Journal of Pharmaceutical and Biomedical Analysis 196 (2021) 113906

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

journal homepage: www.elsevier.com/locate/jpba

Copper nanocluster-based sensor for determination of vancomycin in exhaled breath condensate: A synchronous fluorescence spectroscopy

Elaheh Rahimpour[a,b], Maryam Khoubnasabjafari[c,d], Mohammad Bagher Hosseini[e], Abolghasem Jouyban[b,f,*]

[a] Pharmaceutical Analysis Research Center and Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, 5165665811, Iran
[b] Food and Drug Safety Research Center, Tabriz University of Medical Sciences, Tabriz, 5165665811, Iran
[c] Tuberculosis and Lung Diseases Research Center and Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, 5165665811, Iran
[d] Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, 5165665811, Iran
[e] Pediatrics Research Center, Tabriz University of Medical Sciences, Tabriz, 5165665811, Iran
[f] Kimia Idea Pardaz Azarbayjan (KIPA) Science Based Company, Tabriz University of Medical Sciences, Tabriz, 5165665811, Iran

ARTICLE INFO

Article history:
Received 17 November 2020
Received in revised form 6 January 2021
Accepted 14 January 2021
Available online 16 January 2021

Keywords:
Vancomycin
Copper nanocrystal
Synchronous fluorescence spectroscopy
Exhaled breath condensate
Response surface method
Central composite design

ABSTRACT

A synchronous fluorescence spectroscopy (SFS) nanoprobe is developed for the determination of vancomycin in exhaled breath condensate (EBC) samples. The synthesized nanoprobe is copper nanoclusters (Cu NCs) and its SFS peak is located at 405 nm with $\Delta\lambda = 80$. The affinity of Cu NCs to complex formation with vancomycin results in blocking non-radiative e^-/h^+ recombination defect sites on the surface of NCs and consequently enhancing the SFS signal intensity. Central composite design and response surface methodology is used for the optimization of reaction conditions. Under the optimized conditions, a linear relationship is found between the SFS intensity and the concentration of vancomycin in the range of 0.1−8 μg/mL. The validated method is applied for the determination of vancomycin in EBC of newborns receiving vancomycin treatment.

1. Introduction

Vancomycin as a glycopeptide antibiotic is used for treatment of infections caused by certain methicillin-resistant staphylococci. It is also the chosen antibiotic for the treatment of bacterial infections in patients allergic to β-lactam antibiotics [1]. It is not appreciably absorbed orally and after administration of a single dose, it is removed initially from the renal route, with >80 %–90 % recovered unchanged in urine within 24 h [2]. Therapeutic concentration range reported for vancomycin in plasma and serum samples is 5.0–40 μg/mL and >40 μg/mL is considered as toxic level for it [3]. Ototoxicity which caused damages in the auditive nerve as well as nephrotoxicity is the side effect of vancomycin. The ototoxicity is observed in 2–5.5 % of the patients in blood concentration > 80 mg/L and occurs in 5–7 % of the patients in the serum vancomycin concentration > 10 mg/L. However, these ratios can reach 35 %, if vancomycin is prescribed with aminoglycoside drugs [4,5].

The knowing vancomycin concentrations in the biological samples, the determination of a therapeutic range, and their correlation to antibacterial efficacy and drug toxicity in the clinical setting are controversial. Moreover, monitoring its concentration is highly recommended for patients with altered renal function, particularly for individuals with co-administrated drugs such as aminoglycoside or other nephrotoxic drugs; to maintain the adequate concentration for patients under renal dialysis; for those with altered distribution volume, patients with cancer; pregnant women; and those who require high antibiotic doses [6]. To adjust its appropriate dose, and for satisfactory results with minimum side effects, it is really necessary to determine vancomycin concentration in blood or other biological fluids. For this purpose, it needs to use a simple and reliable method for quantitatively analyze the vancomycin concentration in the biological samples. In the last years, various methods such as chemiluminescence [7,8], spectrophotometry [9], spectrofluorimetry [10], electrochemical methods [11], RP-HPLC [12], LC/MS-MS [13], and capillary electrophoresis [14,15] have been reported for the determination of vancomycin in the biological and pharmaceutical samples. Although each developed method has advantages and disadvantages for application in clinical routes, however, development of a new and easy-to-use method

* Corresponding author at: Food and Drug Safety Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
E-mail address: ajouyban@hotmail.com (A. Jouyban).

