Int. J. Electrochem. Sci., 14 **(2019)** 9552 – 9561, doi: 10.20964/2019.10.03

International Journal of ELECTROCHEMICAL SCIENCE
www.electrochemsci.org

An Electrochemical Sensitive Sensor for Determining Sulfamethoxazole Using a Modified Electrode Based on Biosynthesized NiO Nanoparticles Paste Electrode

Sadegh Salmanpour[1], *Mohammad A. Khalilzadeh*[1,*], *Hassan Karimi-Maleh*[2,3,] *and Daryoush Zareyeea*[1]

[1] Department of Chemistry, Qaemshahr Branch, Islamic Azad University, Qaemshahr, Iran
[2] Department of Chemical Engineering, Laboratory of Nanotechnology, Quchan University of Technology, Quchan, Iran
[3] Department of Applied Chemistry, University of Johannesburg, P. O. Box 17011, Doornfontein Campus, 2028, Johannesburg, South Africa,
[*]E-mail: khalilzadeh73@gmail.com

Received: 6 June 2019 / *Accepted:* 28 July 2019 / *Published:* 30 August 2019

In this research, we describe a new type of sulfamethoxazole electrochemical sensor based on a carbon paste electrode (CPE) modified with NiO nanoparticle (NiO-NPs) and 1-methyl-3-octylimidazolium tetrafluoroborate (1M3OIMZTFB). The NiO nanoparticle was biosynthesized with a diameter of ~ 18.0 nm by *Mentha aquatic* extract and characterized by AFM, FESEM, XRD and EDS methods. The oxidation peak of sulfamethoxazole was recorded at +1130 mV and +995 mV at surface of CPE and 1M3OIMZTFB/NiO-NPs/CPE. Meanwhile, the oxidation signal of sulfamethoxazole was improved by ~20.32 times compared to unmodified CPE. The 1M3OIMZTFB/NiO-NPs/CPE exhibited good catalytic activity toward sulfamethoxazole with a dynamic range 0.003-400.0 μM and limit of detection 1.0 nM. The 1M3OIMZTFB/NiO-NPs/CPE was used as useful tool for determination of sulfamethoxazole in real samples.

Keywords: Sulfamethoxazole, NiO nanoparticle, Biosynthesis, Electrochemical Sensor

1. INTRODUCTION

Sulfamethoxazole is an important antibiotic prescribed in the treatment of a variety of bacterial infections such as intestinal infections, middle ear and respiratory infections in combination with the trimethoprim under the brand name Bactrim [1]. Excessive consumption of sulfamethoxazole is associated with many health effects such as shortness of breath, feeling light-headed, and rapid heart rate [2]. The determination of sulfamethoxazole could be useful for controlling drug dose in human body and determination of drug dose in tablet and other pharmaceutical samples. There are many published papers

on determination of sulfamethoxazole using HPPLC [3,4], capillary zone electrophoresis [5], visible and UV spectrophotometry [6] and electrochemical methods [7,8]. Due to fast response and low cost of electrochemical analysis, electrochemical sensors have found more popularity compared to other analytical sensors for drug analysis in recent years [9-12].

Although the electrochemical sensors are of choice for fabrication of drug sensors [13-15], the high overvoltage and weak oxidation current of sulfamethoxazole are the main problems for determination of this drug at low level concentrations [16]. For overcoming to these problems, modified sensors are appropriate choices given their high conductivity and low charge transfer resistance [17].

Nanomaterials and especially metal oxide nanoparticles (MONs) have shown a high surface [18-21] area and good electrical conductivity for modification of electrode surfaces in recent years [22-24]. According to papers, MON could improve the oxidation/reduction signals of drugs and also reduce the redox over-potential of electroactive compounds [25-32]. On the other hand, ionic liquids (IL) with high electrical conductivity have been suggested as high performance mediator for modification of voltammetric sensors and especially a good choice for replacing paraffin oil in carbon paste matrix [23-36].

Herein, we used the coupling of 1-methyl-3-octylimidazolium tetrafluoroborate and biosynthesized NiO nanoparticle for fabrication of 1M3OIMZTFB/NiO-NPs/CPE as a powerful electrochemical sensor in sulfamethoxazole. The NiO/NPs were biosynthesized by *Mentha aquatic* extract and revealed high electrical conductivity for fabrication of 1M3OIMZTFB/NiO-NPs/CPE.

