

Prospective of Ultrasensitive Nanometal Oxides Electrochemical Sensors for Pharmaceutical Analysis of Antihistamine Drug Fexofenadine Hydrochloride

Amal M. Al-Mohaimed, Nawal A. Alarfaj, Maha F. El-Tohamy*, Hajar Al-Harbi

Department of Chemistry, College of Science, King Saud University, P.O. Box 22452, Riyadh 11495, Saudi Arabia

*E-mail: moraby@ksu.edu.sa

Received: 8 January 2020 / Accepted: 10 February 2020 / Published: 10 April 2020

Promising advancement in nanoscience and nanomaterials has witnessed various triumphs of metal oxide nanoparticles due to their unique properties and wide applications. The exotic and multi-functional activity of ZnO and CuO nanoparticles, encourage the scientific researchers payed an extensive attention to these metal oxides as a remarkable and active materials in the electrochemical and sensing applications. The suggested study described a comparative evaluation of sensitivity and selectivity of two fabricated coated wire membrane sensors enriched with zinc oxide and copper oxide nanoparticles with other conventional types for the quantification of antihistamine drug fexofenadine hydrochloride (FFN). The outcome results revealed linear behavior of the enriched ZnO and CuO nano sensors over the concentration ranges 1.0×10^{-9} - 1.0×10^{-2} , 1.0×10^{-10} - 1.0×10^{-2} mol L⁻¹, respectively, with respect to 1.0×10^{-6} - 1.0×10^{-2} mol L⁻¹ for the conventional coated wire types. The regression equations were $E_{mV} = (52.1 \pm 0.7) \log(\text{FFN}) + 521$, $E_{mV} = (59.7 \pm 0.3) \log(\text{FFN}) + 744.31$ for enriched nanometal oxides, respectively, $E_{mV} = (55.0 \pm 0.5) \log(\text{FFN}) + 510.4$ and $E_{mV} = (60.083 \pm 0.4) \log(\text{FFN}) + 821.94$ for conventional type with correlation coefficients 0.9995, 0.9999, 0.9997 and 0.9998 for the previously mentioned sensors respectively.

Keywords: Fexofenadine hydrochloride; Electrochemical sensors; Metal oxide nanoparticles

1. INTRODUCTION

Recently, nano-scale materials are considered the potential key in sensors, constructions of materials, medicine, electronics, drug delivery systems, and cancer. Scientists are still trying to grow their research area, where, the unique properties of nano-scale materials can be potentially modified our life cycle and utilized for the benefit of ultra-sensitive sensor construction [1]. The matter in nano size exhibits different and amazing properties which are considered as a possible solution to many current

problems. It makes a new essential contribution to solving global and environmental challenges [2]. Among nanomaterials, metal oxides such as zinc oxide, copper oxide, etc., which play an important role in chemistry, physics, and material science [3].

Nowadays, the detection and quantification of pharmaceutical compounds using metal oxide sensors have major attention. The advanced physical and chemical properties of Zinc oxide nanoparticles (ZnONPs) and copper oxide (CuONPs), encourage, their use in various applications including medical products, drug delivery systems, electrochemical sensors, biomedical application [4-6]. The high iso-electric stability and the powerful binding features of ZnO and CuO nano-sized particles enhanced the development of electrochemical sensors [7, 8]. The literature survey addressed various reported articles concerned with the role of ZnONPs and CuONPs in electrochemical sensors [9-12].

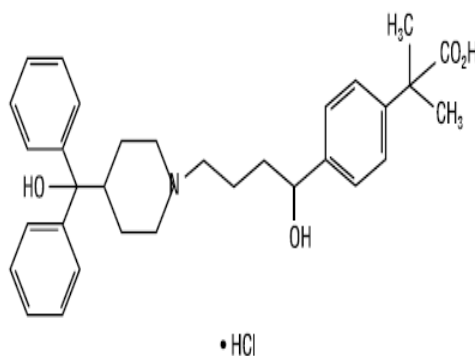


Figure 1. Structural formula of *fexofenadine* hydrochloride

Fexofenadine hydrochloride (FFN) is known as a carboxylate metabolic derivative of terfenadine (Figure 1). It is a second generation antihistamine medication. Upon administration, it binds with the peripheral H1-receptors to prevent the binding of histamine and reduce its action [13]. Fexofenadine hydrochloride was previously determined by several analytical methods, including chromatographic separation and identification using stability indicating and reversed phase liquid chromatography [14-16], thin layer chromatography [17] and capillary zone electrophoresis [18, 19]. Also, different spectroscopic methods for the determination of FFN were reported [20-24]. Moreover, few electrochemical techniques were addressed for the determination of FFN [25, 26].

The present study, aimed to fabricate new and simple coated wire electrochemical membrane sensors enriched with ZnO and CuO nano-sized particles to improve these sensors to detect Fexofenadine hydrochloride. Furthermore, a comparative study was carried out between the enriched sensors with metal oxide nanoparticles and the conventional fabricated sensors.

2. EXPERIMENTAL

2.1. Materials and solvents

Pure fexofenadine HCl, Zinc acetate and copper acetate were provided by Al-Qassim pharmaceutical industries, Saudi Arabia. Commercial product (Telfast 120 mg/tablet) was given by (Sanofi Aventis). Different chemicals and reagents were purchased from Sigma Aldrich Hamburg,

Germany) such as polyvinyl chloride (PVC), ortho-nitrophenyloctyl ether (*o*-NPOE), phosphomolybdic acid (PMA) and tetraphenylborate (TPB), tetrahydrofuran (THF) 97.0 %, acetone 99.9 %, methanol 99.9 % and ethanol 99.9 %.

2.2. Instrumentation

All analysis measurements were performed using a digital pH/mV (HANNA, model 211) with an indicator electrode and Ag/AgCl as reference one. pH-meter (Metrohm model 744) was applied to adjust the pH.

