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An amplified sensor based on improved carbon paste electrode with 1,3-Dipropylimidazolium Bromide and MgO/SWCNTs Nanocomposite for tradamol determination

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The electrochemical behavior of tramadol at carbon paste electrode amplified with the 1,3-dipropylimidazolium bromide and MgO/SWCNTs nanocomposite (1,3-DI-Br/MgO/SWCNTs/CPE) has been studied in aqueous solutions. The oxidation of tramadol at the pH range of 6.0-9.0 has been investigated. At the optimum condition of pH 8.0, the tramadol shows an irreversible signal at 0.81 V. The scan rate investigation confirms a diffusion process for the electro-oxidation of tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE. Square wave voltammetric investigation shows a linear relation between the tramadol current and concentration within the range of 0.05-280 μM with a detection limit of 8.0 nM. The 1,3-DI-Br/MgO/SWCNTs/CPE has been applied to analyze the tramadol in injection and urine samples.

Keywords: Tramadol, MgO/SWCNTs nanocomposite, 1,3-dipropylimidazolium bromide, Electrochemical sensor

1. INTRODUCTION

The attention to fabrication of electrochemical sensors for analyzing drugs in biological and pharmaceutical samples increased during the past decades [1-10]. Significant growth in the design of electrochemical sensors can be attributed to the need to use non-fake drugs and determine the concentration of drugs in blood and urine samples. Although some analytical methods such as HPLC [11], spectroscopy [12], chemiluminescence [13], flow injection [14] and electrochemical methods [15-20] were reported for analyzing drugs and biological samples, electrochemical-based sensors have

shown more attention between analytical scientists due to fast response and low cost [21-25]. The low oxidation/reduction signals of drugs can be counted among the main disadvantages of electrochemical sensors for their determination. Hence, electrochemists use modified electrochemical sensors for improving the sensitivity of analytical sensors in drug analysis [26-30]. For example, MgO/SWCNTs coupled with 2-Chloro-N′-[1-(2,5-dihydroxyphenyl) methylidene]aniline, is suggested for the modification of carbon paste electrode [31]. The suggested sensor shows high sensitivity for glutathione, acetaminophen and tyrosine. In other examples, the pencil graphite electrode modified with DNA, SWCNTs, and polypyrrole were suggested as biosensor for determination the ciprofloxacin anticancer drug [32]. Moreover, a modified electrode amplified with Pt/MWCNTs and ionic liquids was used as voltammetric sensor for simultaneous determination of 6-mercaptopruine, 6-thioguanine and dasatinib [33]. On the other hand, many published papers show the high conductivity of nanomaterials for increasing the electrical conductivity of electrodes [34-43].

Following the reported papers and literature [44-50], we found that the coupling of nano-materials and room temperature ionic liquids can be useful for fabrication of the highly sensitive electrochemical sensors for drug or drugs sample analysis. Therefore, we described in this research a new electrochemical sensor based on the carbon paste electrode modified with the 1,3-dipropylimidazolium bromide and MgO/SWCNTs nano-composite for the determination of tramadol ((1S,2S)-2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexan-1-ol). The 1,3-DI-Br/MgO/SWCNTs/CPE showed an interesting ability for the determination of tramadol in injection and urine samples.

2. MATERIALS AND METHODS

2.1. Materials

Tramadol, sodium hydroxide, magnesium nitrate hydrate, single wall carbon nanotubes, and graphite powder were purchased from Sigma-Aldrich. Paraffin oil was purchased from Merck. A 0.01 M stock solution of tramadol was prepared by dissolving 0.075 g tramadol hydrochloride ≥99.0% in the 25 mL phosphate buffer solution at pH=8.0.

2.2. Characterization

The electrochemical investigation was performed by μ-Autolab PGSTAT 12. The device output of μ-Autolab was connected with Ag/AgCl/KCl_{sat}, Pt wire and 1,3-DI-Br/MgO/SWCNTs/CPE as reference, counter and working electrodes. The TEM (Philips, CM300) apparatus was used for morphological investigation.