2. EXPERIMENTAL

2.1. Reagents and apparatus

For synthesis of NiO nanoparticles: The *Mentha aquatic* plant was prepared from Mazandaran Province, Iran. Nickel nitrate hexahydrate and sodium hydroxide were purchased from Merck Co.

For electrochemical investigation: sulfamethoxazole, paraffin oil, phosphoric acid, graphite powder, and1-methyl-3-octylimidazolium tetrafluoroborate were purchased from Sigma-Aldrich Co.

The electrochemical optimization and determination of sulfamethoxazole were initiated by μ-Autolab via NOVA software. In all of the voltammetric investigations, the Ag/AgCl/KClsat was used as a reference electrode. The NAMA AFM nanotechnology system corporation (ATSYCO) machine, Iran and the FESEM model Mira 3-XMU were used for morphological investigation of the biosynthesized NiO/NPs.

2.2. Biosynthesis of NiO/NPs using Mentha aquatic extract

Mentha aquatic leaves were collected from, Qaemshahr, Mazandaran, Iran. The collected leaves were washed with distilled water ten times and then dried for 12 days at room temperature. Next, 5.0 g of dried leaves were grinded for 1.5 h into pestle and mortar. Thereafter, the powder obtained from the

dried leaves was added into 150 mL distilled water and then boiled for 150 min. The Mentha aquatic extract was filtered and kept at 4 ˚C.

Subsequently, 15 mL *Mentha aquatic* extract was placed in Erlenmeyer flask after which 5 mL nickel nitrate hexahydrate (0.05 M) was added dropwise to the previous solution under stirring for 2 hours at 65 ˚C. The solution changing color from black-green to black confirmed the biosynthesis of NiO-NPs. The black sediment was then filtered and dried at 80 ˚C for 10 h and eventually annealed at 350 ˚C.

2.3. Fabrication of 1M3OIMZTFB/NiO-NPs/CPE

The 1M3OIMZTFB/NiO-NPs/CPE was prepared by mixing 0.96 g graphite powder + 0.04 g NiO-NPs in the presence of suitable amounts of paraffin oil and 1M3OIMZTFB as binders into pestle and mortar through hand mixing for 2 h.

2.4. Real sample preparation

The Bactrim tablet and pharmaceutical serum samples were selected as real sample for investigation of 1M3OIMZTFB/NiO-NPs/CPE ability in real sample analysis. The tablet sample was grinded into pestle and mortar and then dissolved in ethanol/water solution. The sample was filtered and utilized for real sample analysis. The pharmaceutical serum sample was added into buffer solution and used directly for real sample analysis.

3. RESULTS AND DISCUSSION

3.1. Characterization of the biosynthesized NiO nanoparticles

The NiO nanoparticle biosynthesized by *Mentha aquatic* extract was evaluated by XRD method. The presence of six planes with miller indexes [111], [200], [220], [311] and [222] at 2ɵ ~37.240°, 43.287°, 62.823°, 75.345° and 79.274° matched the XRD pattern for NiO-NPs with JCPDS file No. 22-1189 (Figure 1A) [37]. The mean value of NiO diameter was calculated as ~18 nm using Scherrer equation. In addition, the elemental analysis was used to investigate the purity of biosynthesized NiO-NPs via the Mentha aquatic extract. The presence of Ni and O elements in the biosynthesized NiO-NPs confirmed the high purity of nanoparticles (Figure 1B).