2.3. Synthesis of metal oxide nanoparticles

To prepare ZnONPs, an equivalent amount of zinc acetate was dissolved at room temperature in methanol to prepare 0.2 mol L⁻¹ zinc acetate solution. The prepared solution was stirred at 25°C for 2h. Then, approximately, 0.02 mol L⁻¹ of NaOH was dropped in the solution and stirred for 1 hour. Then it kept aside to form a white precipitate. The formed ZnONPs was filtered, rinsed with methanol and dried at 80 °C for 15 min [27].

The preparation of CuONPs using copper nitrate started by preparing 100 mL of 0.1 mol L⁻¹ of copper nitrate in deionized water. Under magnetic stirring, a solution of 0.1 mol L⁻¹ sodium hydroxide was added dropwise. At pH 14 a black precipitate was observed. DI water and ethanol were used to neutralize the formed CuONPs and then dried at 80°C for 16 h [28].

2.4. Microscopic and spectroscopic characterization of nanoparticles

Ultraviolet-visible (UV-Vis) spectral analysis was carried out using UV 2450 Spectrophotometer (Shimadzu Corporation, Kyoto, Japan) in the range of 100-800 nm. Fluorolog 3 spectrometer (FL-3-11, Horiba JobinYvon, USA) was used to measure the emission and excitation spectra of the synthesized ZnONPs and CuONPs.

Fourier-Transform Infrared spectroscopy (FT-IR) analysis was performed on the Spectrum BX spectrometer, (PerkinElmer, Waltham, USA) to detect the possible functional groups that were present in the as-prepared ZnONPs and CuONPs.

Transmission electron microscope (TEM) (JEM-2100F, JEOL Ltd, USA) was applied to study the surface morphology and particle size of ZnONPs and CuONPs using an accelerating voltage of 100 kV. Energy-dispersive X-ray spectroscopy (EDX) analysis was carried out using a JEM-2100F transmission electron microscope; to confirm the presence of Zn and Cu in the suspension as well as to detect other elementary components of the particles.

2.5. Preparation of stock solution

A stock solution of 1.0×10^{-2} mol L⁻¹ was obtained by dissolving 0.60 g of FFN in 100 mL of distilled water. Different concentrations were prepared for analysis using the same solvent.

2.6. Preparation of ion pairs

Two different ion pair's fexofenadine-phosphomolybdate (FFN-PM) and fexofenadine tetraphenylborate (FFN-TPB) were prepared by adding separately 50 mL of 1.0×10^{-2} mol L⁻¹ of FFN solution to the same volume of 1.0×10^{-2} mol L⁻¹ of PMA and TPB solutions. Faint yellow and white precipitates of FFN-PM and FFN-TPB were obtained, respectively, after filtration and washing the formed precipitates were dried overnight at room temperature.

2.7. Sensor construction and membrane composition

Four different coated wire sensors were fabricated using coated membrane prepared by dissolving 190 mg of high molecular weight polyvinyl chloride (PVC), 10 mg of ion-pair (FFN-PM or FFN-TPB) for the conventional coated wire sensors and 0.35 mL of plasticizer *o*-NPOE in 5 mL of THF. The solution was mixed well and allowed to evaporate at ambient temperature. The modified electrode was fabricated by forming a thin layer of the prepared ZnONPs or CuONPs on the surface of Al wire sensors and dried at ambient temperature for one day. Finally, the modified sensors were immersed in the previously prepared membrane solutions to obtain FFN-PM-ZnONPs or FFN-TPB-CuONPs.

2.8. Calibration graphs

Ten mL amounts of 1.0×10^{-7} - 1.0×10^{-3} mol L⁻¹ standard solution of fexofenadine HCl were tested and the sensor in conjunction with Ag/AgCl reference electrode was immersed in each solution. The recorded potentials were plotted vs. $-\log [\text{FFN}]$. Between each measurement the sensor should be cleaned using distilled water and dried by tissue paper, respectively.

2.9. Factors affecting the potential readings

The influence of pH of 1.0×10^{-3} mol L⁻¹ of drug test solution on the potential value of the fabricated sensors was investigated. The pH was recorded in approximately, 50 mL aliquots of the tested drug using the fabricated sensors in conjunction with reference sensor Ag/AgCl and combined glass electrode. The change in pH was performed by adding 0.1 mol L⁻¹ hydrochloric acid or a few drops of 0.1 mol L⁻¹ of sodium hydroxide. The pH values were plotted against the potential readings.

Separate solution method [29] is the common method which is used to evaluate the selectivity of the fabricated sensor in such study.

The dynamic response time was obtained from the potential response corresponding to drug concentration over the range of $1.0 \times 10^{-2} - 1.0 \times 10^{-9} \text{ mol L}^{-1}$.

2.10. Analytical Applications

Five individual tablets of Telefast[®] tablets (120 mg/tablet) were finely powdered and 0.53 g was dissolved in distilled water to obtain $1.0 \times 10^{-2} \text{ mol L}^{-1}$ standard solution. Working solutions were prepared to obtain different concentrations of FFN in the range $1.0 \times 10^{-3} - 1.0 \times 10^{-6} \text{ mol L}^{-1}$. The suggested sensors FFN-PM-ZnONPs and FFN-TPB-CuONPs were separately used to determine each concentration of the investigated drug.

3. RESULT AND DISCUSSION

3.1. Characterization of the synthesized nanoparticles

The produced ZnONPs and CuONPs were characterized using microscopic techniques including TEM and SEM. FT-IR was also used to prove the formation of ZnONPs and CuONPs. The TEM images showed that the prepared ZnONPs and CuONPs are uniformly distributed, cube and spherical in shape, respectively. The size of the as-prepared ZnONPs and CuONPs was 32 and 20 nm for the previously prepared nanoparticles, respectively. The surface morphology of the prepared ZnONPs and CuONPs was revealed by SEM analysis (Figure 2).

