

## Comparative Potentiometric Study for Determination of Azithromycin Using Conventional PVC and Multi-Walled Carbon Nanotubes Sensors

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A new simple, accurate and reliable potentiometric method for determination of azithromycin was proposed and validated. Four types of sensors were fabricated. Conventional PVC plastic membrane (I), coated wire (II), carbon paste (III) and modified multi-wall carbon nanotubes carbon paste type (IV). The fabrication of all sensors based on the incorporation of azithromycin with phosphotungstic acid to form azithromycin-phosphotungstate as electroactive materials. The proposed sensors exhibit Nernstian response ( $55.10 \pm 0.19$ ,  $55.52 \pm 0.20$ ,  $57.09 \pm 0.14$  and  $58.04 \pm 0.11$  mV decade<sup>-1</sup>) over concentration ranges  $1.0 \times 10^{-6}$ - $1.0 \times 10^{-2}$ ,  $5.0 \times 10^{-7}$ - $1.0 \times 10^{-2}$ ,  $1.0 \times 10^{-7}$ - $1.0 \times 10^{-2}$  and  $1.0 \times 10^{-8}$ - $1.0 \times 10^{-2}$  mol L<sup>-1</sup> for sensor I, II, III and IV, respectively. The influence of several parameters such as pH, selectivity of sensors, response time and soaking time, etc. was studied. The proposed method was successfully applied for the determination of azithromycin in its pure form, pharmaceutical dosage forms and biological fluids. The obtained results were statistically analyzed and compared with those obtained by the reported method.

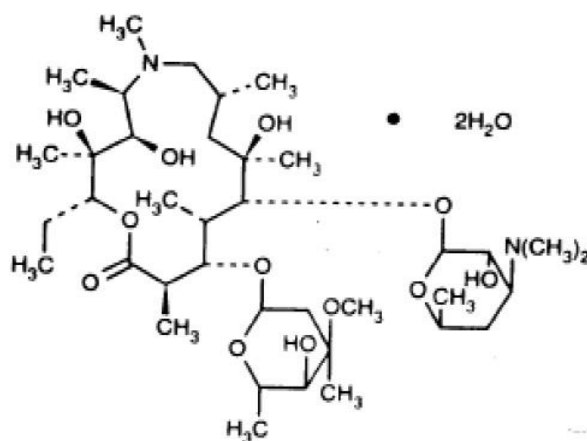
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**Keywords:** Azithromycin; Potentiometry; Conventional sensors; Coated wire sensor; Modified multi-wall carbon nanotubes carbon paste sensor

### 1. INTRODUCTION

Azithromycin, (Figure 1) is a member of macrolide antibiotics class called azalide. It is derived from erythromycin; however, it differs chemically from erythromycin in that a methyl-substituted nitrogen atom is incorporated into the lactone ring. Azithromycin is used to treat certain infections caused by bacteria, such as bronchitis; pneumonia; sexually transmitted diseases (STD); and infections of the ears, lungs, skin, and throat. It works by stopping the growth of bacteria. Azithromycin is also used sometimes to treat pylori infection, early Lyme disease, and other infections.

It is also used sometimes to prevent heart infection in patients having dental or other procedures and to prevent STD in victims of sexual assault [1].



**Figure 1:** Chemical structure of azithromycin dihydrate

Several methods have been reported for determination of azithromycin including high performance liquid chromatography [2-6], liquid chromatography coupled with mass spectrometry [7-9], thin Layer chromatography [10], spectrophotometry [11-14], voltammetry [15], capillary electrophoresis [16] and chemiluminescence [17].

From the literature survey, no potentiometric sensors were developed for the determination of azithromycin yet. In the present investigation, an attempt has been made to develop simple, accurate, and reproducible potentiometric sensors for the determination of azithromycin in pure form, pharmaceutical dosage forms and biological fluids. Moreover, the use of modified multi-wall carbon nanotubes carbon paste sensor plays an important role in terms of low cost, mass production, easy and highly reproducible sensors. Also the main attention is undertaken with a comparative study between four fabricated sensors and investigates the best performance characteristics of these sensors for the determination of the selected drug.