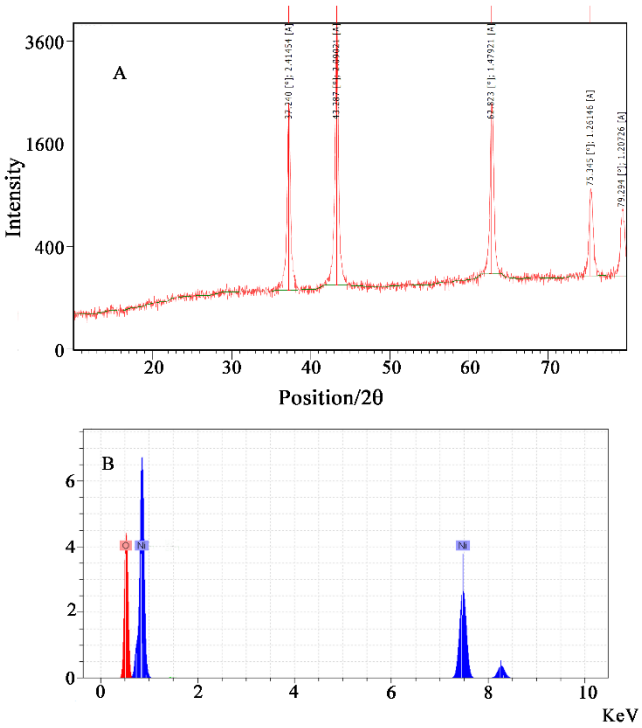


Figure 1. XRD (A) and EDAX (B) pattern of biosynthesized NiO nanoparticles

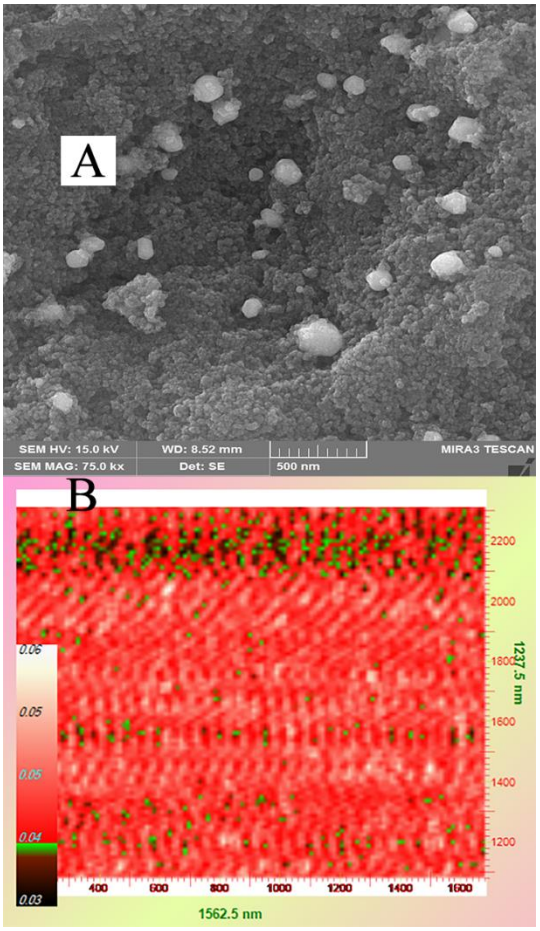


Figure 2. FESEM (A) and AFM (B) images of biosynthesized NiO nanoparticle

The biosynthesized NiO-NPs morphology was investigated using FESEM and AFM methods (Figure 2A). The spherical shaped biosynthesized NiO-NPs can be observed in the results obtained in Figure 2B.

3.2. Electrochemical oxidation of sulfamethoxazole at the surface of sulfamethoxazole

The electro-oxidation of sulfamethoxazole was investigated by cyclic voltammetric method with the recorded signals being available in Figure 3 inset. The characterization of oxidation potential of recorded signals vs. pH is seen in Figure 3 with the results confirming a linear relationship between E_{pa} vs. pH with slope 0.0534 mV/pH for one electron and one proton oxidation mechanism (Scheme 1) [38].