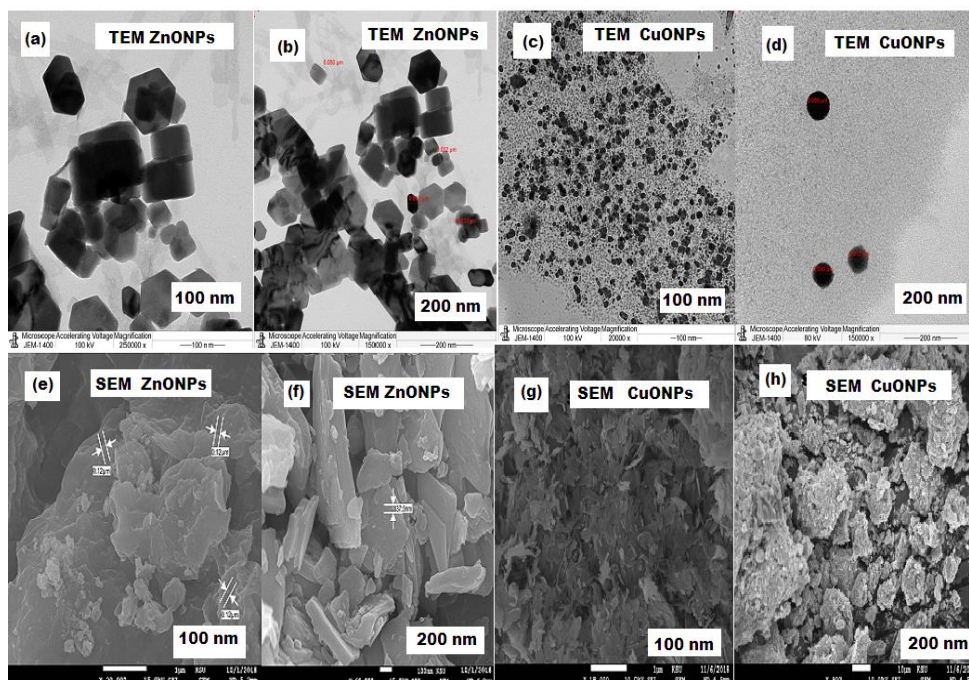


Figure 2. Transmission electron microscope (TEM) and scanning electron microscope (SEM) images of ZnONPs and CuONPs using different magnifications

Furthermore, FT-IR spectra of the prepared ZnONPs and CuONPs displayed significant bands at 3755.25 cm^{-1} and 3435.69 cm^{-1} which were assigned to be related to OH-stretching groups. An absorption band at 2367.79 cm^{-1} confirmed the presence of CH-stretching. The bands at 1597.25 cm^{-1} and 1400.11 cm^{-1} and 1337.32 cm^{-1} were assigned to be related to a C=O group of carboxylic acid and C=C group of equines, respectively.