## 2. EXPERIMENTAL

### 2.1. Materials and reagents

All chemicals used were of analytical grade. Pure grade azithromycin was kindly supplied from Saudi Arabian Japanese Pharmaceutical Co. Limited (SAJA). The pharmaceutical preparation (Zithromax<sup>®</sup> 600 mg/tablet) was provided by Pfizer, USA. Methanol 99.0%, Acetone 99.9%, *o*-nitrophenyloctylether (*o*-NPOE) 99.0% and tetrahydrofuran (THF) 97.0% were provided by Fluka, Switzerland. Poly (vinyl chloride) (PVC) high molecular weight, phosphotungstic acid 99.1 %, high purity graphite powder (1-2  $\mu\text{m}$ ) and multi-wall carbon nanotubes powder (carbon >95.0%, O.D. x L 6-9 nm x 5  $\mu\text{m}$ ) were purchased from Sigma-Aldrich, Germany.

## 2.2. Instrumentation

The electrochemical measurements were carried out with HANNA instruments pH 211 microprocessor pH-meter. Saturated calomel electrode (SCE) was used as an external reference electrode while Ag/AgCl was used as an internal reference electrode.

## 2.3. Standard drug solution

Stock azithromycin solution  $0.1 \text{ mol L}^{-1}$  was freshly prepared daily by dissolving 1.963 g in 25 mL methanol. Working solutions ( $1.0 \times 10^{-8}$ - $1.0 \times 10^{-1} \text{ mol L}^{-1}$ ) were prepared by appropriate dilution with distilled water.

## 2.4. Preparation of azithromycin ion pair

The ion-pair was prepared by mixing 150 mL of  $1.0 \times 10^{-2} \text{ mol L}^{-1}$  azithromycin and 50 mL of  $1.0 \times 10^{-2} \text{ mol L}^{-1}$  phosphotungstic acid. The resulting white precipitate was filtered, washed thoroughly with distilled water and air dried at room temperature for 24 h.

## 2.5. Membrane composition

In order to optimize the membrane composition for the conventional PVC plastic membrane sensor and coated wire sensor, the membrane composition was studied by varying the percentages (w/w %) of the ion pair, poly (vinyl chloride) PVC and plasticizer (*o*-NPOE), until the optimum composition that exhibits the best performance characteristics was obtained. The membranes were prepared by dissolving the required amount of the ion-pair, PVC and (*o*-NPOE), in 5 mL tetrahydrofuran (THF). The solution mixture was poured into a petri dish (3 cm diameter), covered with a filter paper and the solvent was allowed to evaporate slowly at room temperature.

## 2.6. Sensor construction

*Conventional plastic membrane sensor:* A circular membrane was attached to a poly-ethylene tube (8 mm diameter) in sensor configuration by means of PVC-THF solution. The internal solution was prepared by mixing equal volumes of  $1.0 \times 10^{-3} \text{ mol L}^{-1}$  azithromycin and  $1.0 \times 10^{-3} \text{ mol L}^{-1}$  potassium chloride solution and the Ag/AgCl reference electrode was dipped in it. The constructed sensor was pre-conditioned after preparation by soaking for at least 24 h in  $1.0 \times 10^{-3} \text{ mol L}^{-1}$  azithromycin and stored in the same solution. All potentiometric measurements were performed using the following cell assembly: Ag/AgCl / Internal solution / membrane / test solution // KCl salt bridge // SCE.

*Coated wire sensor:* A coated wire sensor was prepared by insulating pure aluminum wire of 4.0 cm length by polyethylene tube leaving 1.0 cm at one end for coating and 0.5 cm at the other end

for connection. The polished aluminum surface was washed with a detergent, thoroughly rinsed with water, and dried with acetone. Then it was coated with the coating solution which was described under (2.5. membrane composition). The prepared sensor was conditioned by soaking for 6 h in  $1.0 \times 10^{-3}$  mol L<sup>-1</sup> azithromycin solution. All potentiometric measurements were performed using the following cell assembly: Al / membrane / test solution // KCl salt bridge // SCE.

