Biogenic green synthesis of metal oxide nanoparticles using oat biomass for ultrasensitive modified polymeric sensors

Salma A. Al-Tamimi
Department of Chemistry, College of Science, King Saud University, Riyadh, Saudi Arabia

ABSTRACT
This study describes Green synthesis of two metal oxide nanoparticles MnO₂NPs and CuONPs using the oat biomass. The electrocatalytic activity of the synthesized metal oxide nanoparticles was investigated by fabricating two modified sensors enriched with MnO₂NPs and CuONPs as a coated layer on the surface of the sensors and utilized to quantify antibacterial drugs cephalexin (CPX) and cefazolin (CFZ) in their commercial products and biosamples. The tested drugs were incorporated with the precipitating agents phosphomolybdic acid and phosphotungstic acid to form CPX-PM and CFZ-PT as electroactive materials, respectively. Conductivity enhancement of the fabricated modified sensors CPX-PM-MnO₂NPs and CFZ-PT-CuONPs was determined and the outcomes compared to the results obtained from the conventional types of the same sensors. Linear relationships were recorded between the sensory potentials of the enriched metal oxide nanoparticles in the ranges of 1.0 × 10⁻⁸-1.0 × 10⁻² and 1.0 × 10⁻¹⁰-1.0 × 10⁻² mol L⁻¹ with lower limits of detection 5.6 × 10⁻⁹ and 5.7 × 10⁻¹¹ mol L⁻¹ for CPX-PM-MnO₂NPs and CFZ-PT-CuONPs with respect to 1.0 × 10⁻⁶-1.0 × 10⁻² mol L⁻¹ of their conventional coated wire types. The fabricated sensors provide excellent sensitivity and selectivity towards the determination of CPX and CFZ in its commercial and biosamples.

1. Introduction
Nanotechnology is a term concerned with the utility of the techniques or nanomaterials in various applications. It is an innovative facilitating technology with the potential to engineer novel materials has the ability to introduce new nano-specific features of products, instruments, and systems in wide-ranging professional and consumer applications (1).

Currently, nanomaterials have gained much attention in electrochemical and sensing applications, due to their unique physical and chemical properties such as high mechanical strength, large surface area, excellent electrocatalytic potential, and conductivity. The nanoscale materials reveal significant and amazing characteristics which are considered as a possible key to solving many global and environmental problems (2).
Scientists are still trying to improve their research area, where, the extraordinary features of nanomaterials can be potentially modified our life cycle. The unique characteristics of these nanomaterials and the multifunctional properties of metal oxides play an important role in the fabrication of various modified chemo and biosensors (3–4).

The unique physical and chemical characteristics of metal oxide nanoparticles, including a large specific surface area, ability of strong adsorption, high catalytic efficiency, and biocompatibility, they have been reported for many applications such as biomedical applications (5), catalysis (6), drug delivery systems (7), and sensing technology (8). The last decades have also seen phenomenal advancement in the synthesis of metal oxides nanoparticles using various chemical and biogenic methods (9–10). Accordingly, eco-friendly, benign methods are necessary to be ascribed for synthesis of nanomaterials. Indeed, the formation of energy-efficient, low-cost, and nontoxic metal oxides nanoparticles using plant extracts, and microorganisms have been reported (11–12).

The Oat (Avena sativa L.) is a species of cereal grains usually grown worldwide to provide a potential food staple for people in many countries. It is commonly eaten or administered as a medicinal supplement for its high health benefits (13). The use of oat biomass or extract can be useful for biogenic preparation of nanoparticles (14–15).

In recent years, the researchers started employing metal oxide nanoparticles based sensors in the estimation and quantification of medical drugs. The unique advanced physicochemical features of metal oxide nanoparticles such as manganese dioxide nanoparticles (MnO2NPs) and copper oxide (CuONPs), encourage their use in various applications such as semiconductors, drug delivery systems, and biomedical properties (16–20). The literature review revealed various reported articles that discussed the role of MnO2NPs and CuONPs in electrochemical sensors (21–22).