2.3. Synthesis of MgO/SWCNTs nanocomposite

For the synthesis of MgO/SWCNTs, 1.0 g SWCNTs dispersed in 50 mL sodium hydroxide (0.1 M) and stirred for 30 min at 35 ^{0}C. In continuous, 50 mL magnesium nitrate (0.05 M) drop wise in the previous solution and stirring continued for 30 min. The precipitated sample was washed with the ethanol: water (1:1 v/v) solution and dried for 12 h at 100 ^{0}C. In the final step the sample was calcinated at 600 ^{0}C for 2 h.

2.4. Fabrication of 1,3-DI-Br/MgO/SWCNTs/CPE

Now, 0.04 g of the MgO/SWCNTs was mixed with 0.96 g graphite powder in the presence of diethyl ether as a solvent. After hand mixing, 13.3% (v/v) 1,3-DI-Br and 86.7 (v/) paraffin oil was added to previous mixture, and a paste input was obtained at the end of the glass tube in the presence of the copper wire.

2.5. Real sample preparation

The injection sample after purchasing local pharmacy was used directly as the real sample. The urine sample was prepared in accordance with our previous procedure [39].

3. RESULTS AND DISCUSSION

3.1. MgO/SWCNTs characterization

We used precipitation method for synthesis of MgO/SWCNTs nano-composite according to our previous reported procedure [50]. Figure 1 illustrates the morphological structure of MgO/SWCNTs recorded by TEM method. As can be seen, the MgO nanoparticles decorated at a surface of single wall carbon nanotubes that is useful for application as stable conductive mediator for modification of electrochemical sensors.

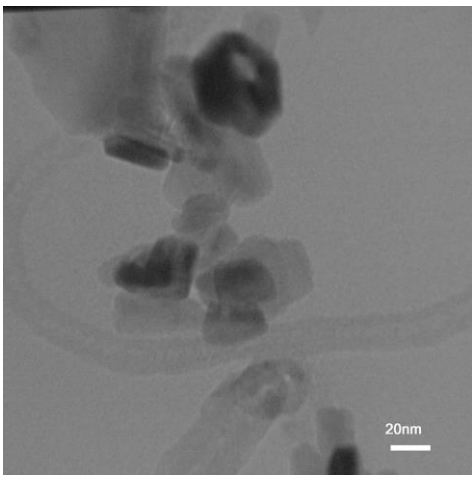

Figure 1. TEM image of MgO/SWCNTs

3.2. Electrochemical behavior of tramadol

According to the reported paper of Hathoot et al. [41], the electro-oxidation reaction of tramadol is relative to the pH of the solution. Therefore, we recorded cyclic voltammograms of 500.0 µM tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE (figure 2 insert) within the pH range of 6.0-9.0. As can be seen, by moving pH=6.0 to pH=9.0, the oxidation potential shifted to a negative value (slope 0.0691 V/pH), thus confirming that the electro-oxidation of tramadol is relative to the pH of the solution with equal value of electron and proton [52]. Moreover, the maximum oxidation signal can be observed at pH=8.0 so that this condition is selected as the optimum for the electrochemical determination of tramadol.

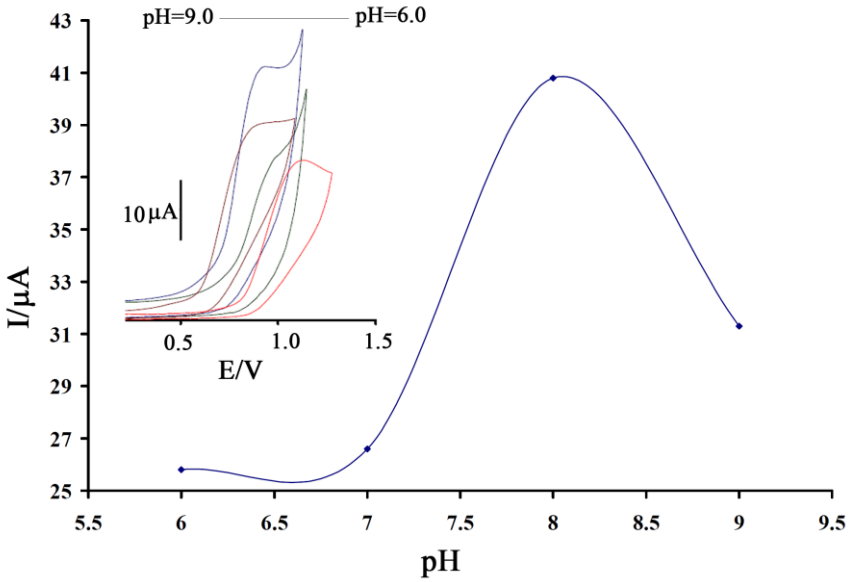

Figure 2. The current-pH curve for electro-oxidation of 500 µM tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE in the pH range 6.0-9.0. Insert) cyclic voltammograms of 500.0 µM tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE in the pH range 6.0-9.0