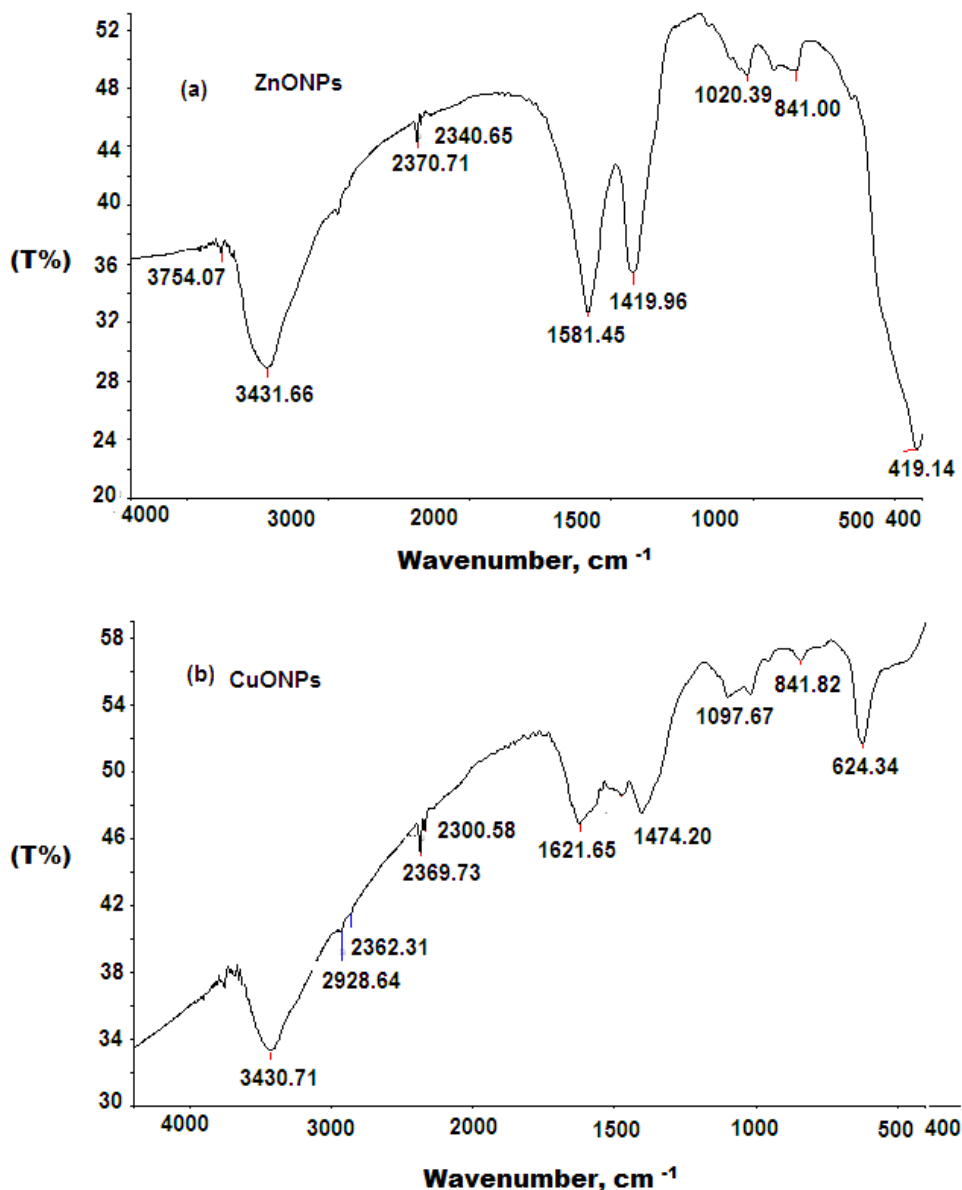


Figure 3. FT-IR spectra of ZnONPs and CuONPs at wavenumber from 4000-400 cm^{-1}

The peak of 1022.80 cm^{-1} is assigned to be related to the CO group of acetate and the peak assigned at 455.32 cm^{-1} confirmed the formation of Zn metal stretching (Figure 3a). In case of CuONPs, well defined bands at 3756.10 cm^{-1} , 3693.25 cm^{-1} , 3654.46 cm^{-1} and 3465.91 cm^{-1} were observed for OH-stretching groups. However, the absorption band 2340.46 cm^{-1} confirmed the presence of CH-

stretching. The band at 1656.16 cm^{-1} was assigned to be related to a C=O group of a carboxylic acid (Figure 3b).

3.2. The behavior of the fabricated sensors

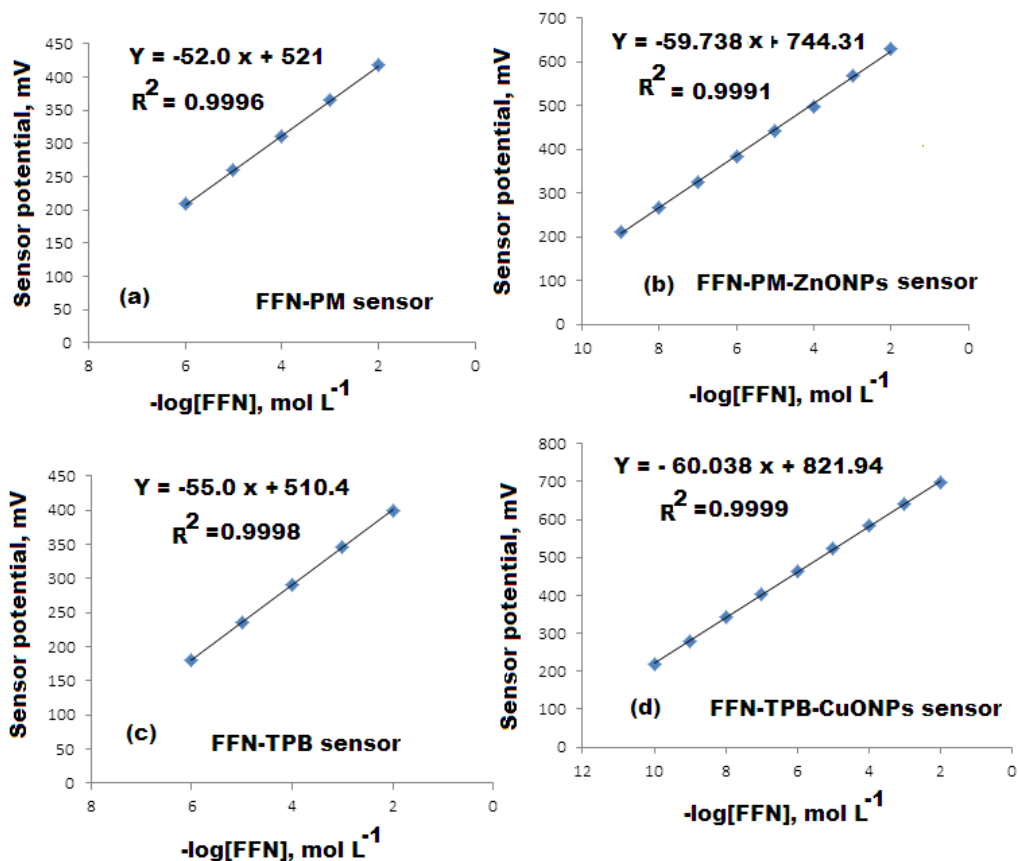


Figure 4. Calibration graphs of the fabricated (a, c) Conventional FFN-PM and FFN-TPB, (b, d) modified FFN-PM-ZnONPs, FFN-TPB-CuONPs

Table 1. Electrochemical response characteristics of conventional coated wire FFN-PM and FFN-TPB, modified FFN-PM-ZnONPs and FFN-TPB-CuONPs sensors

Parameter	Conventional coated wire FFN-PM sensor	Modified FFN-PM-ZnONPs sensor	Conventional coated wire FFN-TBP sensor	Modified FFN-TPB-CuONPs sensor
Slope (mV. Decade ⁻¹)	52.1±0.7	59.7± 0.3	55.0±0.5	60.083± 0.4
Intercept	521	744.31	510.4	821.94
Regression equation	$E_{mV} = (52.1±0.7) \log(\text{FFN})+521$	$E_{mV} = (59.7±0.3) \log(\text{FFN})+744.31$	$E_{mV} = (55.0±0.5) \log(\text{FFN}) + 510.4$	$E_{mV} = (60.08±0.4) \log(\text{FFN}) + 821.94$
Correlation coefficient, r	0.9997	0.9995	0.9998	0.9999
Linear range (mol L ⁻¹)	$10 \times 10^{-6} - 1.0 \times 10^{-2}$	$1.0 \times 10^{-9} - 1.0 \times 10^{-2}$	$10 \times 10^{-6} - 1.0 \times 10^{-2}$	$1.0 \times 10^{-10} - 1.0 \times 10^{-2}$
LOD	4.9×10^{-7}	6.0×10^{-10}	5.0×10^{-7}	5.8×10^{-11}
Response time/ s	60	30	45	30
Working pH range	3-7	3-7	3-7	3-7
Lifetime/day	21	30	15	25
Temperature, °C	25	25	25	25
Accuracy (%)	99.33 ± 0.46	99.70 ± 0.27	99.19 ± 0.63	99.84 ± 0.16