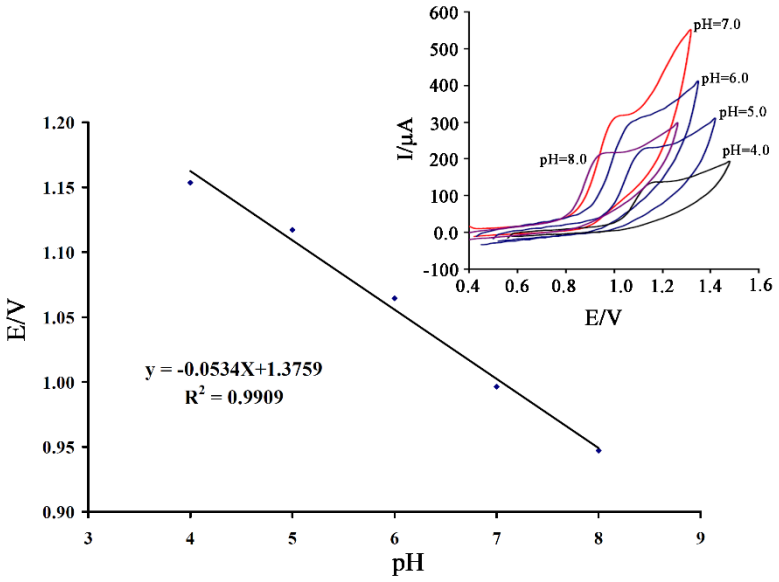
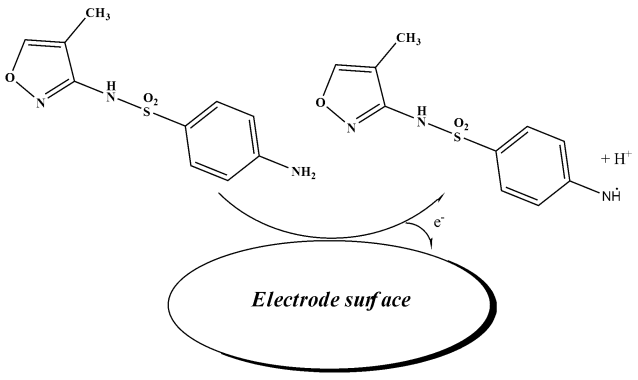


Figure 3. A) The plot of Epa vs. pH for electro-oxidation of 700 µM sulfamethoxazole at a surface of 1M3OIMZTFB/NiO-NPs/CPE in the pH range 4.0-8.0. Insert) the cyclic voltammograms of 700 µM sulfamethoxazole at a surface of 1M3OIMZTFB/NiO-NPs/CPE in the pH range 4.0-8.0.



Scheme 1. The electro-oxidation mechanism of sulfamethoxazole.

In addition, with elevation of pH from 4.0 to pH=7.0, the oxidation current of sulfamethoxazole increased and then decreased. This point could be useful for selection of the best pH value for next voltammetric investigation of sulfamethoxazole on the surface of 1M3OIMZTFB/NiO-NPs/CPE.

In the next step, the electro-oxidation signal of sulfamethoxazole was recorded on the surface of CPE (Figure 4, curve a), NiO-NPs/CPE (Figure 4, curve b), 1M3OIMZTFB/CPE (Figure 4, curve c) and 1M3OIMZTFB/NiO-NPs/CPE (Figure 4, curve d).

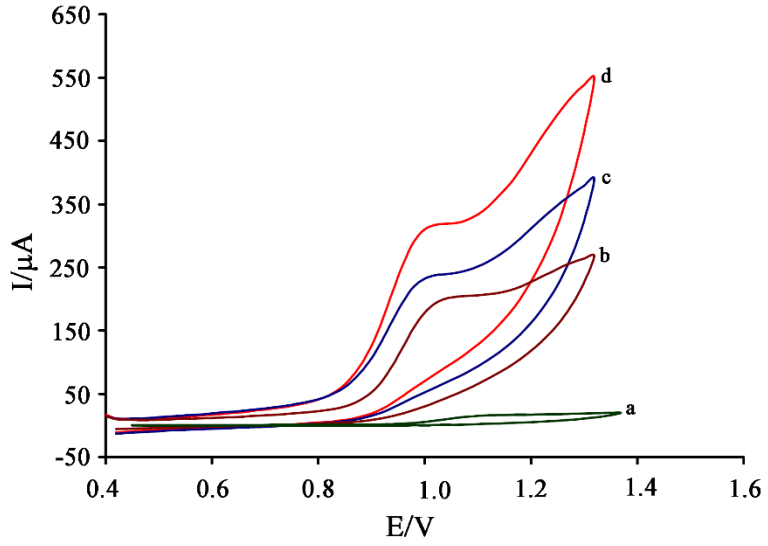


Figure 4. The cyclic voltammograms of 700 µM sulfamethoxazole (pH=7.0) at a surface of CPE (a); NiO-NPs/CPE (b); 1M3OIMZTFB/CPE (c) and 1M3OIMZTFB/NiO-NPs/CPE (d).