Figure 3 shows the cyclic voltammograms 150.0 µM of tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE (curve a), 1,3-DI-Br/CPE (curve b), MgO/SWCNTs/CPE(curve c) and CPE (curve d) in pH=8.0. With addition of SWCNTs or 1,3-DI-Br to carbon paste matrix the oxidation current of tramadol increased ~4.2 and ~6.7 times compare to CPE, respectively. On the other hand, after the modification of the carbon paste electrode with SWCNTs and 1,3-DI-Br the oxidation of tramadol increased ~ 8.7 times compared to the unmodified sensor that confirmed synergic effect of these conductive mediators for modification of carbon paste electrode. Moreover, the obtained data confirmed the current density reported data, which is shown in figure 3 insert. As can be seen, the mediators increased the active surface area and electrical conductivity of electrode surface. Moreover, the oxidation potential of tramadol reduced by moving carbon paste electrode to MgO/SWCNTs/CPE that is relative to good electrical conductivity of mediators at a surface of carbon paste electrode.

The cyclic voltammograms of 100.0 µM tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE were recorded within the scan rate range of 20-150 mV/s (figure 4 insert). As can be seen, the catalytic current showed a linear relation with $\nu^{1/2}$ (figure 4), thus confirming the

diffusion process for electro-oxidation of tramadol in this study. In addition, with increases in scan rate, the oxidation potential shifted to more a positive value that can be relative to kinetic limitation in the electro-oxidation process.

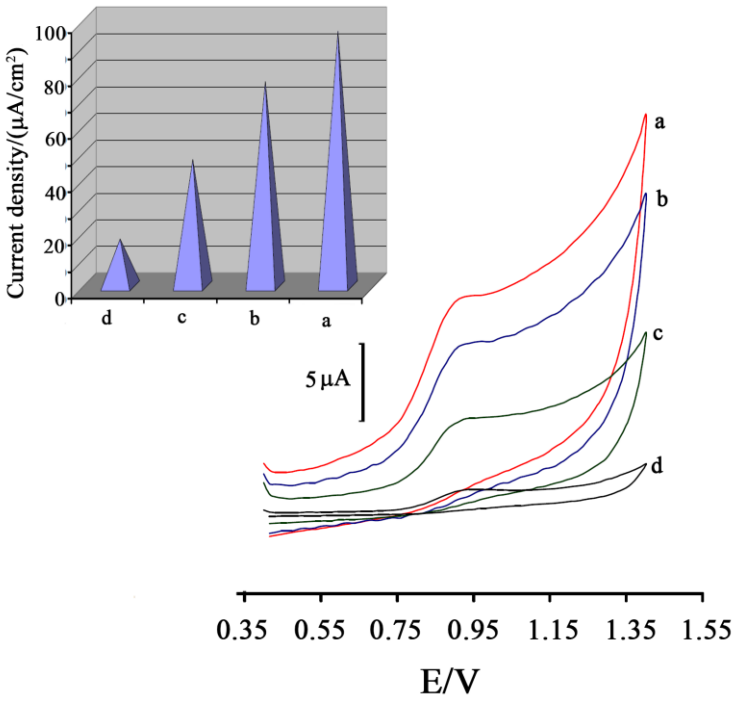

Figure 3. Cyclic voltammograms of 150.0 μM of tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE (curve a), 1,3-DI-Br/CPE (curve b), MgO/SWCNTs/CPE(curve c) and CPE (curve d) in the pH=8.0. Insert) current density data obtained from cyclic voltammograms.