https://doi.org/10.1016/j.jpba.2021.113906
0731-7085/

based on the modern science for determination of drug concentrations in biological samples has always been of interest to analytical chemists and clinicians. Nowadays, increasing attention has been focused on using nanomaterials-based probes [16]. Nanoclusters (NCs) with unique optical and electronic features such as size-controlled fluorescence, high quantum yields, stability and efficiency, good solubility, low toxicity, and biocompatibility suggests high efficient tools for sensing and biosensing [17,18]. To the best of our knowledge, optical nanoprobe based on quantum dots (QDs) or NCs are rarely used for the quantification of vancomycin and there are only three reports in the literature [7,8,10]. Khataee et al. in one study used L-cysteine capped cadmium sulfide QDs sensitized $KMnO_4$ –morin chemiluminescence system for determination of vancomycin in the concentration range of 0.004–19 μg/mL [7] and in another study they used CuO nanosheets sensitized luminol–H_2O_2 chemiluminescence system for determination of vancomycin in the concentration range of 0.5–40 μg/mL [8]. It should be noted that in none of these reports, QDs are not used as a direct probe for the determination of vancomycin. In other words, QDs were used as a catalyst and involved in the improvement of chemiluminescence signal, not vancomycin detection. The only report for the determination of vancomycin by using QDs as the sensor is performed by Liang et al. [10] in serum samples. They synthesized glutathione capped CdTe QDs and found that a fluorescence quenching was observed after vancomycin adding in the range of 1.534 ng/mL –20 μg/mL, due to electron transfer.

On the other hand, the current work is the first effort for vancomycin analysis in exhaled breath condensate (EBC). EBC has been introduced as an alternative biological sample for drug monitoring [19] owing to possessing low interfering compounds compared with other matrices such as plasma, blood, sputum, and urine [20]. To continue our researches on EBC analysis, in the current study, we use copper nanocrystal (Cu NCs) as a nanoprobe for the determination of vancomycin in EBC samples of newborns receiving vancomycin treatment. Herein, synchronous fluorescence spectroscopy (SFS) as a multidimensional fluorescence technique based on Cu NCs is optimized by response surface methodology (RSM) and fully validated for the determination of vancomycin. SFS technique involves simultaneously scanning of the excitation and emission monochromators. This method presents several advantages such as simplification of spectra, spectral resolution owing to the narrow spectral bands, the selectivity improvement and, decreasing the interference owing to light scattering which makes it an effective method for quantitative analysis [21].

2. Experimental

2.1. Reagents and solutions

Ultrapure deionized water (Ghazi Pharmaceutical Co., Tabriz, Iran, www.sgco-infusion.com), hydrazine hydrate ($H_4N_2.H_2O$, Sigma-Aldrich, www.sigmaaldrich.com), citric acid ($C_6H_8O_7 \cdot H_2O$, Merck), cetyl trimethyl ammonium bromide (CTAB, $C_{19}H_{42}BrN$, Merck, www.merck.com), and copper nitrate ($Cu(NO_3)_2.3H_2O$, Sigma-Aldrich, www.sigmaaldrich.com) are used reagents for the synthesis of Cu NCs. A solution of 1000 mg/L vancomycin HCl is prepared by dissolving its proper amount in water. The working solutions of vancomycin are daily prepared by diluting the standard solution with deionized water.

2.2. Apparatus and software

SFS spectrum is recorded at room temperature on an FP-750 spectrofluorometer (Jasco Corp., Japan, www.jasco.co.jp) with synchronous mode, 20 nm slit width in both excitation and emission paths and the medium sensitivity. A digital pH-meter model 744 (Metrohm Ltd., Switzerland, www.metrohm.com) for pH adjustments and an electronic analytical balance model AB204-S (Mettler Toledo, Switzerland, www.mt.com) are used in the current work. A CM30 transmission electron microscopy (Philips, The Netherlands, www.philips.com) is used for the identification of shape and size of synthesized nanocrystals.

Experimental design and ANOVA analysis are performed on MINITAB (Minitab Inc. Release 17.0, www.minitab.com/en-us/products/minitab) software.

2.3. Synthesis of Cu NCs

The synthesis of Cu NCs is previously reported in a literature [22]. In brief, 0.0182 g CTAB and 0.05 mL citric acid of 0.1 mol/L (0.5 mmol/L in 10 mL) is added to 10 mL of 2 mol/L aqueous solution of hydrazine hydrate and stirred for 30 min and named solution "A". Then, solution "B" is prepared by dissolving 0.0482 g $Cu(NO_3)_2.3H_2O$ and adding 0.0182 g CTAB and 0.05 mL citric acid of 0.1 mol/L to 10 mL of the deionized water. The obtained solutions are mixed and the mixture is agitated for 3 h at room temperature. Initially, the solution is colorless and gradually turned into a deep red color passing through bright red to reddish brown indicating Cu NCs formation. After that, the solution shows no further change in color indicating the completion of the reaction. The prepared NCs are stored at 4 °C in a dark place. A diluted aqueous solution of the synthesized nanoparticles is prepared, sonicated and used for providing TEM images.

2.4. Sample preparation

Newborns or premature babies under mechanical ventilation has been chosen for collecting the EBC samples from the waste of the ventilator [23]. EBC is a low-protein and highly diluted aqueous matrix, so the collected samples are directly analyzed without any sample preparation procedure or pretreatment. EBC samples analyzed for investigation of method applicability are obtained from five patients after the administration of vancomycin. One of the parents of the sample donors signed a consent form approved by the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1399.479).