The oxidation current and potential relative to the above electrodes have been 1030 mV, 1030 mV, 1000 mV, and 995 mV and 15.6 µA, 201 µA, 237 µA and 317 µA, respectively. As can be seen, the oxidation potential of sulfamethoxazole was reduced with the transition from curve a to curve b. Further, the oxidation current of sulfamethoxazole was also improved through modification of CPE with biosynthesized NiO/NPs and 1M3OIMZTFB/CPE. These changes in the oxidation current and potential of sulfamethoxazole have occurred with regards to the good electrical conductivity of NiO-NPs and 1M3OIMZTFB/CPE at surface of CPE. In addition, the reducing resistance charge transfer of CPE could be observed after modification with NiO/NPs and 1M3OIMZTFB.

The current and potential changing of sulfamethoxazole was investigated by altering the scan rate effect within the range 5.0-120 mV/s (figure 5). The linear relationship between I_{pa} and $\nu^{1/2}$ of sulfamethoxazole and shift in E_{pa} of sulfamethoxazole with elevation of ν suggested the diffusion process [39] as well as irreversible process for electro-oxidation of sulfamethoxazole on the surface of 1M3OIMZTFB/NiO-NPs/CPE.

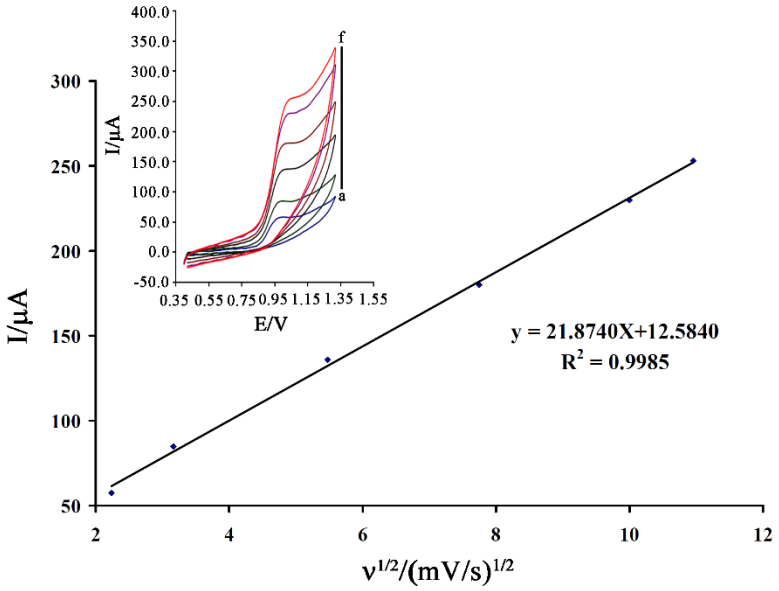


Figure 5. the cyclic voltammograms of 400 µM sulfamethoxazole at a surface of 1M3OIMZTFB/NiO-NPs/CPE at a scan rate a) 5; b) 10; c) 30; d) 60; e) 100 and f) 120 mV/s and pH=7.0.

The Tafel plot for oxidation of 400.0 µM sulfamethoxazole at surface of 1M3OIMZTFB/NiO-NPs/CPE has been recorded in Figure 6. Using the slope of Tafel at scan rate 30.0 mV/s, the value of electron transfers coefficient (α) was determined as ~0.68 confirming an irreversible process for oxidation of sulfamethoxazole on the surface of 1M3OIMZTFB/NiO-NPs/CPE.