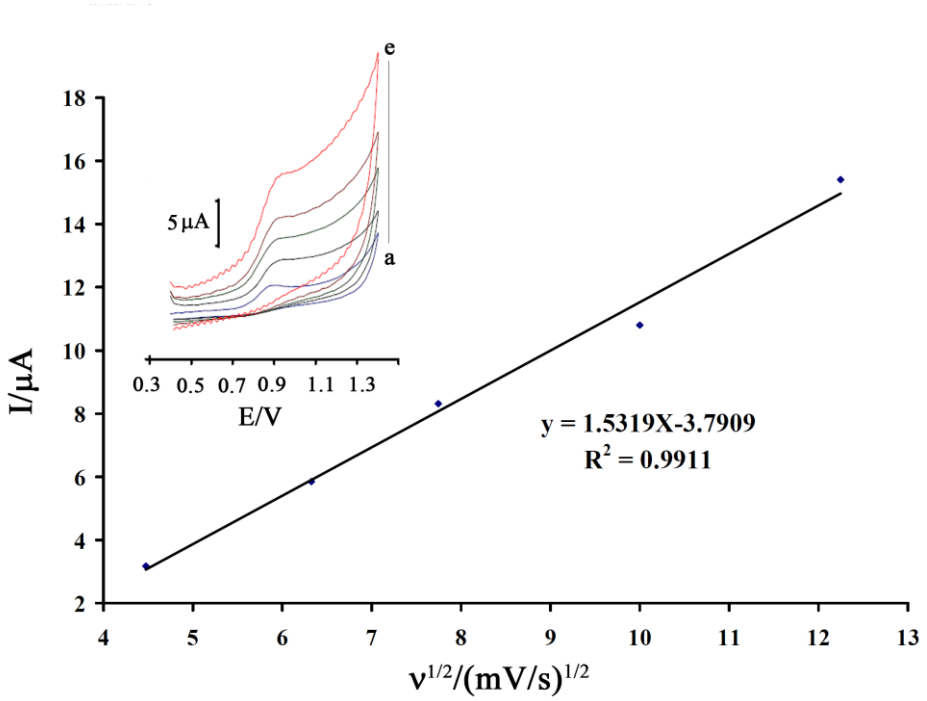

Figure 4. Cyclic voltammograms of 100.0 μM of tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE at scan rate a) 20.0; b) 40.0; c) 60.0; d) 100.0 and e) 150 mV/s.

In the next step, we recorded chronoamperograms 300 and 500 μM tramadol with the applied potential of 1.0 V (figure 5 A). As can be seen, the current of chronoamperograms increased with the concentration of tramadol due to the diffusion process of tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE. This confirms that the 1,3-DI-Br/MgO/SWCNTs/CPE can be useful for the study of electro-oxidation of tramadol. The obtained data from diffusion part of chronoamperograms showed a linear relationship between the current and $t^{-1/2}$, thus confirming the diffusion process (figure 5 B). Using the slopes, we calculated the diffusion coefficient tramadol to be 3.43 $\times 10^{-5}$ cm^2 s^{-1}.