FFN reacts with PM or TPB to form a stable FFN-PM and FFN-TPB ion pairs which are soluble in an organic solvent such as THF. Ortho-nitrophenyloctyl ether (*o*-NPOE) is the solvent mediator which used with the active materials FFN-PM and FFN-TPB in the presence of PVC. The response of the fabricated sensors was determined and the critical response characteristics were summarized in Table 1. The fabricated sensors gave Nernstian responses with slopes of 52.1 ± 0.7 , 59.7 ± 0.3 , 55.0 ± 0.5 and 60.08 ± 0.4 mV over the drug concentration ranges of 10×10^{-6} – 1.0×10^{-2} , 1.0×10^{-9} – 1.0×10^{-2} , 10×10^{-6} – 1.0×10^{-2} and 1.0×10^{-10} – 1.0×10^{-2} mol L⁻¹ for conventional FFN-PM and FFN-TPB, modified FFN-PM-ZnONPs and FFN-TPB-CuONPs, respectively (Figures 4a, 4b, 4c and 4d). Fast dynamic responses without changes in the sensor parameters were noticed in 60, 21, 45 and 30 s for 21, 30, 15, 25 days for the previously mentioned sensors. The influence of pH of conventional and modified sensors potential was examined to evaluate the safe pH range which is suitable for FFN determination. The outcome results concluded that both conventional FFN-PM and FFN-TPB, modified FFN-PM-ZnONPs and FFN-TPB-CuONPs sensors were practically independent in pH range 3-7, and this range can be safely used for FFN determination. It was also noticed that in the acidic medium pH 3, the potential readings were slightly elevated due to the presence of H⁺ ions. However, the increase of OH⁻ ions in alkaline medium caused significant decrease in potential readings [30].

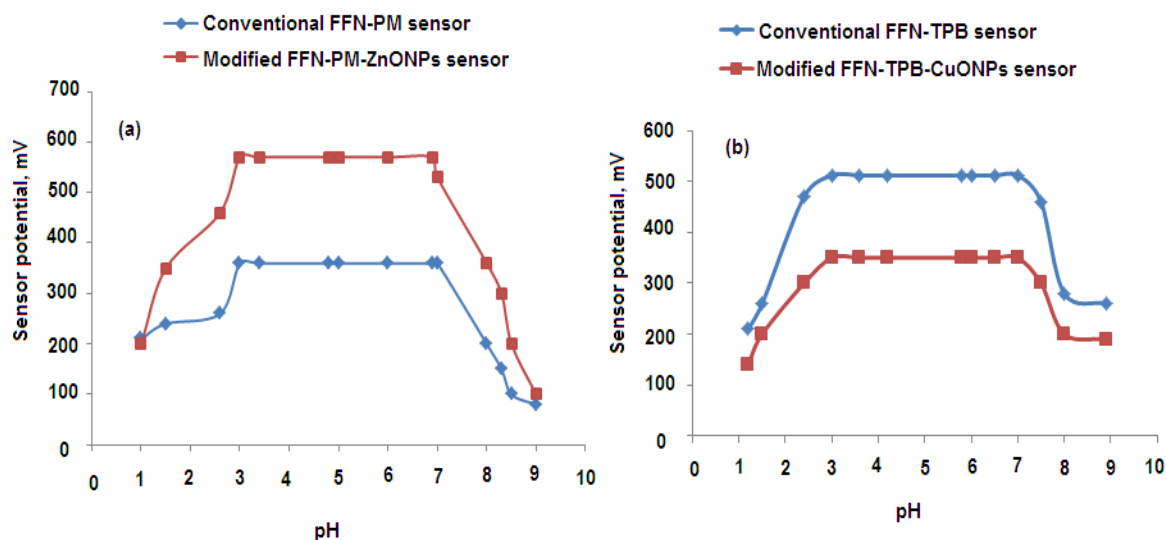


Figure 5. Effect of pH on the conventional and modified metal oxide nanoparticles coated wire sensors using 1.0×10^{-3} mol L⁻¹ of FFN solution

In order to estimate the selectivity of the fabricated sensors towards the investigated drug, the suggested sensors examined to analyze 1.0×10^{-3} mol L⁻¹ of various inorganic cations, sugars and amino acids. Very high selectivity was observed by using the modified sensors FFN-PM-ZnONPs and FFN-TPB-CuONPs. Due to the reduced particle size and the unique physical and chemical features of the metal oxide nanoparticles, the addition of ZnONPs and CuONPs increases the conductivity of the fabricated sensors and the selectivity toward the investigated drug also increased. Also, the selectivity of the FFN coated membrane sensors is referred to the free energy of transfer of FFN⁺ between aqueous and coated membrane phases. No interference was noticed by using the suggested sensors in the

detection of inorganic cations because of their ionic size differences, their mobility and permeability as compared with FFN⁺.

Table 2. Selectivity coefficient ($K^{Pot}_{FFN^+}$) of of conventional coated wire FFN-PM and FFN-TPB, modified FFN-PM-ZnONPs and FFN-TPB-CuONPs sensors by the separate solution method using 1.0×10^{-3} mol L⁻¹ FFN