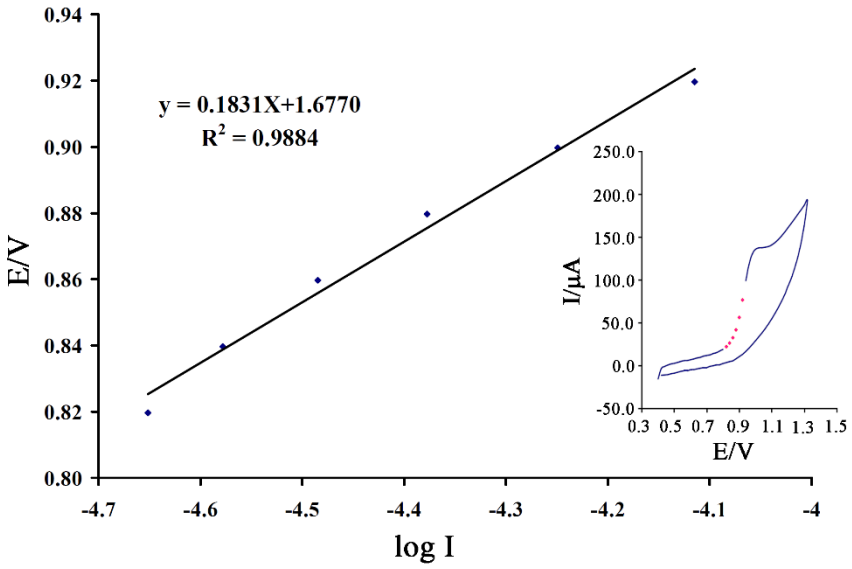


Figure 6. A) The plot of electro-oxidation 400 µM sulfamethoxazole at a surface of 1M3OIMZTFB/NiO-NPs/CPE with scan rate 30 mV/s.

According to the results obtained from the scan rate investigation of sulfamethoxazole at the surface of 1M3OIMZTFB/NiO-NPs/CPE and confirming diffusion process for this drug, we tried to determine the diffusion coefficient (D) using chronoamperometric method (Fig. 7A). The linear

relationship between I_{pa} of sulfamethoxazole and $t^{-1/2}$ was used for determination of D in the aqueous solution. Using the Cottrell equation, the mean value of D for diffusion of sulfamethoxazole was calculated as ~ 5.24×10^{-5} cm^2/s.

3.3. Analytical investigation

The differential pulse volatmmetric method was used as a strategy for determination of sulfamethoxazole within the concentration rage 0.003-400 µM (LDR) with detection limit 1.0 nM (LOD=3SB/m).

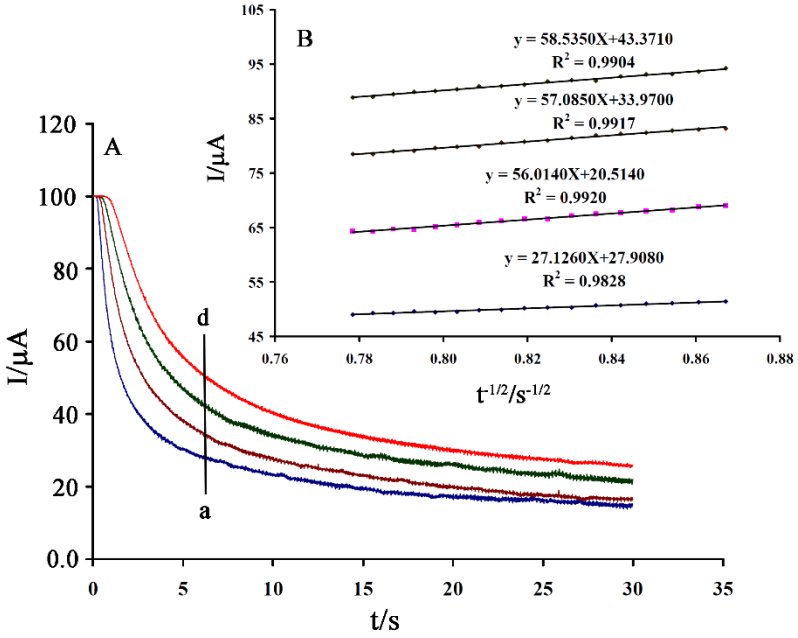


Figure 7. (A) Chronoamperograms obtained at the 1M3OIMZTFB/NiO-NPs/CPE in the presence of (a) 300; (b) 400; (c) 500 and (d) 400 µM sulfamethoxazole. (B) Plots of I vs. $t^{-1/2}$ for electro-oxidation of sulfamethoxazole obtained from chronoamperometry.