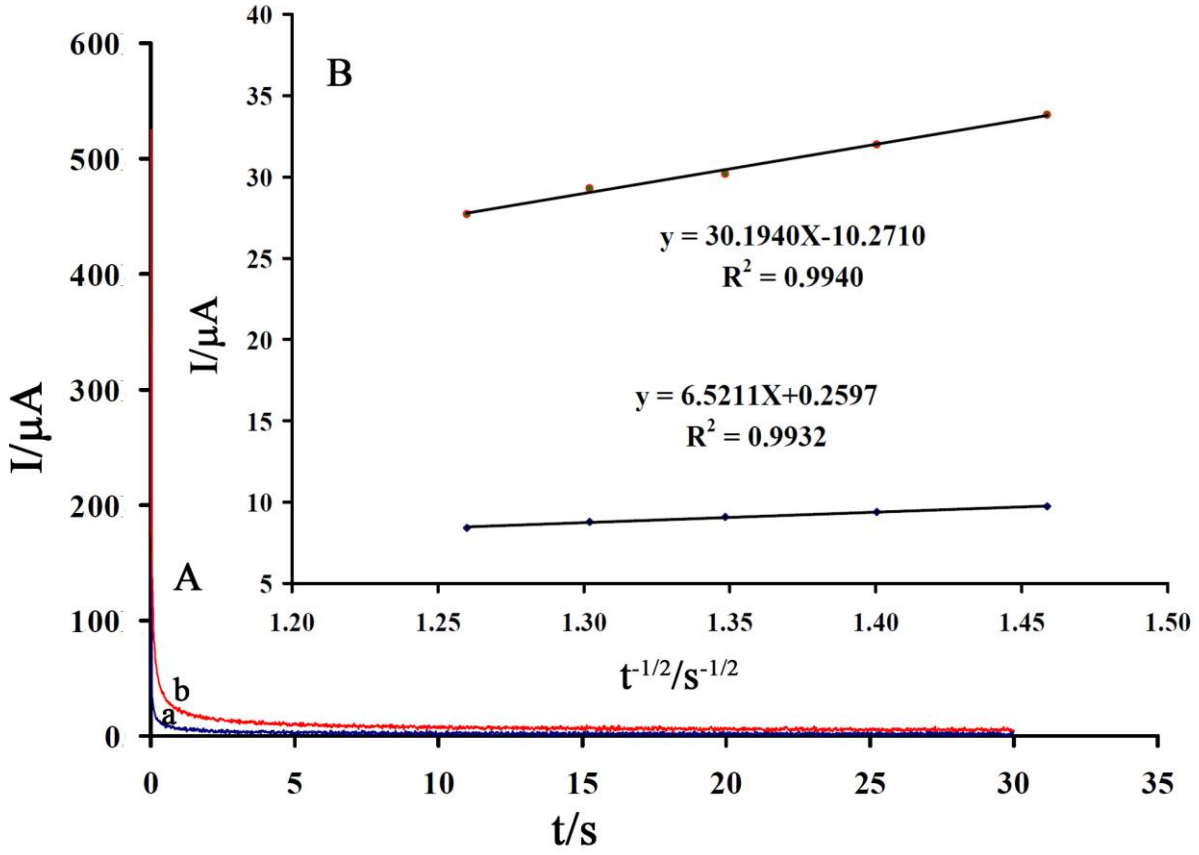

Figure 5. A) Chronoamperograms obtained at the 1,3-DI-Br/MgO/SWCNTs/CPE in the presence of (a) 300 and (b) 500 μM tramadol. B) Plots of I vs. $t^{-1/2}$ obtained from chronoamperometry.

Figure 6 insert showed the square wave voltammetric response of tramadol at a surface of 1,3-DI-Br/MgO/SWCNTs/CPE in the phosphate buffer solution with pH=8.0. We found a relationship between the oxidation current of tramadol and its concentration within the range 0.05-280 μM (with sensitivity 0.056 μA/μM), with the detection limit of 8.0 nM. This value of the linear dynamic range and the limit of detection are comparable or better than other suggested electrochemical sensors for the determination of tramadol (table 1).

The selectivity of 1,3-DI-Br/MgO/SWCNTs/CPE for the determination of tramadol was checked by recording the voltammetric response of the 20.0 μM drug in the absence and in the presence of some usual interferences with an acceptable error rate of 5%. The results showed that

1000-fold Na^+, Br^-, K^+, Cl^- and Mg^{2+} and 200-fold methionine, alanine, glycine, vitamin B_2 and uric acid did not have any significant interference for the determination of tramadol. This confirm the good selectivity of 1,3-DI-Br/MgO/SWCNTs/CPE as an electrochemical sensor for determination of tramadol in the real samples.

Table 1. The comparison of proposed sensors with published electrochemical sensors for determination of tramadol

Electrode	pH	LOD (µM)	LDR (µM)	Ref.
pencil graphite electrode	9.2	0.038	0.1-1.5	[52]
platinum electrode modified with poly 8-(3-acetylimino-6-methyl-2,4-dioxopyran)-1-aminonaphthalene	0.1 M H_2SO_4	0.327	5.0-30.0	[51]
glassy carbon electrode modified with carbon nanoparticles	7.0	1.0	10-1000	[53]
Carbon paste electrode modified with nano-molecularlyimprintedpolymer	7.0	0.004	0.01-20.0	[54]
1,3-DI-Br/MgO/SWCNTs/CPE	8.0	0.008	0.05-280.0	The presence work