Cephalexin (CPX) is a semi-synthetic antibiotic that belongs to the cephalosporin group, which is a medication used in the treatment of various bacterial infections (Figure 1). Its action is conducted by stopping the bacterial cell growth. Various analytical methods were reported in the literature for the quantification of Cephalexin monohydrate in its commercial products such as reversed-phase high-performance liquid chromatography (23), UV–spectrophotometry (24), spectrofluorimetry (25). Also, electrochemical methods were addressed including, voltammetry (26) and potentiometry (27–28).

Cefazolin sodium (CFZ) is a first-generation cephalosporin (Figure 1), which is active mainly against Gram-positive and Gram-negative organisms. It is mainly recommended to treat various bacterial infections, including skin, bone, lung, joint, stomach, and urinary tract (29). Furthermore, it is also used before surgical operations (30). Methods of analysis have been reported for CFZ quantification in commercial formulations including, spectroscopic analysis using spectrophotometry and spectrofluorimetry (31–32), chemiluminescence (33), densitometry (34) and high-performance liquid chromatography (35). Few reports were concerned with the electrochemical determination of CFZ using voltammetry and potentiometry (26–36).

Despite these analytical techniques provide sensitive detection, they still have certain drawbacks such as expensive instrumentations, consuming a long time of analysis and may require a tedious precondition procedure.

Nowadays, numerous polymeric potentiometric sensors have been developed for the determination of drug species, mainly for quality control of commercial preparations. Because of their sensitivity, selectivity and simplicity, potentiometric sensors are among the most commonly applied electrochemical techniques for various rapid measurements of drugs (37). Although few reports were addressed for the determination of CPX and CFZ, those developed sensors showed poor
reproducibility, narrow concentration ranges and high detection limits. Therefore, the objective of this study is to synthesize MnO₂ and CuO nanoparticles using oat biomass as a green reducing agent. Various spectroscopic and microscopic techniques were used to confirm the synthesis of MnO₂ and CuO nanoparticles. The synthesized metal oxides were used to fabricate simple and ultrasensitive new CPX-PM-MnO₂NPs and CFZ-PT-CuONPs coated wire membrane sensors for the determination of CPX monohydrate and CFZ sodium in their commercial products and biosamples. In addition, a comparative study was performed between the modified sensors and their conventional types with respect to the potential response, selectivity, the quantification range and the detection limit. The suggested potentiometric method was also validated according to the International council for harmonization of technical requirements for pharmaceuticals for human use (ICH) guidelines (38).

2. Experimental

2.1. Chemicals

Pure grade of cephalixin and cefazolin was gifted by Memphis Co. for Pharmaceutical and Chemical Industries (Cairo, Egypt). Commercial cephalixin (Keflex® 500 mg/tablets) and (Zinol 500 mg/vial) were purchased from local drug markets. The used chemicals and reagents such as tetrahydrofuran (THF), acetic acid, ortho-nitrophenylctyl ether (ω-NPOE), high molecular weight polyvinyl chloride (PVC), acetone 99.9%, methanol 99.9%, ethanol 99.9%, acetonitrile, hydrochloric acid 37%, phosphomolybdic acid (PMA) and phosphotungstic acid (PTA) were supplied by (Sigma Aldrich, Hamburg, Germany). Manganese acetate 99.9%, copper sulfate 99.0%, potassium monobasic phosphate, zinc sulfate (ZnSO₄·7H₂O), potassium dibasic phosphate, sodium acetate and sodium hydroxide 99.9% were purchased from (WinLab, East Midlands, UK). Multi-Serum Normal, Randox Laboratories (Crumlin, Antrim, UK) is the suppliers of commercial serum samples.

2.2. Characterization and instruments

UV 2450 Spectrophotometer (Shimadzu Corporation, Kyoto, Japan) was employed to investigate the crystalline nature of the synthesized MnO₂NPs and CuONPs. Furthermore, Transmission electron microscope (TEM) (JEM-2100F, JEOL Ltd, USA) and Scanning electron microscope (SEM) (JSM-7610F; JEOL, USA) was used to characterize the surface morphology and particle size using an accelerating voltage of 100 kV. Additionally, all potentiometric measurements were performed using a digital pH-mV (HANNA, model 211) with a fabricated indicator sensor in conjunction with Ag/AgCl as a reference electrode. The pH adjustment was carried out using pH-meter (Metrohm model 744, Romania).