*Carbon paste sensor:* The carbon paste sensor was prepared by hand mixing of 60.0% pure graphite powder (1-2  $\mu$ m) with 30.0 % *o*-NPOE as plasticizing liquid and 10.0% ion-pair (azithromycin-phosphotungstate) in an agate mortar to obtain a homogenous paste. Then the carbon paste was carefully packed in Teflon tube (3 mm in diameter). A fresh surface was obtained by polishing the carbon paste surface using transparent paper to obtain shiny and smooth surface.

*Modified multi-wall carbon nanotubes carbon paste sensor:* The modified multi-wall carbon nanotubes carbon paste sensor was prepared by the same step as previously mentioned for carbon paste sensor but in the modified sensor a small amount of carbon nano particles was added and the paste was homogeneously mixed. Then the packed sensor was dried in air for 24 h.

## 2.7. Sensor calibration

The calibration graphs were carried out using 100 mL of standard drug solutions  $1.0 \times 10^{-8}$ - $1.0 \times 10^{-1}$  mol L<sup>-1</sup>. All potentiometric measurements were recorded using the proposed sensor(s) in conjunction with double junction Ag/AgCl reference electrode. The measured potential was plotted against the logarithm of drug concentration.

## 2.8. Sensor selectivity

The selectivity of the fabricated azithromycin sensors towards different inorganic cationic species, sugars, amino acids and some coformulated substances were examined using separate solution method [18]. The following equation was applied for calculation of the selectivity coefficients of the proposed sensors.

$$\text{Log } K_{\text{Azith}}^{\text{Pot}} J^{z+} = (E_2 - E_1) / S + \log [\text{Azith.}] - \log [J^{z+}]^{1/z}$$

Where,  $E_1$  is the electrode potential in  $1.0 \times 10^{-3}$  mol L<sup>-1</sup> azithromycin solution,  $E_2$  is the potential of the electrode in  $1.0 \times 10^{-3}$  mol L<sup>-1</sup> solution of the interferent ion  $J^{z+}$  and  $S$  is the slope of the calibration plot.

## 2.9. Effect of pH

The influence of pH on the potential of the fabricated sensors was studied using azithromycin test solution  $1.0 \times 10^{-3} \text{ mol L}^{-1}$ . The effect of pH was investigated by varying the potential by the addition of small volumes of  $0.1 \text{ mol L}^{-1}$  of hydrochloric acid or sodium hydroxide and the potential readings recorded was plotted as a function of pH using pH/mV meter.

## 2.10. Standard addition method

Standard addition method [19] was used to determine the investigated drug using small increments of drug test solution vs. the sensor potential. The fabricated sensor(s) was immersed into sample of 50 mL with unknown concentration and the equilibrium potential of  $E_1$  was recorded. Then 0.1 mL of  $0.1 \text{ mol L}^{-1}$  of standard drug solution was added into the testing solution and the equilibrium potential of  $E_2$  was obtained. One can determine the concentration of the testing sample from the change of potential  $\Delta E$  ( $E_2 - E_1$ ).

## 2.11. Analytical Applications

### 2.11.1. Determination of azithromycin in tablets

The proposed sensors were used to determine the investigated drug in its pharmaceutical dosage form using standard addition method. Ten tablets of zithromax<sup>®</sup> (600 mg/tablet) were accurately weighed and finally powdered. An amount of powder equivalent to 100 mg of azithromycin was transferred into a small conical flask. Methanol 3x30 mL portion was used to extract the contents. The working solutions were prepared in the range of  $1.0 \times 10^{-6}$ - $1.0 \times 10^{-2} \text{ mol L}^{-1}$  by appropriate dilution with distilled water.

### 2.11.2. Content uniformity assay of azithromycin tablets

The content uniformity assay for zithromax<sup>®</sup> (600 mg/tablet) was investigated using azithromycin-phosphotungstate sensors. This was carried out by dissolving ten tablets separately in 100 mL of methanolic water (50:50 v/v). Each sensor was immersed in the drug sample separately. The mean potential was recorded and used to evaluate the content uniformity from the calibration graph.