Interferences	Conventional coated wire FFN-PM sensor ($K^{Pot}_{FFN^+}$)	Modified FFN-PM-ZnONPs sensor ($K^{Pot}_{FFN^+}$)	Conventional coated wire FFN-TPB sensor ($K^{Pot}_{FFN^+}$)	Modified FFN-TPB-CuONPs sensor ($K^{Pot}_{FFN^+}$)
Na ⁺	7.2×10^{-3}	3.7×10^{-4}	4.2×10^{-4}	8.1×10^{-5}
K ⁺	1.4×10^{-3}	2.1×10^{-3}	1.6×10^{-3}	5.0×10^{-4}
Ag ⁺	2.7×10^{-3}	1.1×10^{-3}	1.0×10^{-3}	7.5×10^{-4}
Ni ²⁺	3.2×10^{-3}	1.4×10^{-3}	2.1×10^{-3}	1.4×10^{-3}
Cu ²⁺	5.8×10^{-3}	8.9×10^{-4}	1.8×10^{-3}	8.9×10^{-4}
Zn ²⁺	6.3×10^{-3}	1.2×10^{-3}	1.5×10^{-3}	1.2×10^{-3}
L-histidine	5.2×10^{-3}	5.2×10^{-4}	9.2×10^{-4}	5.2×10^{-4}
Ornithine	4.1×10^{-3}	3.9×10^{-4}	2.4×10^{-3}	3.9×10^{-4}
Glycine	4.5×10^{-3}	6.3×10^{-4}	1.4×10^{-3}	6.3×10^{-4}
Starch	5.2×10^{-3}	1.1×10^{-3}	6.3×10^{-4}	1.1×10^{-3}
Lactose	1.8×10^{-3}	9.2×10^{-4}	2.0×10^{-3}	9.2×10^{-4}
Glucose	2.3×10^{-3}	1.4×10^{-3}	2.4×10^{-3}	2.0×10^{-5}

Additionally, the smaller energy of cation hydration cation causes the greater the response of coated membrane. Therefore, the suggested modified sensors based FFN-PM-ZnONPs and FFN-TPB-CuONPs exhibit good tolerance towards sugars (Table 2).

3.3. Quantification of fexofenadine hydrochloride

Table 3. Statistical analysis of data obtained from the determination of FFN in bulk powder using conventional coated wire FFN-PM and FFN-TPB, modified FFN-PM-ZnONPs and FFN-TPB-CuONPs sensors

Statistical analysis	Conventional FFN-PM coated wire sensor			Modified FFN-PM ZnONPs sensor		
	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery
	6.0	5.96	99.3	9.0	8.97	99.7
5.3	5.24	98.9	8.3	8.26	99.5	
5.0	4.95	99.0	8.0	7.94	99.3	
4.3	4.30	100.0	7.0	6.96	99.4	
4.0	3.98	99.5	6.0	6.00	100.0	
3.3	3.26	98.8	5.0	4.99	99.8	
3.0	2.97	99.0	4.0	4.00	100.0	

	2.3 2.0	2.29 2.00	99.6 100.0	3.0 2.0	2.99 2.00	99.7 100.0
Mean±SD	99.35±0.5			99.71±0.3		
n	9			9		
Variance	0.25			0.09		
%SE	0.16			0.10		
%RSD	0.50			0.30		
	Conventional FFN-TPB coated wire sensor			Modified FFN-TPB CuONPs sensor		
	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery
Statistical analysis	6.0	5.96	99.3	10.0	10.00	100.0
	5.3	5.27	99.4	9.0	8.99	99.0
	5.0	4.98	99.6	8.0	7.97	99.6
	4.0	3.98	99.5	7.0	6.98	99.7
	3.0	2.97	99.0	6.0	5.99	99.8
	2.0	1.99	99.5	5.0	4.98	99.6
				4.0	3.99	99.8
				3.0	3.00	100.0
				2.0	2.01	100.5
Mean±SD	99.38±0.2			99.78±0.4		
n	6			9		
Variance	0.04			0.16		
%SE	0.08			0.13		
%RSD	0.20			0.40		

$$**SE (\%Error) = \%RSD/\sqrt{n}$$

The suggested conventional and modifying sensors were exploited to determine FFN in its authentic powder and the percentage recoveries were 99.35 ± 0.5 , 99.71 ± 0.3 % and 99.38 ± 0.2 and 99.78 ± 0.4 for FFN-PM, FFN-PM-ZnONPs and FFN-TPB, FFN-TPB-CuONPs, respectively (Table 3). The sensitivity of the modified sensors was attributed to the unique physical and chemical characteristics of the added nanoparticles. Additionally, it was noticed that the modified sensor by CuONPs displayed an excellent sensitivity and selectivity towards the investigated drug and this due to the high dielectric constant of CuONPs rather than ZnONPs.

3.4. Method validation

The suggested method was validated [31]. A rectilinear relationships were displayed by the fabricated sensors over 1.0×10^{-9} - 1.0×10^{-2} , 1.0×10^{-10} - 1.0×10^{-2} mol L⁻¹, respectively, with respect to

1.0×10^{-6} – 1.0×10^{-2} mol L⁻¹ for the conventional coated wire types. The regression equations were $E_{mv} = (52.1 \pm 0.7) \log(\text{FFN}) + 521$, $E_{mv} = (59.7 \pm 0.3) \log(\text{FFN}) + 744.31$ for enriched nanometal oxides, respectively, $E_{mv} = (55.0 \pm 0.5) \log(\text{FFN}) + 510.4$ and $E_{mv} = (60.083 \pm 0.4) \log(\text{FFN}) + 821.94$ for conventional type with correlation coefficients 0.9995, 0.9999, 0.9997 and 0.9998 for the previously mentioned sensors respectively.