2.3. Plant gathering and oat biomass preparation

The seeds of oat (Avena Sativa L) were collected and identified by prof. Hesham Oraby, Crop Department of Agriculture, Zagazig University, Egypt. The collected seeds were washed with deionized water and dried at 80°C for 15 days. The dried oat seeds (0.5 kg) were ground and sieved through a sieve with a nominal mesh aperture of 180 μm to obtain a homogenous powder.

2.4. Green synthesis of MnO₂ nanoparticles

Green synthesis of MnO₂NPs was conducted by mixing 10 g of oat powder with 250 mL of distilled water and boiled for 10 min and centrifuged at 3500 rpm for 10 min. Then 25 mL of aqueous solution manganese acetate (1.0 × 10⁻⁵ mol L⁻¹) at alkaline pH 8 was mixed with 100 mL of the oat biomass under continuous stirring for 1 h at ambient temperature. After centrifugation, the obtained precipitate was washed with deionized water followed by ethanol three times and dried at 100°C (Scheme 1(a)).

2.5. Green synthesis of CuO nanoparticles

The green synthesis of CuONPs was carried out by adding a quantity of 1.0 × 10⁻² mol L⁻¹ copper sulfate solution (10 mL) to 30 mL of aqueous oat biomass and mixed well under magnetic stirring. Then, the solution was heated at 80 °C in a water bath for 60 min. The change of color solution from brownish-yellow to dark brown revealed the formation of CuONPs (Scheme 1(b)).

2.6. Preparation of standard drug solution

Standard aqueous CPX and CFZ solutions of 1.0 × 10⁻² mol L⁻¹ were prepared by dissolving 0.347 g and 0.476 of CPX and CFZ in 100 mL distilled water. Testing
solutions for experimental studies with various concentrations were prepared using the same solvent for serial dilutions.

2.7. Preparation of electroactive materials

The electroactive materials of CPX-PM and CFZ-PT were prepared by adding 50 mL of $1.0 \times 10^{-2}$ mol L$^{-1}$ of each CPX and CFZ solution to the same volume of $1.0 \times 10^{-2}$ mol L$^{-1}$ of PMA and PTA, respectively. A light yellow precipitate of CPX-PM and a white precipitate of CFZ-PT were formed. The obtained solutions were filtered and washed thoroughly three times using distilled water and left aside to dry in room temperature for 12 h.

2.8. Sensor fabrication and membrane composition

Four different coated wire sensors CPX-PM, CPX-PM-MnO$_2$NPs, CFZ-PT and CFZ-PT-CuONPs were fabricated by mixing 10 mg of ion-pair CPX-PM or CFZ-PT with 190 mg of high molecular weight polyvinyl chloride (PVC) and 0.35 mL of plasticizer o-NPOE in the presence of 5 mL of THF. The mixed solution of each electroactive material was allowed to evaporate slowly in a Petri dish (3 cm in diameter) at room temperature until an oily membrane solution was formed. An aluminum wire was cleaned and washed with acetone, then immersed many times in the membrane solution to fabricate the conventional CPX-PM and CFZ-PT sensors. The modified sensors were fabricated by coating the surface of the sensor with a modified coated membrane cocktail containing MnO$_2$NPs or CuONPs (5 mg). A polymeric CPX-PM-MnO$_2$NPs or CFZ-PT-CuONPs was used to form a thin layer on the surface of the sensor then after drying the sensor immersed several times in the coated membrane mixture to form thick coated wire membrane as shown in Scheme 2.

2.9. Calibration graphs

The calibration graphs of the fabricated conventional and modified sensors were constructed by plotting the potential readings of each sensor vs. -logarithm of drug concentrations. Approximately, 20 mL of $1.0 \times 10^{-10}$–$1.0 \times 10^{-2}$ mol L$^{-1}$ CPX or CFZ standard solution was analyzed using the fabricated sensors separately in conjunction with Ag/AgCl as a reference electrode. Between each measurement, the surface of the sensors should be washed carefully with distilled water and dried with tissue paper.