### 2.11.3. Application to biological fluids

The proposed sensors were used for determination of azithromycin in biological fluids such as human serum and urine. Spiking technique was used by adding a small volume of standard methanolic solution of azithromycin containing 100 mg of the drug to 5 mL of serum and urine samples. For

serum sample which previously adjusted to pH 6 using phosphate buffer, 20 mL of diethyl ether was added and the sample was centrifuged at 1500 rpm for 5 min. Working solutions for serum and urine were prepared in the range of  $1.0 \times 10^{-6}$ - $1.0 \times 10^{-2}$  mol L<sup>-1</sup>, by appropriate dilution with distilled water and then the analysis for samples carried out using general analytical procedures.

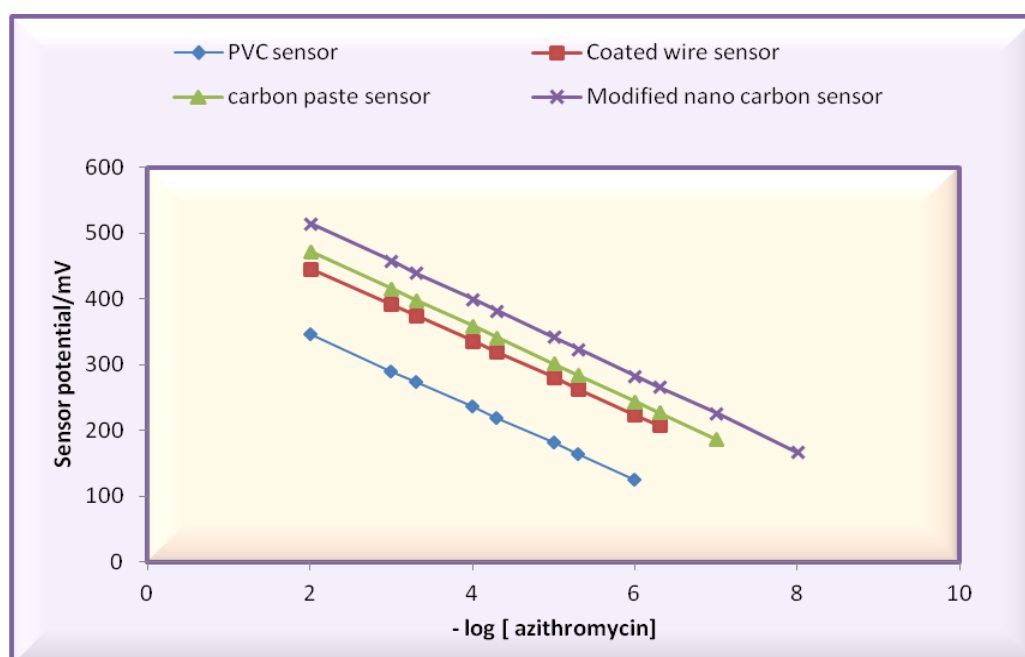
### 3. RESULTS AND DISCUSSION

#### 3.1. Optimization of membrane composition

Azithromycin reacts with phosphotungstic acid to produce azithromycin-phosphotungstate ion-pair as electroactive material which is insoluble in water but readily soluble in organic solvents such as tetrahydrofuran. Also, to improve the physical properties of the membrane, a suitable amount of plasticizer should be used. So, an increase in the amount of plasticizer improves to a large extent the adhesive properties of the membrane but, it aids in the deterioration of the membrane depending on the properties of both the ion-pair and the matrix.

In the present study, the percentages of PVC, ion-pair and plasticizer were varied until reach the optimum performance characteristics of the membrane sensors. For conventional and coated wire azithromycin sensors, the best performances were obtained using 48.0 w% PVC, 42.0 w% *o*-NPOE and 10.0 w% ion pair for PVC plastic membrane sensor and 65.0 w% PVC, 30.0 w% (*o*-NPOE) and 5.0 % ion-pair for coated wire sensor.