3.4. Stability and reproducibility of 1M3OIMZTFB/NiO-NPs/CPE

The DP voltammograms of 700.0 µM sulfamethoxazole were recorded on the surface of five 1M3OIMZTFB/NiO-NPs/CPEs fabricated under the same conditions. The results showed the RDS values 0.31% and 0.6 % for the current and potential that confirm good reproducibility of 1M3OIMZTFB/NiO-NPs/CPE for determination of sulfamethoxazole. In addition, the DP voltammogram 700.0 µM sulfamethoxazole was recorded within 30 days. As can be seen in Figure S2, 93.7% of 700.0 µM sulfamethoxazole can be observed after 30 days compared to its first oxidation signal. It suggests good stability of 1M3OIMZTFB/NiO-NPs/CPEs for determination of 700.0 µM sulfamethoxazole.

3.5. Real sample analysis and selectivity study

The ability of 1M3OIMZTFB/NiO-NPs/CPEs for determination of sulfamethoxazole in Bactrim tablet and pharmaceutical serum was tested using standard addition strategy (Table 1). According to the table, the recovery values within 99.06-103.9% confirm powerful ability of 1M3OIMZTFB/NiO-NPs/CPEs for determination of sulfamethoxazole in real samples.

The interference of trimethoprim, ascorbic acid, glucose, vitamin B2, as well as some anions and cations was checked on the oxidation signal of 20.0 µM sulfamethoxazole. The obtained results confirming high selectivity of 1M3OIMZTFB/NiO-NPs/CPEs for determination of sulfamethoxazole.

Table 1. The real sample analysis of sulfamethoxazole

Sample	Added (µM)	Expected (µM)	Founded (µM)	Recovery %
Tablet sample	---	5.00	4.96±0.34	99.2
	10.00	15.00	15.28±0.54	101.8
Pharmaceutical sample	---	---	<LOD	---
	10.00	10.00	10.39±0.54	103.9
	15.00	15.00	14.86±0.52	99.06

4. CONCLUSION

Herein, the NiO nanoparticle was biosynthesized using Mentha Herein, the NiO nanoparticles were biosynthesized using Mentha aquatic extract with a diameter ~18 nm and used for modification of CPE. Further, the 1M3OIMZTFB/NiO-NPs/CPEs was introduced as a two-fold amplified electrochemical sensor for determination of sulfamethoxazole with a low detection limit (1.0 nM). The 1M3OIMZTFB/NiO-NPs/CPEs was successfully used as a powerful sulfamethoxazole analytical sensor. The1M3OIMZTFB/NiO-NPs/CPEs revealed good stability and reproducibility for determination of 700.0 µM sulfamethoxazole.

References

1. G. M. Eliopoulos and P. Huovinen, *Clin. Infect. Dis.,* 32 (2001) 1608.
2. R. Weening, P. Kabel, P. Pijman and D. Roos, *J. Pediatr,* 103 (1983) 127.
3. A. Pereira and Q. Cass, Journal of Chromatography B, 2005, 826, 139-146.
4. H. Amini and A. Ahmadiani, *J. Pharmaceut. Biomed. Anal.* 43 (2007) 1146.
5. D. Teshima, K. Otsubo, K. Makino, Y. Itoh and R. Oishi, *Biomed. Chromatogr.* 18 (2004) 51.
6. S. V. Chamundeeswari, E. J. J. Samuel and N. Sundaraganesan, *Spectrochim. Acta A,* 118 (2014) 1.
7. C. Chen, Y.-C. Chen, Y.-T. Hong, T.-W. Lee and J.-F. Huang, *Chem. Eng. J.* 352 (2018) 188-197.
8. P. Balasubramanian, R. Settu, S.-M. Chen and T.-W. Chen, *Microchim. Acta,* 185 (2018) 396.
9. M. A Khalilzadeh and Z. Arab, *Curr. Anal. Chem.* 13 (2017) 81.
10. M. A. Khalilzadeh and M. Borzoo, *J. Food Drug Anal.* 24 (2016) 796.
11. M. L. Yola and N. Atar, *Mat. Sci. Eng. C,* 96 (2019) 669.