2.5. General procedure

Analysis procedure is made in a 2 mL microtube by a batch method. 50 μL of 0.1 mol/L phosphate buffer (pH 6.0) is added into the microtube containing a proper volume of vancomycin standard solution or real sample and finally, 50 μL of Cu NPs is added to it. The volume of the mixture is set in 0.5 mL and incubated for 5 min. The SFS spectrum is recorded at λ_{max} = 405 nm when $\Delta\lambda$ = 80.

3. Results and discussion

3.1. Characterization of Cu-NCs

TEM is used to characterize the shape and size of the prepared NCs. As shown in Fig. 1, Cu NCs have a spherical morphology with an average diameter of 3.0 ± 1.2 nm.

3.2. Detection mechanism discussion

Emission mechanisms for fluorescent compounds are related to the band gap transitions or transitions arising from surface defects in QDs [24]. These transitions affects by the surface modification or interaction with surrounding compounds [25,26]. These effects appearance as (i) activation of fluorescence resulting from blocking

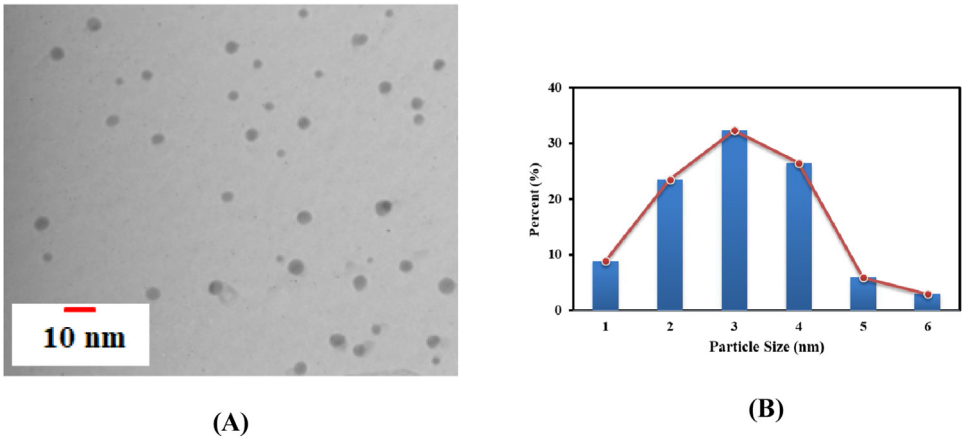

Fig. 1. TEM image of the Cu NCs (A) and particle size distribution curve (B).