#### 3.2. Nature and response characteristics of the sensors



**Figure 2.** Typical calibration graphs of azithromycin-phosphotungstate sensors

The nature and response characteristics of plastic membrane, coated wire, carbon paste and modified multi-wall carbon nanotubes carbon paste sensors were determined and the results were summarized in Table 1.

**Table 1.** Critical response characteristics of azithromycin-phosphotungstate sensors

Parameter <sup>a</sup>	PVC plastic membrane sensor	Coated wire sensor	Carbon paste sensor	Modified multi-wall carbon nanotubes carbon paste sensor
Slope (mV decade <sup>-1</sup> )	55.10±0.19	55.52±0.20	57.09±0.14	58.04±0.11
Intercept	456.00	557.86	586.88	601.75
Standard deviation of slope (S <sub>b</sub> )	0.19	0.20	0.14	0.11
Standard deviation of intercept (S <sub>a</sub> )	0.81	0.93	0.67	0.59
Correlation coefficient ( r )	0.9999	0.9998	0.9999	0.9999
Linear range (mol L <sup>-1</sup> )	1.0x10 <sup>-6</sup> -1.0x10 <sup>-2</sup>	5.0x10 <sup>-7</sup> -1.0x10 <sup>-2</sup>	1.0x10 <sup>-7</sup> -1.0x10 <sup>-2</sup>	1.0x10 <sup>-8</sup> -1.0x10 <sup>-2</sup>
LOD (mol L <sup>-1</sup> )	5.0 x10 <sup>-7</sup>	2.3 x10 <sup>-7</sup>	5.0x10 <sup>-8</sup>	4.9x10 <sup>-9</sup>
Response time (s)	35	30	25	20
Working pH range	3-8	3-8	3-8	3-8
Lifetime /day	20	30	30	40
Accuracy (%)	99.59	99.80	99.23	99.61
Standard deviation	0.38	0.42	0.52	0.41
Robustness <sup>b</sup>	99.28±0.38	99.62±0.42	99.48±0.81	99.74±0.22
Ruggedness <sup>c</sup>	99.43±0.25	99.01±0.19	99.87±0.48	99.44±0.59

<sup>a</sup> Mean of six measurements

<sup>b</sup> A small variation in method parameters were carried out as pH of phosphate buffer (pH 6±1)

<sup>c</sup> Comparing the results by those obtained by different sensors assemblies using (Jenway 3510 pH meter)

The obtained results clarified that the azithromycin sensors exhibit Nernstain response over the concentration range from 1.0 x 10<sup>-6</sup>-1.0 x 10<sup>-2</sup>, 5.0 x 10<sup>-7</sup>-1.0 x 10<sup>-2</sup>, 1.0 x10<sup>-7</sup>-1.0 x10<sup>-2</sup> and 1.0 x 10<sup>-8</sup>-1.0 x 10<sup>-2</sup> mol L<sup>-1</sup> azithromycin for sensors I, II,III and IV respectively, with slopes of 55.10±0.19, 55.52±0.0.2, 57.09±0.14 and 58.04±0.11 mV decade<sup>-1</sup> change in concentration for the four mentioned sensors, respectively as in Figure 2. The response time of the sensors was tested for 1.0x10<sup>-8</sup>-1.0x10<sup>-1</sup> mol L<sup>-1</sup> azithromycin solutions. The results obtained revealed that the proposed modified nano carbon sensor exhibits better responses in terms relevant to the concentration range, sensitivity, response time and sensor stability. Also a fast dynamic response of 35, 30, 25 and 20 s for a period of 20, 30, 30 and 40 days was recorded for sensors I, II, III and IV, respectively without significant change in the sensor parameters.