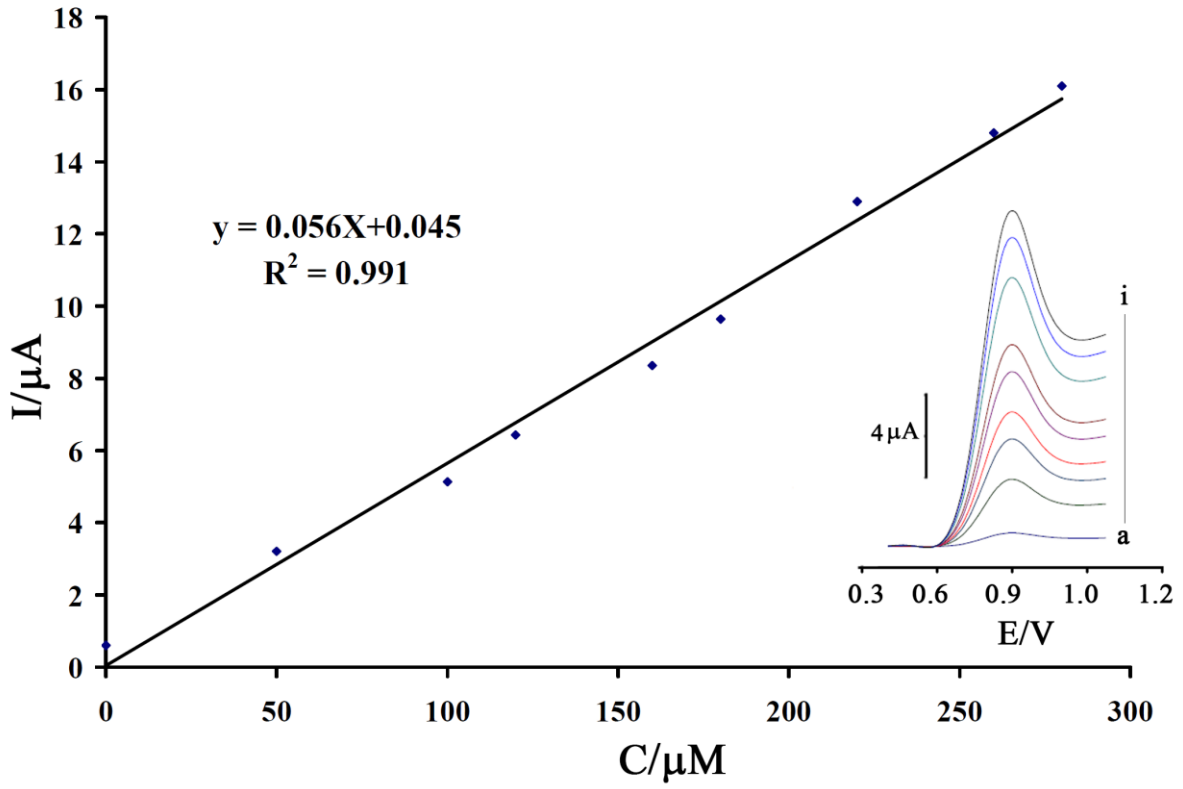

Figure 7. The linear relation between current and tramadol concentration. Insert) square wave voltammograms of 1,3-DI-Br/MgO/SWCNTs/CPE in the presence of a) 0.05, b) 50.0, c) 100.0, d) 120.0, e) 160.0, f) 180.0, g) 220.0, h) 260.0 and i) 280 µM tramadol.

Table 2. The obtained data for determination of tramadol in real samples

Sample	Added (μM)	Expected (μM)	Founded (μM)	Recovery%
Injection	---	3.00	3.06±0.81	102.0
	12.00	15.00	14.87±0.81	99.13
Urine	---	---	<LOD	---
	10.00	10.00	10.43±0.78	104.3
	20.00	20.00	20.87±0.96	104.35

In addition, the ability of 1,3-DI-Br/MgO/SWCNTs/CPE was checked for the determination of tramadol in injection and urine samples by the standard addition method (n=5). The obtained data are presence in table 2 and confirms the interesting ability of the sensor in the tramadol determination.

4. CONCLUSION

In this study, we fabricated the 1,3-DI-Br/MgO/SWCNTs/CPE as a highly sensitive sensor for the determination of tramadol with the detection limit of 8.0 nM. The application of 1,3-DI-Br and MgO/SWCNTs improved the oxidation current tramadol ~ 8.7 times when compared to the unmodified sensor. The 1,3-DI-Br/MgO/SWCNTs/CPE was used for the determination of tramadol without any significant interferences. Finally, the 1,3-DI-Br/MgO/SWCNTs/CPE successfully used for determination of tramadol in the injection and urine samples.

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