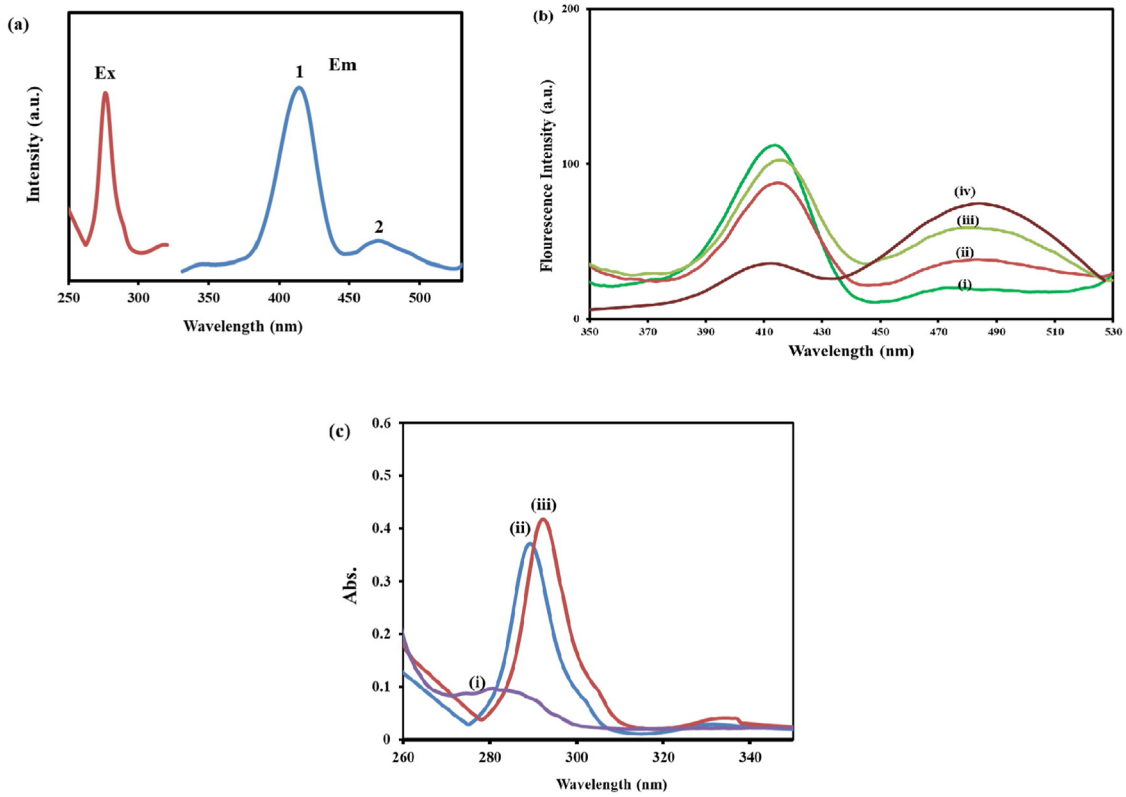

Fig. 2. Excitation and emission spectrum of the Cu NCs (a); fluorescence spectrum of the Cu NCs in the absence (i) and presence of vancomycin in the concentration of (ii) 1, (iii) 2 and (iv) 4 μg/mL (b); and UV–vis spectrum of (i) vancomycin, (ii) Cu NCs and (iii) Cu NCs in the presence of vancomycin (4 μg/mL) (c).

non-radiative electron/ hole (e^-/h^+) recombination defect sites on the surface of QDs, (ii) creation a new trap on QDs surface causing appearance a new emission peak, and (iii) quenching QDs fluorescence due to energy or charge transfer [27,28]. In this study, Cu NCs as fluorescent nanoprobe synthesize and use for its determination according to the high affinity of copper to form a complex with vancomycin [29]. In the high concentration of Cu NCs and under single wavelength excitation at 290 nm, the Cu-NCs shows two fluorescent bands centered at 415 and 480 nm (Fig. 2a). Herein, the low concentration of NCs is used for detection of vancomycin; thus, in the absence of vancomycin, the synthesized NCs emits only a well-resolved emission peak at 415 nm. Upon the addition of vancomycin, the fluorescence spectra show an enhanced emission peak centered at 480 nm which according to mechanisms mentioned for fluorescence variation after interaction with analyte, the possible mechanism can belong to class (i) and blocking the defects on nanoparticles surface. However, in the primary investigation, only a smooth increase was observed in Cu NCs conventional fluorescence intensity (Fig. 2b). So, based on the optical properties of SFS technique compared with conventional fluorescence, we use SFS for determination instead of conventional fluorescence. As can be seen in Fig. 3, Cu NCs show a week SFS peak centered at 405 nm with $\Delta\lambda$ = 80 that increases with vancomycin adding and shows a linear relationship with its concentration in the range of 0.1–8 μg/mL. We suggest that the interaction of Cu NCs with vancomycin results in blocking non-radiative e^-/h^+ recombination defect sites on the NCs surface and consequently enhancing the SFS intensity of NCs. UV–vis spectrum of NCs and its partial shift in the presence of vancmycin provides an evidence for interaction between Cu NCs and vancomycin (Fig. 2c).

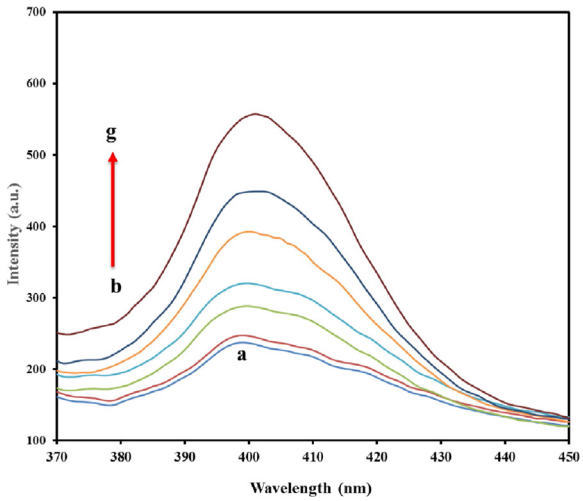

Fig. 3. SFS spectrum of the Cu NCs in the absence (a) and presence of vancomycin in the concentration range of 0.1 – 8 μg/mL (b-g). Conditions: pH 6, Cu NCs volume=0.05 mL, [phosphate buffer] = 0.01 mol/L, and time =5 min. λ_{max} = 405 nm when $\Delta\lambda$ = 80.