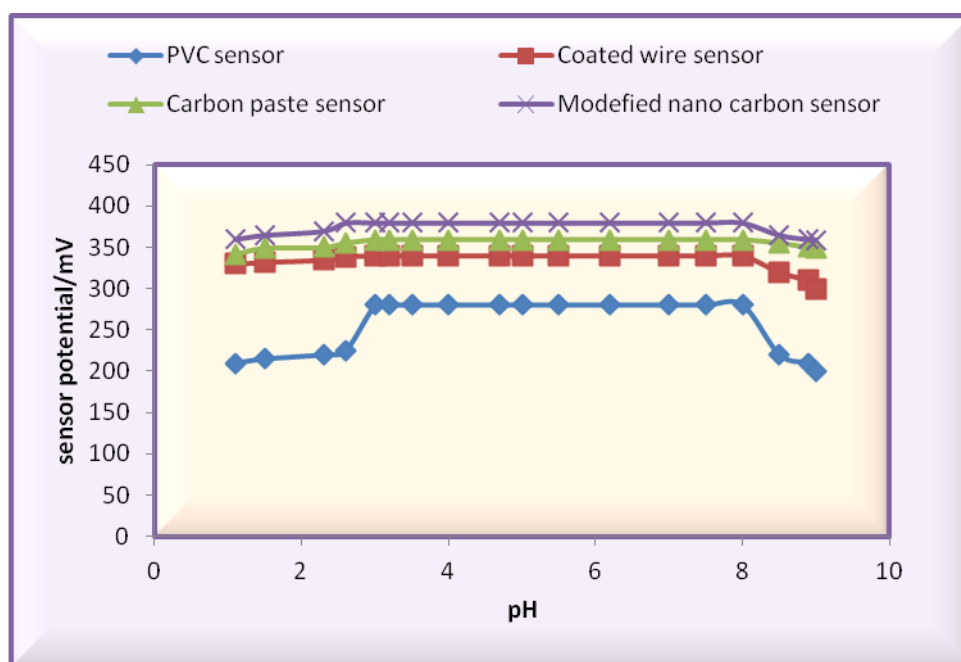
### 3.3. Effect of immersion time

The effect of immersion time on the sensor performance was investigated. The sensor(s) was soaked in 1.0x10<sup>-3</sup> mol L<sup>-1</sup> solution of azithromycin. It was clarified that the optimum immersion time was 24 and 6 h for PVC plastic membrane and coated wire sensors, respectively. Also, the influence of immersion time on the performance characteristics of carbon paste and carbon nanotubes modified sensor was investigated and from the results obtained it was found that the life span of the

conventional sensors was longer than that of carbon paste but the modification using multi-wall carbon nanotubes increase the life span of the sensor. The slopes of the calibration curves were  $55.10 \pm 0.19$ ,  $55.52 \pm 0.20$ ,  $57.09 \pm 0.14$  and  $58.04 \pm 0.11$  mV decade<sup>-1</sup>, at 25 °C for electrodes I, II, III and IV, respectively. Continuous immersing of the sensors affect negatively on the sensor performance. After 20 days the slopes were gradually decreased to 52.12, 53.86, 55.23 and 56.12 for the four mentioned sensors, respectively. Moreover, continuous immersing of sensors for 30 days caused sharp decrease in the sensor performance and the slopes were dropped to 50.41, 51.69, 52.12 and 54.37 for sensors I, II, III and IV, respectively. This revealed that immersing of the sensor for long time causes negative effect on the sensor response due to the leaching of electroactive material in the drug test solution.

### 3.4. Effect of pH

In order to investigate the influence of pH on the potential of the proposed sensors, azithromycin  $1.0 \times 10^{-4}$  mol L<sup>-1</sup> solution was tested. The potential reading of the azithromycin-phosphotungstate sensors was recorded after acidification of the drug test solution using 0.1 mol L<sup>-1</sup> hydrochloric acid then the pH value was increased gradually using 0.1 mol L<sup>-1</sup> sodium hydroxide. Figure 3 showed that within pH range 3-8 the proposed sensors were independent of pH. This can be attributed to below pH 3, the potential of the sensor increased with the increase of analyte acidity which may be ascribed to extraction of H<sup>+</sup> ions by membrane. While at pH more than 8, the response of the electrode decreased this may be due to increase of OH<sup>-</sup> concentration [20].