2.10. Optimization of potential readings conditions

The potential readings of the fabricated sensors can be greatly affected by the pH of the testing solution. To investigate the pH effect, $1.0 \times 10^{-4}$ mol L$^{-1}$ of CPX or CFZ test solution was acidified by adding a few drops of 0.1 mol L$^{-1}$ hydrochloric acid. After increasing the pH using 0.1 mol L$^{-1}$ sodium hydroxide, the potential readings were determined using the fabricated

---

**Scheme 1.** Illustration of (a) preparation of MnO$_2$NPs and (b) preparation of CuONPs using oat biomass.

**Scheme 2.** The preparation steps of modified coated wire sensors using polymeric coated membrane cocktail containing CPX-PM-MnO$_2$NPs or CFZ-PT-CuONPs as modified ion-pairs.
conventional and modified sensors separately in conjunction with Ag/AgCl as a reference electrode and a combined glass electrode for detecting pH values. The pH values were plotted as a function of potential readings of each sensor and the pH graphs were obtained.

A separate solution method (39) was applied to evaluate the selectivity of the fabricated sensors towards the determination of CPX and CFZ solutions. The same molar concentration (1.0 x 10^-3 mol L^-1) of CPX or CFZ solution and interfering species was analyzed and the selectivity of the fabricated sensors was expressed as tolerable values which were calculated using the previously reported equation (40).

Furthermore, the dynamic response time and lifetime of the fabricated sensors should be determined by measuring the potential response time of the investigated drugs using the concentration range 1.0 x 10^-10–1.0 x 10^-2 mol L^-1.

2.11. Analysis of CPX and CFX in pharmaceuticals

Ten tablets of Keflex® (500 mg/tablets) were ground to a fine powder and an amount 0.347 g equivalent to obtain 1.0 x 10^-2 mol L^-1 CPX standard solution was dissolved in 100 mL distilled water. Testing solutions in the range of 1.0 x 10^-9–1.0 x 10^-2 mol L^-1 were prepared using serial dilutions with distilled water. The potential readings of modified CPX-PM-MnO2NPs were recorded to determine CPX in its tablets. To determine of CFZ in its injections Zinol® (500 mg/vial), the powder of five vials mixed well and accurate amount 0.476 g equivalent to obtain 1.0 x 10^-2 mol L^-1 CFZ standard solution was dissolved in 100 mL distilled water and serial dilutions to obtain concentration range 1.0 x 10^-10–1.0 x 10^-2 mol L^-1 was performed and the fabricated CFZ-PT-CuONPs was applied to determine CFZ in its pharmaceutical injections.

2.12. Analysis of CPX and CFZ in biosamples

The fabricated modified CPX-MnO2NPs and CFZ-PT-CuONPs sensors were used to detect CPX and CFZ in serum samples using a spiking technique. The pH of the samples was adjusted using acetate buffer pH 3 (CPX) or pH 2 (CFZ). To the previously adjusted serum samples, an accurate amount of the tested CPX or CFZ was added. Approximately, 1.0 mL of each previously spiked sample was mixed with 1.0 mL acetonitrile, 0.1 mL of 0.1 mol L^-1 sodium hydroxide and 1.0 mL ZnSO4 ·7H2O (5.0%, w/v) for deproteination. The sample was centrifuged at 2500 rpm for 15 min and filtered.

3. Results and discussion

3.1. Characterization of MnO2 and CuO nanoparticles

Different spectroscopic methods were used to characterize the green synthesized MnO2 and CuO nanoparticles. UV–Vis spectroscopy is an utmost reliable and useful method suitable for characterizing and confirming the shape, size and stability of the biogenic green synthesized metal oxide nanostructures in their aqueous suspensions (41). UV–Vis spectra of MnO2NPs and CuONPs demonstrated two broad absorption peaks at 387 and 270 nm, respectively (Figure 2). This can be due to photo excitation of electrons from the valence band to the conduction band. Eg = hv = hc/λ formula was used to calculate the band gap of nanoparticles, where h is Planck’s constant, c is the velocity of light and λ is the wavelength. The band gaps of MnO2NPs and CuONPs were found to be 3.45 and 3.36 eV, respectively. The bandgap values confirmed that these nanoparticles are semiconductors. The results obtained were in agreement with those previously reported in (42–43).