Table 4. Intra-day and Inter-day assay of fexofenadine hydrochloride by using modified FFN-PM-ZnONPs and FFN-TPB-CuONPs coated wire sensors

Statistical analysis	Modified FFN-PM-ZnONPs coated wire sensor					
	Intra-day assay			Inter-day assay		
	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery
	6.0	5.96	99.33	6.0	6.00	100.00
	5.0	4.95	99.00	5.0	4.99	99.80
	4.0	3.98	99.50	4.0	4.00	100.00
Mean±SD	99.27±0.3			99.93±0.2		
n	3			3		
Variance	0.09			0.04		
%SE*	0.17			0.11		
%RSD	0.30			0.20		
Statistical analysis	Modified FFN-TPB-CuONPs sensor					
	Intra-day assay			Inter-day assay		
	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery
	6.0	5.99	99.83	6.0	5.98	99.67
	5.0	4.98	99.60	5.0	4.98	99.60
	4.0	3.98	99.50	4.0	4.01	100.25
Mean±SD	99.64±0.2			99.84±0.4		
n	3			3		
Variance	0.04			0.16		
%SE**	0.11			0.23		
%RSD	0.20			0.40		

**SE (%Error) = %RSD/√n

The lower limit of detection was recorded for all sensors after the potential reading of the slope was dropped by 17.9 mV. The obtained results were found to be 4.9×10^{-7} , 6.0×10^{-10} , 5.0×10^{-7} and 5.8×10^{-1} mol L⁻¹. The accuracy of the described method was tested using nine concentrations and the mean percentage recoveries were calculated as 99.27 ± 0.3 %, 99.93 ± 0.2 % and 99.64 ± 0.2 % and 99.84 ± 0.4 % for the previously mentioned sensors, respectively. The intermediate precision was also

evaluated via inter-day and intra-day assay and the percentage relative standard deviation (% RSD) was calculated. The % RSD for the fabricated FFN-PM and FFN-PM-ZnONPs were 0.3 % and 0.2 % and for FFN-TPB and FFN-TPB-CuONPs were 0.2 % and 0.4 % all outcome results are less than 2 % revealing a high precise technique. The robustness of the current probe were evaluated by adding acetate buffer pH 3±0.5 and the percentage recoveries were found to be 99.77 ± 0.2 %, 99.62 ± 0.1 % for a conventional FFN-PM and 99.62 ± 0.11 % for modified FFN-PM-ZnONPs, while the outcome results of a conventional FFN-TPB and modified FFN-TPB-CuONPs were 99.49 ± 0.2 % and 99.60 ± 0.1 %, respectively. A further study was carried out to ensure the ruggedness of the suggested method by using a different model of pH meter (Jenway-3510). The calculated mean percentage recoveries were 99.88 ± 0.2 %, and 99.55 ± 0.1 %, 99.36 ± 0.5 % and 99.45 ± 0.1 % for the tested sensors. The outcome data revealed acceptance with other data from the proposed method and no significant difference was observed.

3.5. Quantification of the drug in tablets

Table 5. Statistical analysis of data obtained from the determination of FFN in Telfast® tablets using conventional coated wire FFN-PM and FFN-TPB, modified FFN-PM-ZnONPs and FFN-TPB-CuONPs sensors

Statistical analysis	Conventional FFN-PM coated wire sensor			Modified FFN-PM ZnONPs sensor			Reference Method [20]
	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery	
	6.0	5.97	99.5	7.0	6.98	99.7	
5.3	5.24	98.9	6.0	5.96	99.3		
5.0	4.95	99.0	5.0	4.99	99.8		
4.0	3.96	99.0	4.0	4.00	100.0		
3.0	2.98	99.3	3.0	3.00	100.0		
2.0	2.00	100.0	2.0	2.00	100.0		
Mean±SD	99.28±0.4			99.80±0.3			99.35±0.5
n	6			6			
Variance	0.16			0.09			
%SE**	0.16			0.12			
%RSD	0.40			0.30			
t-test	0.273 (2.228)***			1.929 (2.228)***			
F-test	1.56 (5.05)***			2.78 (5.05)***			
Statistical analysis	Conventional FFN-TPB coated wire sensor			Modified FFN-TPB CuONPs sensor			Reference
	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery	Test solution -log Conc. mol L ⁻¹	Found -log Conc. mol L ⁻¹	% Recovery	

	6.0	5.99	99.8	9.0	8.97	99.7	Method [20]
	6.3	6.27	99.5	8.0	7.95	99.4	
	5.0	4.96	99.2	7.0	6.96	99.4	
	4.0	3.97	99.3	6.0	5.99	99.8	
	3.0	2.98	99.3	5.0	5.00	100.0	
	2.0	1.95	97.5	4.0	4.00	100.0	
Mean±SD	99.10±0.8			99.72±0.3			99.35±0.5
n	6			6			
Variance	0.64			0.09			
%SE**	0.33			0.12			
%RSD	0.81			0.30			
t-test	0.648 (2.228)***			1.929 (2.228)***			
F-test	2.56 (5.05)***			2.78 (5.05)***			

**SE (%Error) = %RSD/ \sqrt{n}

*** The tabulated values of "t" and "F" at confidence level $p=0.05$

In order to evaluate analytical usefulness of the fabricated sensors, FFN was determined in Telefast[®] tablets (120 mg/tablet). The recorded results were statistically analyzed using t-student's test and F-test [32] and the results compared with those obtained by spectrophotometric method [20] which is measured the absorbance of formed pale yellow complex between FFN and bromothymol blue at 412 nm and the pH was adjusted at 2.6. The outcome of the data revealed an excellent sensitivity of the proposed sensors towards the determination of FFN in its tablet solution and the calculated % recoveries were 99.28±0.4, 99.80±0.3, 99.10±0.8 and 99.72±0.3 for the fabricated FFN-PM and FFN-PM-ZnONPs, FFN-TPB and FFN-TPB-CuONPs, respectively.

4. CONCLUSION

The suggested potentiometric study was conducted by fabricating two coated wire membrane sensors enriched with zinc oxide and copper oxide nanoparticles. The potential readings of the modified sensors were compared to the conventional types for the quantification of antihistamine drug fexofenadine hydrochloride. The developed sensors revealed good and advantageous over the other conventional sensors due to their sensitivity and selectivity. Also, the use of ZnONPs and CuONPs as electro enhanced materials increased the sensitivity of the sensors and facilitate the detection of the investigated drug with a low limit and in wide concentration range. Therefore, the fabricated sensors can be used for routine analysis of fexofenadine hydrochloride in pharmaceutical industries, hospitals and research laboratories.

ACKNOWLEDGMENT

This research project was supported by a grant from the "Research Center of the Female Scientific and Medical Colleges", Deanship of Scientific Research, King Saud University.