12. M. L. Yola and N. Atar, *Biosens. Bioelectron.,* 126 (2019) 418.
13. B. J. Sanghavi, S. Sitaula, M. H. Griep, S. P. Karna, M. F. Ali and N. S. Swami, *Anal. Chem.,* 85 (2013) 8158.
14. B. J. Sanghavi and A. K. Srivastava, *Electrochim. Acta,* 55 (2010) 8638.
15. N. F. Atta, E. H. El Ads, A. Galal and A. E. Galal, E *Electroanalysis 31 (2019) 448.*
16. A. Yari and A. Shams, *Anal. Chim. Acta,* 1039 (2018) 51.
17. A. Samadzadeh, I. Sheikhshoaie and H. Karimi-Maleh, *Curr. Anal. Chem.* 15 (2019) 166.
18. S. Ben Hammouda, F. Zhao, Z. Safaei, I. Babu, D.L. Ramasamy and M. Sillanpaa, *Appl. Catal. B-Environ.,* 218 (2017) 119.
19. S. Ben Hammouda, F. Zhao, Z. Safaei, V. Srivastava, D.L. Ramasamy, S. Iftekhar and M. Sillanpää, *Appl. Catal. B-Environ.* 215 (2017) 60.
20. S.B. Hammouda, F. Zhao, Z. Safaei, D.L. Ramasamy, B Doshi and M Sillanpä, *Appl. Catal. B-Environ.* 233 (2018) 99.
21. M. Khoobi, T. Modiri Delshad, M. Vosooghi, M. Alipour, H. Hamadi, E. Alipour, M. Pirali Hamedani, Z. Safaei, A. Foroumadi, A. Shafiee. *J. Magn. Magn. Mater.* 375 (2015) 217.
22. S. A. Alavi-Tabari, M. A. Khalilzadeh and H. Karimi-Maleh, *J. Electroanal. Chem.,* 811 (2018) 84.
23. S. A. Alavi-Tabari, M. A. Khalilzadeh, H. Karimi-Maleh and D. Zareyee, *New J. Chem.,* 42 (2018) 3828.
24. M. Miraki, H. Karimi-Maleh, M. A. Taher, S. Cheraghi, F. Karimi, S. Agarwal and V. K. Gupta, *J. Mol. Liq.* 278 (2019) 672.
25. A. F. Mulaba-Bafubiandi, H. Karimi-Maleh, F. Karimi and M. Rezapour, *J. Mol. Liq.* 285 (2019) 430.
26. M.A. Diva, K. Pourghazi and M.A. Diva, *J. Nanostruct.* 9 (2019) 238.
27. A.A. Ensafi, H. Bahrami, B. Rezaei and H. Karimi-Maleh, *Mater. Sci. Eng. C* 33 (2013) 831.
28. S. Sarafraz, H.A. Rafiee-Pour, M. Khayatkashani and A. Ebrahimi, *J. Nanostruct.* 9 (2019) 384.
29. H. Karimi-Maleh, A.L. Sanati, V.K. Gupta, M. Yoosefian, M. Asif and A. Bahari, *Sensor. Actuat. B-Chem.* 204 (2014) 647.
30. H. Karimi-Maleh, K. Ahanjan, M. Taghavi and M. Ghaemy, *Anal. Methods* 8 (2016) 1780.
31. H. Karimi-Maleh, F. Tahernejad-Javazmi, V.K. Gupta, H. Ahmar and M.H. Asadi, *J. Mol. Liq.* 196 (2014) 258-263
32. Z. Amani-Beni and A. Nezamzadeh-Ejhieh, *Anal. Chim. Acta,* 1031 (2018) 47.
33. M. Shabani-Nooshabadi and M. Roostaee, *J. Mol. Liq.* 220 (2016) 329.
34. Z. Song, G. Sheng, Y. Cui, M. Li, Z. Song, C. Ding and X. Luo, *Microchim. Acta,* 186 (2019) 220.
35. M. Opallo, A. Lesniewski, *J. Electroanal. Chem.* 656 (2011) 2.
36. M. Najafi, M. A. Khalilzadeh and H. Karimi-Maleh, *Food Chem.* 158 (2014) 125.
37. F. Farzaneh, S. Haghshenas Kashani, *J. Ceram. Process. Res.* 14 (2013) 673.
38. T. You, X. Yang, E. Wang, *Analyst* 123 (1998) 2357.
39. H. Karimi-Maleh, M. Sheikhshoaje, I. Sheikhshoaje, M. Ranibar, J. Alizadeh, N.W. Maxakato, A. Abbaspourrad, *New J. Chem*., 43 (2019) 2362