The FTIR analysis of MnO2NPs and CuONPs was carried out in the range 400–4000 cm^-1. The absorption bands for MnO2NPs were 3430, 2928, 2862, 1597, 1071, and 527 cm^-1. The noticed band at 3430 cm^-1 is related to the O–H bond stretching vibration. The

Figure 2. UV–vis spectra of MnO2 NPs and CuONPs using wavelength scan range 200–400 nm.
recorded bands at 2928 and 2862 cm$^{-1}$ revealed the presence of medium C–H stretching vibration bands. The observed absorption bands around 1597 cm$^{-1}$ indicated the presence of an O–H vibrating mode of adsorbed water. A strong peak at 1071 cm$^{-1}$ was recorded which is attributed to C–O of secondary alcohol in cellulose and other carbohydrates present in oat biomass. The observed band at 534 cm$^{-1}$ confirmed the formation of O–Mn–O stretching vibration (Figure 3(a)).

FTIR spectrum of CuONPs showed two significant bands at 3432 and 2928 cm$^{-1}$ which corresponding to O–H and C–H stretching vibrations, respectively. The recorded absorption band at 2369 cm$^{-1}$ indicated the presence of carbon dioxide (CO$_2$–stretching) vibration. The O–H stretching mode of water is confirmed by the appearance of absorption band at 1622 cm$^{-1}$. Characteristic bands of CuO are ranging from 1000 to 400 cm$^{-1}$. The observed bands around 842 and 624 cm$^{-1}$ can be attributed to the formation of Cu–O (Figure 3(b)).

To estimate and detect the crystalline forms of the green synthesized metal oxide nanoparticles, XRD diffractometer with Cu-ka at ($\lambda = 1.5406$ Å) with accelerating voltage 220/50 Hz was used to determine the crystal structure of MnO$_2$NPs and CuONPs. The XRD analysis of MnO$_2$NPs showed diffraction peaks at $2\theta = 38.2\degree$, 40.0\degree, 44.3\degree, 48.7\degree, 56.4\degree, 63.2\degree, 66.3\degree, and 72.2\degree corresponding to MnO$_2$ (110), (101), (200), (111), (211), (220), (002) and 310, respectively. However, CuONPs displayed different peaks at $2\theta = 29.2\degree$, 31.5\degree, 33.2\degree, 35.7\degree, 42.3\degree, 45.2\degree, 51.3\degree, 62.1\degree, 73.5\degree, 83.2\degree, and 84.2\degree for CuO (110), (002), (111), (202), (020), (202), (113), (311), (220), (311), and (004) plane orientation. The results are in agreement with JCPDS (044-0141) and (JCPDS 80-1268) values of MnO$_2$ and CuO, respectively, and indicated that the formed particles are crystalline and in nanoscale dimensions. All diffraction peaks can be indexed as typical monoclinic in structure and no other phases were observed (Figures 4a and 4b). The particle size of MnO$_2$ and CuO nanoparticles have been estimated.

![Figure 3. FT-IR spectra of (a) MnO$_2$NPs and (b) CuONPs at wavenumber from 4000 to 400 cm$^{-1}$](image)

![Figure 4. XRD patterns of (a) MnO$_2$NPs and (b) CuONPs.](image)
from XRD pattern by using the following Debye–Scherer equation: 
$$D = \frac{0.9\lambda}{\beta \cos \theta}$$
where $\lambda$ of the XRD detection was 0.15406 nm, $\beta$ represents the full width at half maximum, $\theta$ is the diffraction angle, and $D$ is the diameter of the particle. The particle diameter for MnO$_2$ and CuO nanoparticles were found to be 52.3 and 66.8 nm, respectively.