**Figure 3.** Effect of pH on azithromycin-phosphotungstate sensors



### 3.5. Selectivity of the sensors

Selectivity coefficients for azithromycin-phosphotungstate sensors toward some inorganic cations, amino acids, sugar and other coformulated drug were determined using separate solution method [18]. Table 2 reflects that high selectivity was evaluated for the proposed sensors. The mechanism of selectivity is mainly based on the stereospecificity and electrostatic environment, and is dependent on how much matching is present between the locations of the lipophilic sites in the two competing species in the bathing solution side and those present in the receptor of the ion-pair. Good tolerance was obtained towards inorganic cations, sugars and amino acids.

**Table 2.** Selectivity coefficient and tolerance values for azithromycin sensors

Interferent	PVC Plastic membrane sensor	Coated wire sensor	Carbon paste sensor	Modified multi-wall carbon nanotubes carbon paste sensor
Na <sup>+</sup>	1.0x10 <sup>-3</sup>	1.4x10 <sup>-4</sup>	2.5x10 <sup>-3</sup>	4.6x10 <sup>-3</sup>
K <sup>+</sup>	8.8x10 <sup>-3</sup>	1.2x10 <sup>-4</sup>	6.5x10 <sup>-3</sup>	5.0x10 <sup>-3</sup>
NH <sub>4</sub> <sup>+</sup>	3.5x10 <sup>-3</sup>	4.9x10 <sup>-4</sup>	9.2x10 <sup>-3</sup>	4.9x10 <sup>-3</sup>
Mg <sup>2+</sup>	8.2x10 <sup>-4</sup>	5.9x10 <sup>-4</sup>	1.2x10 <sup>-4</sup>	8.8x10 <sup>-4</sup>
Ca <sup>2+</sup>	4.4x10 <sup>-4</sup>	1.5x10 <sup>-3</sup>	6.3x10 <sup>-5</sup>	5.1x10 <sup>-3</sup>
Zn <sup>2+</sup>	6.1x10 <sup>-4</sup>	1.7x10 <sup>-3</sup>	2.2x10 <sup>-3</sup>	6.6x10 <sup>-4</sup>
Cd <sup>2+</sup>	1.4x10 <sup>-3</sup>	1.5x10 <sup>-3</sup>	6.9x10 <sup>-3</sup>	9.6x10 <sup>-3</sup>
Thymine	2.1x10 <sup>-4</sup>	1.9x10 <sup>-3</sup>	2.8x10 <sup>-3</sup>	2.3x10 <sup>-4</sup>
Glycine	4.0x10 <sup>-4</sup>	2.7x10 <sup>-3</sup>	4.6x10 <sup>-4</sup>	7.1x10 <sup>-4</sup>
Glutamine	7.2x10 <sup>-4</sup>	1.2x10 <sup>-3</sup>	7.8x10 <sup>-4</sup>	7.2x10 <sup>-4</sup>
Uracil	1.1x10 <sup>-3</sup>	3.8x10 <sup>-3</sup>	2.6x10 <sup>-3</sup>	1.2x10 <sup>-5</sup>
Starch	2.7x10 <sup>-4</sup>	3.2x10 <sup>-4</sup>	7.1x10 <sup>-5</sup>	2.0x10 <sup>-4</sup>
Glucose	5.6x10 <sup>-4</sup>	2.9x10 <sup>-4</sup>	6.6x10 <sup>-4</sup>	4.8x10 <sup>-5</sup>
Talc	8.2x10 <sup>-4</sup>	9.2x10 <sup>-5</sup>	8.9x10 <sup>-4</sup>	8.7x10 <sup>-4</sup>
Mg stearate	1.5x10 <sup>-4</sup>	3.7x10 <sup>-4</sup>	2.0x10 <sup>-5</sup>	1.1x10 <sup>-4</sup>
Sodium lauryl sulfate	6.4x10 <sup>-4</sup>	8.6x10 <sup>-4</sup>	3.9x10 <sup>-4</sup>	3.6x10 <sup>-5</sup>

The interference of magnesium stearate and sodium lauryl sulfate as coformulated drug with azithromycin was investigated and the sensors showed insignificant interferent effect during the determination of azithromycin.