3.3. Optimization of reaction conditions by an experimental design

Central composite design (CCD) is chosen for the investigation of the relationship between the response function and variables by considering the interactive effects of independent factors. The studied factors for obtaining maximum response are pH, phosphate buffer concentration, Cu NCs volume and reaction time. The coded values for these parameters are set at five levels: −α (minimum), -1, 0 (central) +1, and +α (maximum). Respective data and tables are given in electronic supporting material (ESM). Difference between SFS intensity in the presence and absence of vancomycin is considered as analytical response and the EBC sample spiked with 2.0 μg/mL vancomycin is used for all measurements. To see the influence of each investigated factors and their interactions, the three dimensional graphs of the parameter's effect on response are plotted and are given in Fig. 4. In Fig. 4a, the response surface is plotted as a function of pH and Cu NCs volume at the center level of other parameters. As can be seen, fluorescence intensity shows a maximum value in acidic pH and decreases in pH higher than 6. On the other hand, better results in the analytical signal are obtained as the Cu NCs volume raises to 0.05 mL and increase more than this value leads to decrease in response owing to fluorescence quenching by the excess amount of NCs via non-radiative de-activation pathways. Fig. 4b shows the response surface of the analytical signal as a function of pH and phosphate buffer concentration. A maximum response can be seen for 0.01 mol/L of phosphate buffer which is adequate for buffering the reaction system. Furthermore, fluorescence intensity increases with an increase in time and remains relatively constant after 5 min (Fig. 4c). The optimum values obtained for each parameter to reach the maximum signal intensity are: pH 6, Cu NCs volume=0.05 mL, [phosphate buffer] = 0.01 mol/L, and time =5 min.

The trained equation according to conduct experiments designed by CCD in uncoded units is as:

$$Y = -63.897 + 16.470X_1 + 2039.982X_2 + 3.916X_4 + 55254.252X_2X_3 + 82.601X_2X_4 - 1.574X_1^2 - 22532.295X_2^2 - 121340.368X_3^2 - 0.552X_4^2 \quad (1)$$

In which X_1, X_2, X_3 and X_4 are pH, Cu NCs volume, buffer concentration and time, respectively.

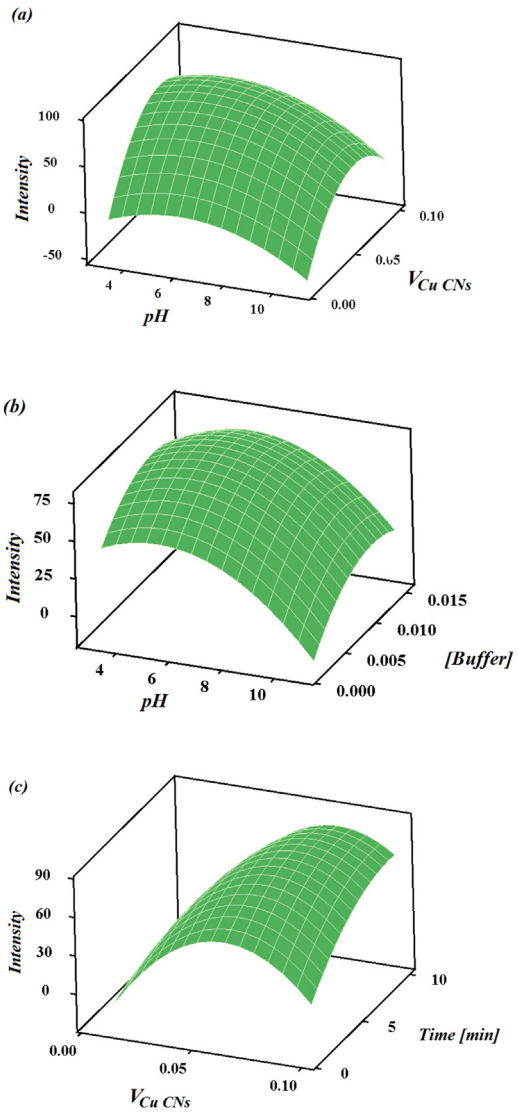

Fig. 4. The response surface of the analytical signals as a function of (a) pH and Cu NCs volume, (b) pH and [Buffer] (c) Cu NCs volume and time, respectively.

3.4. Interferences study

The selectivity of Cu NCs toward vancomycin in the presence of some co-administered and/or non-prescribed over-the-counter drugs such as pain killers etc. is studied by considering the SFS intensity variation for a reaction solution with 1.0 μg/mL vancomycin upon the addition of different concentrations of interferents. It means that a set of sample solutions containing a constant amount of vancomycin (1.0 μg/mL) and different concentrations of the under evaluation interference drugs are analyzed by the developed method and their SFS signals are compared with that in the presence of vancomycin alone to find tolerance limit for each of them. The tolerance limit is defined as the maximum concentration of the interfering substance that causes a relative error less than ±5% for the determination of vancomycin. The results are listed in Table 1. The results demonstrate that the presence of most of the investigated drugs (with exceptions for gentamicin, aspirin, and naproxen) does not affect the response of the nanoprobe. However, the tolerance concentrations of these drugs in determination 1.0 μg/mL of vancomycin by the developed method are 10 times higher than that of vancomycin. It means that the interfering concentration for the mentioned drugs is about 10.0 μg/mL. It should be

Table 1
Tolerance limits of some co-administrated and over-the-counter drugs in the determination of 1.0 μg/mL of vancomycin.