Further investigations were carried out using TEM and SEM microscopes, to study the surface morphology, shape and size of the synthesized nanoparticles. The picked images of MnO$_2$NPs and CuONPs using TEM confirmed that the prepared nanoparticles are uniformly distributed with rode and spherical particles in shape for MnO$_2$NPs and CuONPs, respectively (Figures 5a and 5c). The prepared nanoparticles were found to be in the range of 50–100 nm. The obtained results were in agreement with those estimated from XED analysis. The surface morphology of the as-prepared MnO$_2$NPs and CuONPs, was investigated under SEM and the resulting images confirmed that the synthesized particles are highly aggregated crystals (Figures 5b and 5d).

### 3.2. The nature of the fabricated sensors

CPX and CFZ interact with PMA or PTA to form stable CPX-PM or CFZ-PT complexes, which are soluble in THF. Conventional and modified coated wire sensors were fabricated by mixing the active materials CPX-PM or CFZ-PT with (O-NPOE) as a solvent mediator in the presence of PVC. In this study, ortho-nitrophenyloctyl ether (O-NPOE) acts as a fluidizer facilitating homogenous dissolution of the ion-pairs and allowing their diffusion mobility inside the membranes. The membrane selectivity towards the tested analytes is greatly affected by using O-NPOE of high dielectric constant ($\epsilon = 24$) that enhances the dissolution of ion pairs within the active membranes and consequently increases their partition coefficient in the prepared membranes and improves the mechanical feature of the membranes (44).

The potential response and the critical characteristic performance of the fabricated CPX-PM, CFZ-PT, CPX-PM-MnO$_2$NPs and CFZ-PT-CuONPs were summarized in Table 1. The results demonstrated that the above-mentioned sensors displayed Nernstian responses with slopes 52.12 ± 0.8, 51.60 ± 0.5, 57, 39 ± 0.3 and 58.65 ± 0.2 mV over the drug concentration ranges of 10 × 10$^{-6}$–1.0 × 10$^{-2}$ ($r = 0.9997$) for both conventional types and 1.0 × 10$^{-8}$–1.0 × 10$^{-2}$ and 10 × 10$^{-10}$–1.0 × 10$^{-2}$ mol L$^{-1}$ ($r = 0.9999$) for modified CPX-PM-MnO$_2$NPs and CFZ-PT-CuONPs sensors, respectively (Figures 6a–d). The obtained data showed that both modified CPX-PM-MnO$_2$NPs and CFZ-PT-CuONPs sensors exhibited a higher potentiometric response to a wide linear concentration range over the conventional...
one. The high sensitivity of these sensors towards the quantification of CPX and CFZ can be due to the large surface area of the coated metal oxide nanoparticles layer that enhances the conductivity of the sensor surface. Moreover, it was observed that the modified CuONPs sensor provided higher results than MnO2NPs and this can be attributed to the high dielectric permittivity value of CuO ($\approx 104$) over MnO2 ($\approx 101.5$) at room temperature ($45–46$).

The dynamic response time is defined as the time taken between the instant at which the potential of the cell becomes equal to its steady-state value within 1 mV. It should be measured under experimental conditions, including the use of constant magnetic stirring and precondition of the sensor in test sample prior to measuring the potential readings ($47$). The dynamic response of the fabricated sensors was determined and it was observed that fast dynamic responses 80, 75, 45, and 30 s for 25, 20, 60, and 80 days were recorded for CPX-PM, CFZ-PT, CPX-PM-MnO2NPs, and CFZ-PT-CuONPs, respectively. The fast and high stability of the modified metal oxide nanoparticles sensors can be due to the physicochemical properties of these nanomaterials. These nanoparticles have a high surface area to volume ratio that improves the interaction with targets in the test solution. Furthermore, the exceptional electrical characteristics, such as high charge transfer and extraordinary electrical capacities generated at the

Table 1. Performance characteristics of fabricated conventional CPX-PM and CFZ-PT, modified CPX-PM-MnO2NPs and CFZ-PT-CuONPs coated wire sensors.

