>
<td>2.5</td>
<td>5.6</td>
<td>98.2</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>5.0</td>
<td>8.3</td>
<td>101.2</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>7.5</td>
<td>10.6</td>
<td>99.1</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>10.0</td>
<td>13.5</td>
<td>102.3</td>
<td>3.2</td>
</tr>
<tr>
<td>Urine of healthy</td>
<td>0</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>volunteer</td>
<td>10.0</td>
<td>10.1</td>
<td>101.0</td>
<td>3.3</td>
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<tr>
<td></td>
<td>15.0</td>
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<td>98.7</td>
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</tr>
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<td>97.5</td>
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<tr>
<td></td>
<td>25.0</td>
<td>25.7</td>
<td>102.8</td>
<td>3.2</td>
</tr>
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</table>
deviation (RSD). The results show that this sensor can be used for samples from patients that use sertraline.

The repeatability and stability of La$_2$O$_3$/Co$_3$O$_4$/SPE

The long-term stability of the La$_2$O$_3$/Co$_3$O$_4$/SPE was tested over a 3 weeks period that were stored in atmosphere at room temperature. Then, the experiments were repeated and cyclic voltammograms (CVs) were recorded. According to CVs, no change was observed in the peak potential of sertraline oxidation, but the current signals showed less than 2.4 % decrease relative to the initial response.

The antifouling properties of the La$_2$O$_3$/Co$_3$O$_4$/SPE toward sertraline oxidation and its oxidation product were investigated by recording the CVs of the La$_2$O$_3$/Co$_3$O$_4$/SPE before and after use in the presence of sertraline. CVs were recorded in the presence of 50.0 μM of sertraline, after having cycled the potential 12 times at a scan rate of 50 mV s$^{-1}$. The results showed that the peak potentials were unchanged and the currents decreased by less than 2.3 %. Therefore, on the surface of the La$_2$O$_3$/Co$_3$O$_4$/SPE, not only the sensitivity increase, but also the fouling effect of the analyte and its oxidation product decreases.

CONCLUSIONS

The current study reports a simple and sensitive procedure for the electro-analytical determination of sertraline at SPE modified with La$_2$O$_3$/Co$_3$O$_4$ nano-composite. The modified electrode has excellent operating characteristics like low detection limit, sensitivity, stability with rapid response. Step by step CV and DPV investigations of sertraline at La$_2$O$_3$/Co$_3$O$_4$/SPE indicate the significant difference in the anodic peak current and the electrochemical performance which was achieved at the unmodified SPE electrode. The fabricated sensor was effectively applied for the quantification of sertraline in commercially accessible tablet dosage form, within acceptable recovery range.
чему је нађено да висина анодног пика линеарно расте са повећањем концентрације сертравина у опсегу 5,0–400,0 μM са границом детекције од 1,0 μM. Штампана угљенична електрода, која је модификована композитом La₂O₃/Co₃O₄, је успешно примењена за детекцију сертравина у таблетама и узorcima уз одличан степен аналитичког приноса.

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