Interfering substances	Tolerance limit (Times)
Nicotinamide, Clonazepam, Celecoxib, Amoxicillin, Diltiazem, Ibuprofen	1000
Amikacin, Pantoprazole, Diazepam, Losartan	200
Caffeine, Chlordiazepoxide	160
Tobramycin, Paracetamol	100
Oxazepam	40
Gentamicin, Aspirin, Naproxen	10

noted that the therapeutic level in plasma for gentamicin, aspirin, and naproxen was reported to be 4–10 μg/mL, 20–200 μg/mL, and 20–50 μg/mL [30]. Our previous studies on drug analysis in EBC show that the EBC level of drugs is much lower than that in plasma samples. According to these evidences, the concentration of these drugs in EBC is found to be lower than their tolerable level. Furthermore, the effect of various interfering inorganic ions and organic compounds concurrently presented in EBC samples on the determination of vancomycin by the presented method under the optimum conditions is also investigated and the results are sammerized in Table 2. As can be seen, the amounts of most reported coexisting species in EBC of healthy and pulmonary patient subjects are below tolerable concentration. So, it can be concluded that the developed nanoprobe has acceptable selectivity for vancomycin determination.

3.5. Analytical figures of merit

In the obtained optimum conditions, a linear relationship with a regression coefficient of 0.9993 is observed between SFS intensity and the vancomycin concentration in the concentration range of 0.1–8 μg/mL (λ_{max} = 405 nm when $\Delta\lambda$ = 80). The regression equation is $\Delta I_F = 39.427\,C + 4.2121$, where ΔI_F is the analytical response of nanoprobe that is obtained from the subtraction of SFS intensity in the absence and presence of vancomycin and is in an arbitrary unit. C is the concentration of vancomycin in μg/mL. The limit of detection (LOD) and limit of quantification (LOQ) for the developed method are calculated after the employing of the general procedure mentioned in the previous section for six blank samples. LOD and LOQ are defined as $3\,S_b/m$ and $10\,S_b/m$ (in which S_b is the standard deviation of the blank and m is the slope of the calibration curve) and reported to be 0.06 μg/mL and 0.2 μg/mL for the current study. Moreover, the method precision is studied by replicating analysis of a known concentration of vancomycin (1.0 μg/mL) using developed nanoprobe on the same day and different days. The intra-day and inter-day relative standard deviations (*%RSD*) for six repetitive analysis of 1.0 μg/mL are 4.8 % and 6.0 %, respectively. A comparison of our validated nanoparticles-based method with some other reported methods in the literature for the vancomycin analysis is given in Table 3. As can be seen, the analytical characteristic of the validated method is good and comparable with that of other reported methods.

3.6. Vancomycin analysis in EBC samples

The method ability for vancomycin determination on real EBC samples collected from newborns receiving vancomycin is also investigated. Details of the patients and the results of the analysis are summarized in Table 4. The method's accuracy is confirmed using recovery experiments by spiking a known concentration of vancomycin into the investigated EBC samples. As can be seen, the obtained recoveries are in the range of 101 %–104 % which is good

Table 2
Effect of coexisting inorganic ions and organic compounds on the determination of 1.0 μg/mL of vancomycin.using the developed method.

	Concentration range		Examined concentration of coexisting substance (μg/mL)	
Compounds	Healthy subjects (μg/mL)	Patient subjects (μg/mL)		RE[a]%
Acetone	0.10–2.60	0.10–19.80	38.0	4.3
Phosphate	0.09–14.24	–	40.0	4.8
Ammonia	0.40–1.30	0.81–14.70	20.0	4.2
Urea	–	0.04–4.19	6.0	3.8
Malondialdehyde	0.0004–0.0006	0.0004–0.0006	0.2	3.1
Arginine	0.022	0.02	6.0	4.2
NH_4^+	3.74–9.21	2.30–11.93	20.0	4.7
K^+	0.78–3.43	0.04–0.60	43.0	3.2
Ca^{2+}	0.20–0.59	0.08–1.254	50.0	4.9
Mg^{2+}	0.02–0.04	0.01–0.049	50.0	3.9
NO_2^-	0.01–0.08	0.05–0.52	30.0	4.2
NO_3^-	0.02–0.24	0.07–1.10	60.0	4.9
SO_4^{2-}	0.05–0.21	0.02–0.25	12.0	4.1
Fe^{3+}	0.02–0.16	0.004–7.25	40.0	4.9

[a] Relative error.

Table 3
Comparison of analytical characteristics of the presented method with other reported techniques for determination of vancomycin.