CONFLICT OF INTEREST

The authors declare that no competitive of interest associated with this study.

References

1. G. M. Whitesides, *Small*, 1 (2005) 172.
2. European Commission, Research Directorate General. Outcome of the Workshops Organised by the EC. Future Needs and Challenges for Material and Nanotechnology Research. European, (2001).
3. C. Noguera, *Physics and Chemistry at Oxide Surfaces*; Cambridge University Press: Cambridge, UK, (1996)
4. M. Martínez-Carmona, Y. G. ko and M. Vallet-Regi, *Nanomaterials*, 8 (2018) 268. DOI:10.3390/nano8040268
5. H. Sharma, K. Kumar, C. Choudhary, P. K. Mishra and B. Vaidya, *Cells Nanomed. Biotechnol.*, 44 (2016) 672.
6. J. Jiang, J. Pi and J. Cai, *Bioinorg. Chem. Appl.*, 2018, (2018) 1062562. <https://doi.org/10.1155/2018/1062562>
7. M. E. Vazquez, J. R. Lopez, D. Medina-Rodelo, M. Jimenez-Edeza, G. M. Castaneda-Ruelas, A. M. Lopez, J. M. Herrera-Ramirez and P. F. Mendez, *Int. J. Electrochem. Sci.*, 14 (2019) 6366. doi: 10.20964/2019.07.04
8. M. B. Gumpu, N. Nesakumar, B. L. Ramachandra and J. B. B. Rayappan, *J. Anal. Chem.*, 72 (2017) 316.
9. D. Balram, K-Y, Lian and N. Sebastian, *J. Electrochem. Sci.*, 13 (2018) 1542. doi: 10.20964/2018.02.06
10. S. Reddy, K. Swamy and H. Jayadevappa, *Electrochim. Acta*, 61 (2012) 78 doi: [10.1016/j.electacta.2011.11.091](https://doi.org/10.1016/j.electacta.2011.11.091)
11. J. Ping, S. Ru, K. Fan, J. Wu and Y. Ying, *Microchim. Acta*, 171 (2010)117. doi: [10.1007/s00604-010-0420-3](https://doi.org/10.1007/s00604-010-0420-3)
12. F. J. Arevalo, Y. Osuna-Sanchez, J. Sandoval-Cortez, A. D. Toccoa, A. M. Granero, S. N. Robledob, M. A. Zona, N. R. Vettorazzia, J. L. Martínez, E. P. Segurac, A. Ilinac and H. Fernandez, *Sensor Actuator B*, 244 (2017) 949.
13. E. Compalati, R. Baena-Cagnani, M. Penagos, H. Badellino, F. Braido, R. M. Gomez, G. W. Canonica and C. E. Baena-Cagnani, *Int. Arch. Allerg. Immunol.*, 156 (2011) 1. doi: [10.1159/000321](https://doi.org/10.1159/000321)
14. R. V. Rele, *Method Der Pharm. Lett.*, 8 (2016) 224.
15. H. M. Nimje, Shital T. Nimje, R. J. Oswal and S. T. Bhamre, *E-J chem.*, 9 (2012) 1257.
16. M. K. Sharaf El- Din, F. Ibrahim, M. I. Eid and M. E. K. Wahba, *J. Pharm. Res.* 4 (2011) 2377
17. M. P. Sutar, D. A. Bansode and S. S. Dhaneshwar, *Der Pharm. Sinica*, 6 (2015) 30.
18. A. R. Breier, S. S. Garcia, A. Jablonski, M. Steppe and E. E. S. Schapoval, *J. AOAC Int.*, 88 (2005) 1059.
19. P. Mikus, I. Valaskova and E. Havranek, *Drug Dev. Ind. Pharm.*, 31 (2005) 795. doi:10.1080/03639040500217368
20. S. J. Rajput and P. R. Parekh, *East. Pharm.*, 44 (2001) 101.
21. K. S. Kumar, V. Ravichandran, M. R. M. K. Mohan and R. D. Thyagu, *Indian J. Pharm. Sci.*, 68 (2006) 841.
22. H. M. Saleh, M. M. El-Henawee, G. H. Ragab and S. S. A. El-Hay, *Spectrochim. Acta Part A*, 67 (2007) 1284.
23. Z. A. Alothman, N. Bukhari, S. Haider, S. M. Wabaidur, A. A. Alwarthan, *Arab. J. Chem.*, 3 (2010) 251.
24. M. K. Sharaf El-Din, F. A. Ibrahim, M. I. Eid and M. E. K. Wahba, *Acta Chim. Slov.*, 58 (2011) 278.
25. Golcu, Ayşegül, B. Dogan, and S. A. Ozkan. *Anal. Lett.*, 38 (2005) 1913.
26. R. V. Rele, and S. A. Sawant, *J. Chem. Pharm. Res.*, 5 (2013) 286.

27. R. M. Alwan, Q. A. Kadhim, K. M. Sahan, R. A. Ali, R. J. Mahdi, N. A. Kassim and A. N. Jassim, *Nanosci. Nanotechnol.*, 5 (2015) 1.
28. K. Phiwdang, S. Suphankij, W. Mekprasart, W. Pecharapa, *Energy Procedia*, 34 (2013) 740.
29. N. A. Al-alarfaj, F. Aly, M. El-Tohamy, *J. Chil. Chem. Soc.*, 57 (2012) 1140.
30. N. A. Alarfaj, M. F. El-Tohamy, *Asian J. Chem.*, 25 (2013) 6421.
31. ICH-Q2 (R1) Validation and Analytical Procedures: Text and Methodology. International Conference on Harmonization guidelines, Geneva, November, (2005).
32. J. C. Miller and J. N. Miller, *Statistics for analytical chemistry*. 3rd Ed. New York: Ellis Horwood PTR Prentice Hall, (1993).

© 2020 The Authors. Published by ESG (www.electrochemsci.org). This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/4.0/>).