### 3.6. Quantification of azithromycin

The fabricated azithromycin-phosphotungstate sensors were used for direct determination of azithromycin in pure form. The proposed sensors gave mean % recoveries of 99.44±0.49, 99.49±0.72, 99.59±0.14 and 99.93±0.31 for sensors I, II, III and IV, respectively. Furthermore, the results obtained were encouraging so the proposed method was applied for the determination of azithromycin in its pharmaceutical preparations. The results were compared with the reported spectrophotometric method [12] and the results are listed in Table 3.



In order to validate the proposed method, the fabricated azithromycin sensors were used to determine azithromycin in spiked biological fluids. The results were summarized in Table 4. The potential of the azithromycin sensors showed no significant difference of response time between aqueous solution of pure drug and its spiked serum and urine.

### 3.9. Method validation

The method was validated for linearity, accuracy, precision, repeatability, robustness and ruggedness according to ICH guidelines [22].

#### 3.9.1. Linearity

The linearity of the proposed method was evaluated by analyzing seven concentrations of azithromycin ranging from  $1.0 \times 10^{-8}$ - $1.0 \times 10^{-2}$  mol L<sup>-1</sup>. The assay was performed according to the experimental conditions using azithromycin-phosphotungstate sensors. The fabricated sensors exhibit Nernstian response over a concentration range of  $1.0 \times 10^{-6}$ - $1.0 \times 10^{-2}$ ,  $5.0 \times 10^{-7}$ - $1.0 \times 10^{-2}$ ,  $1.0 \times 10^{-7}$ - $1.0 \times 10^{-2}$  and  $1.0 \times 10^{-8}$ - $1.0 \times 10^{-2}$  mol L<sup>-1</sup> azithromycin for sensors I, II, III and IV, respectively. It is obvious that the use of modified multi-wall nano carbontubes carbon paste improves the sensitivity for detection of very small concentrations of azithromycin.

#### 3.9.2. Robustness and ruggedness

The robustness of a method is its ability to remain unaffected by small variation in method parameters. To determine the robustness of the proposed method, a small change in pH using phosphate buffer was carried out. The fabricated sensors were used for determination of the investigated drug at pH 6±1 and the percentage recoveries were 99.28±0.38, 99.62±0.42, 99.48±0.81 and 99.74±0.22 for sensors I, II, III and IV, respectively. These results were closely in agreement with those obtained from standard drug solutions. Also, the reproducibility upon using another model of pH-meter (Jenway 3510) was indicated by the results obtained (Table 1).

#### 3.10.3. Accuracy and precision

The accuracy of the proposed method was tested by the determination of azithromycin in its placebo sample of sodium lauryl sulfate using standard addition method. The results obtained were calculated in terms of mean percentage recoveries values. The calculated % recoveries were (99.59±0.38, 99.80±0.42, 99.23±0.52 and 99.61±0.41) for the previously mentioned sensors, respectively.

The precision of the method was calculated in terms of (intra-day and inter-day). The % RSD values of intra-day and inter-day studies for the repeated determinations were 0.86%, 0.12%, 0.34 and

0.16% for determination of azithromycin in Zithromax<sup>®</sup> (600 mg /tablet) using electrodes I, II, III and IV, respectively. The above % RSD values are less than 2% indicating good precision.

#### 4. CONCLUSION

New four fabricated sensors of different kinds were developed for the determination of azithromycin in pure form, pharmaceutical dosage form and in biological fluids. In this study the comparative analysis for the selected drug was carried out using the fabricated sensors and the obtained results show that the proposed sensors were simple, selective, and accurate for the determination of the investigated drug. The use of carbon nanotubes for modification of the carbon paste sensor improves the sensitivity of the sensor to be more useful and convenient for quality control analysis and content uniformity assay of the drug.

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