Method	Clean up/Pre-concentration method	Real sample	Linear range (μg/mL)	LOD (μg/mL)	Reference
Chemiluminescence	–	Pharmaceutical formulation	0.5–18.0 18.0–40.0	0.1	[8]
Spectrophotometery	Protein precipitation	Serum	12.5–200	0.99	[9]
Spectrofluorimetry	Protein precipitation	Serum	0.0015–20.0	0.000460	[10]
HPLC[a]-UV	Protein precipitation	Plasma	0.1 – 50.0	–	[12]
LC-MS/MS[b]	Protein precipitation	Plasma	0.3–100	–	[13]
Capillary electrophoresis	Protein precipitation	Serum	0.9998 – 99.98	–	[14]
Cu NCs-based SFS	–	EBC	0.1 – 8.0	0.06	This work

[a] High-Performance Liquid Chromatography.
[b] Liquid Chromatography Tandem Mass Spectrometry.

Table 4
Details of the newborns receiving vancomycin and determined vancomycin concentration in their EBC.

No.	Gender	Age (year)	Receiving dosage (mg)	Added (μg/mL)	Found (μg/mL)	Recovery (%)[a]
1	Female	Newborn	32	–	0.55	–
				1.0	1.56	101.0
2	Male	Newborn	32	–	0.83	–
				1.0	1.87	104.0
3	Male	Newborn	32	–	0.68	–
				1.0	1.73	105.0
4	Male	Newborn	25	–	0.38	–
				1.0	1.40	102.0
5	Female	Newborn	20	–	0.36	–
				1.0	1.40	104.0

[a] Recovery (%)=[(Found–Base)/Added] × 100. "Base" and "Found" refer to the amount of the analyte in samples before and after spiking, respectively.

evidence for the accuracy of the validated method for the determination of vancomycin.

4. Conclusions

In the current study, a sensitive Cu NCs -based SFS has been validated for the determination of vancomycin in EBC samples. Based on the characteristics of SFS techniques, the developed method offers some advantages such as high sensitivity, low cost, few interfering substances, and easy operation. The nanoprobe is successfully used for the vancomycin determination in EBC of newborns receiving vancomycin treatment and an average level of 0.56 μg/mL is reported. This is the first effort on EBC analysis for quantification of vancomycin level and it can be a highly in demand method owing to exploit a non-invasive sampling method.

CRediT authorship contribution statement

Elaheh Rahimpour: Investigation, Writing - review & editing, Validation, Data curation. **Maryam Khoubnasabjafari:** Conceptualization, Methodology, Investigation, Project administration. **Mohammad Bagher Hosseini:** Methodology, Visualization. **Abolghasem Jouyban:** Conceptualization, Supervision, Writing - review & editing, Funding acquisition.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

This work was supported by Research Affairs of Tabriz University of Medical Sciences, Tabriz, Iran under grant number 65435.

References

[1] G.L. Cooper, D.B. Given, Vancomycin: A Comprehensive Review of 30 Years of Clinical Experience, Park Row Publ., Incorporated A John Wiley & Sons Medical Group Comp, 1986.
[2] M.J. Rybak, The pharmacokinetic and pharmacodynamic properties of vancomycin, Clin. Infect. Dis. 42 (2006) S35–S39.
[3] M. Schulz, A. Schmoldt, Therapeutic and toxic blood concentrations of more than 800 drugs and other xenobiotics, Pharmazie 58 (2003) 447–474.
[4] C.A. Hammett-Stabler, T. Johns, Laboratory guidelines for monitoring of antimicrobial drugs, Clin. Chem. 44 (1998) 1129–1140.
[5] S. Davani, P. Muret, B. Royer, B. Hoen, J.-P. Kantelip, Interest of the therapeutic drug monitoring of main antibiotics, Ann. Biol. Clin. 60 (2002) 655–661.
[6] D.F. Thompson, M.A. Raebel, C.D. Freeman, R. Quintiliani, C.H. Nightingale, Vancomycin therapeutic drug monitoring: is it necessary? Ann. Pharmacother. 27 (1993) 594–598.
[7] A. Khataee, R. Lotfi, A. Hasanzadeh, A novel permanganate–morin–CdS quantum dots flow injection chemiluminescence system for sensitive determination of vancomycin, RSC Adv. 5 (2015) 82645–82653.
[8] A. Khataee, A. Hasanzadeh, M. Iranifam, M. Fathinia, Y. Hanifehpour, S. Joo, CuO nanosheets-enhanced flow-injection chemiluminescence system for determination of vancomycin in water, pharmaceutical and human serum, Spectrochim. Acta A. 122 (2014) 737–743.
[9] M. Tariq, H. Naureen, N. Abbas, M. Akhlaq, Development and validation of a simple, accurate and economical method for the analysis of vancomycin in human serum using ultracentrifuge protein precipitation and UV spectrophotometer, J. Anal. Bioanal. Tech. 6 (2015) 01–05.
[10] W. Liang, S. Liu, Z. Liu, D. Li, L. Wang, C. Hao, Y. He, Electron transfer and fluorescence "turn-off" based CdTe quantum dots for vancomycin detection at nanogram level in aqueous serum media, New J. Chem. 39 (2015) 4774–4782.
[11] A.A. Gill, S. Singh, N. Agrawal, Z. Nate, T.E. Chiwunze, N.B. Thapliyal, R. Chauhan, R. Karpoormath, A poly (acrylic acid)-modified copper-organic framework for electrochemical determination of vancomycin, Microchim. Acta. 187 (2020) 1–9.
[12] D. Ramadon, A.J. Courtenay, A.D. Permana, I.A. Tekko, E. McAlister, M.T. McCrudden, H.O. McCarthy, R.F. Donnelly, A sensitive HPLC-UV method for quantifying vancomycin in biological matrices: Application to pharmacokinetic and biodistribution studies in rat plasma, skin and lymph nodes, J. Pharm. Biomed. Anal. 189 (2020), 113429.
[13] M. Oyaert, N. Peersman, D. Kieffer, K. Deiteren, A. Smits, K. Allegaert, I. Spriet, J. Van Eldere, J. Verhaegen, P. Vermeersch, Novel LC–MS/MS method for plasma vancomycin: comparison with immunoassays and clinical impact, Clin. Chim. Acta 441 (2015) 63–70.
[14] J. Wang, Y. Cao, S. Wu, S. Wang, X. Zhao, T. Zhou, Y. Lou, G. Fan, Determination of vancomycin in human serum by cyclodextrin-micellar electrokinetic capillary chromatography (CD-MEKC) and application for PDAP patients, Molecules 22 (2017) 538.
[15] K.C. Chong, L.Y. Thang, J.P. Quirino, H.H. See, Monitoring of vancomycin in human plasma via portable microchip electrophoresis with contactless conductivity detector and multi-stacking strategy, J. Chromatogr. A 1485 (2017) 142–146.
[16] M. Nasrollahzadeh, S.M. Sajadi, M. Sajjadi, Z. Issaabadi, Applications of nanotechnology in daily life, Interface Sci. Technol. 28 (2019) 113–143.
[17] R. Gill, M. Zayats, I. Willner, Semiconductor quantum dots for bioanalysis, Angew. Chem. Int. Ed. 47 (2008) 7602–7625.
[18] P. Alivisatos, The use of nanocrystals in biological detection, Nat. Biotechnol. 22 (2004) 47–52.
[19] M. Khoubnasabjafari, E. Rahimpour, A. Jouyban, Exhaled breath condensate as an alternative sample for drug monitoring, Bioanalysis 10 (2018) 61–64.
[20] M.J.N. de Paiva, H.C. Menezes, Z. de Lourdes Cardeal, Sampling and analysis of metabolomes in biological fluids, Analyst 139 (2014) 3683–3694.
[21] D. Patra, A. Mishra, Recent developments in multi-component synchronous fluorescence scan analysis, Trends Analyt. Chem. 21 (2002) 787–798.
[22] S.K. Ghosh, D.S. Rahman, A.L. Ali, A. Kalita, Surface plasmon tunability and emission sensitivity of ultrasmall fluorescent copper nanoclusters, Plasmonics 8 (2013) 1457–1468.
[23] M. Khoubnasabjafari, H. Pourfathi, A. Mahmoodpoor, A. Jouyban, Waste of mechanical ventilators as a biological sample for follow up of biomarkers and drugs, Pharm. Sci. 26 (2020) 343.
[24] S.Y. Lim, W. Shen, Z. Gao, Carbon quantum dots and their applications, Chem. Soc. Rev. 44 (2015) 362–381.
[25] H. Weller, Colloidal semiconductor q-particles: chemistry in the transition region between solid state and molecules, Angew. Chem. Int. Ed. 32 (1993) 41–53.
[26] P.V. Kamat, Photochemistry on nonreactive and reactive (semiconductor) surfaces, Chem. Rev. 93 (1993) 267–300.
[27] A.V. Isarov, J. Chrysochoos, Optical and photochemical properties of nonstoichiometric cadmium sulfide nanoparticles: surface modification with copper (II) ions, Langmuir 13 (1997) 3142–3149.
[28] L. Fan, Y. Hu, X. Wang, L. Zhang, F. Li, D. Han, Z. Li, Q. Zhang, Z. Wang, L. Niu, Fluorescence resonance energy transfer quenching at the surface of graphene quantum dots for ultrasensitive detection of TNT, Talanta 101 (2012) 192–197.
[29] A.R. Junior, M.M. Vila, M. Tubino, Green spectrophotometric method for the quantitative analysis of vancomycin in pharmaceuticals and comparison with HPLC, Anal. Lett. 41 (2008) 822–836.
[30] M. Schulz, S. Iwersen-Bergmann, H. Andresen, A. Schmoldt, Therapeutic and toxic blood concentrations of nearly 1,000 drugs and other xenobiotics, Crit. Care 16 (2012) 1–4.