| Parameter                        | Conventional coated wire CPX-PM sensor | Conventional coated wire CFZ-PT sensor | Modified CPX-PM-MnO2NPs sensor | Modified CFZ-PT-CuONPs sensor |
|----------------------------------|----------------------------------------|----------------------------------------|---------------------------------|--------------------------------|
| Slope (mV. Decade$^{-1}$)        | 52.12 ± 0.8                            | 51.60 ± 0.5                            | 57.39 ± 0.3                     | 58.65 ± 0.2                     |
| Intercept                        | 406.72                                 | 410.05                                 | 578.11                          | 688.34                          |
| Regression equation               | $E_{mv} = (52.12 ± 0.8) \log [\text{CPX}] + 406.72$ | $E_{mv} = (51.60 ± 0.5) \log [\text{CFZ}] + 410.05$ | $E_{mv} = (57.393 ± 0.2) \log [\text{CPX}] + 578.11$ | $E_{mv} = (58.65 ± 0.2) \log [\text{CFZ}] + 688.34$ |
| Correlation coefficient, $r$     | 0.9997                                 | 0.9987                                 | 0.9999                          | 0.9999                          |
| Linear range (mol L$^{-1}$)      | $10 \times 10^{-6}$–$1.0 \times 10^{-2}$ | $10 \times 10^{-6}$–$5.0 \times 10^{-3}$ | $1.0 \times 10^{-8}$–$1.0 \times 10^{-2}$ | $1.0 \times 10^{-10}$–$1.0 \times 10^{-2}$ |
| LOD                              | $5.0 \times 10^{-7}$                   | $4.9 \times 10^{-7}$                   | $5.6 \times 10^{-9}$            | $5.7 \times 10^{-11}$           |
| Response time, s                 | 80                                     | 75                                     | 45                              | 30                              |
| Working pH range                  | 3–6                                    | 2–5                                    | 3–6                             | 2–5                             |
| Lifetime, day                     | 25                                     | 25                                     | 25                              | 25                              |
| Temperature, °C                   | 25                                     | 25                                     | 25                              | 25                              |
| Accuracy (%)                      | 98.9 ± 0.8                             | 99.2 ± 0.6                             | 99.6 ± 0.4                      | 99.8 ± 0.2                      |

Figure 6. Calibration graphs of the fabricated (a and b) Conventional CPX-PM and CFZ-PT, and (c and d) modified CPX-PM-MnO2NPs and CFZ-CuONPs.
interfaces of some nanosized materials, are very impactful when they are applied as the transducing components in potentiometric sensors (48).

The potential response of membrane sensors can be greatly affected by the interference of hydrogen ions. Therefore, it is very important to study and detect the suitable pH range for the determination of CPX and CFZ using the suggested modified sensors. The effect of pH on the potential readings of the suggested sensors was investigated using 1.0 × 10⁻⁴ mol L⁻¹ of CPX or CFZ solution to determine the safe pH range which is suitable for the determination of CPX and CFZ in their tested solutions. The results showed that both conventional (CPX-PM and CFZ-PT) and modified (CPX-PM-MnO₂NPs and CFZ-PT-CuONPs) sensors were practically independent in an acidic pH range 3–6 and 2–5, respectively and CPX or CFZ can be easily determined using the fabricated sensors within these pH ranges (Figure 7(a,b)). It was noticed that in acidic medium below pH 3 (CPX-sensors), or pH 2 (CFZ-sensors) the potential readings were slightly increased due to the presence of H⁺ ions and the formation of protonated ion-pairs that are poorly responsive to CPX or CFZ ions and strong response to hydronium ions in the test solutions. However, at pH values higher than 6 for CPX-sensors or 5 for CFZ-sensors the potential readings decreased gradually. The increase of OH⁻ ions causes a competition between CPX or CFZ ions and OH⁻ ions and consequently decreases the interaction between the ions of the testing drug and the ion-pair sites on the sensor membrane. Thus, the potential responses of the constructed sensors were decreased (49).

The selectivity of the proposed CPX-PM, CFZ-PT, CPX-PM-MnO₂NPs, and CFZ-PT-CuONPs sensors towards the determination of CPX or CFZ using 1.0 × 10⁻³ mol L⁻¹ was studied. The separate solution method (39) was used and various inorganic cations (Na⁺, K⁺, Ag⁺, Ni²⁺, Ca²⁺, Mg²⁺, and Zn²⁺), amino acids (glycine, valine, leucine, lysine, L. histidine and tryptophan) and some sugars (glucose, lactose, and starch) were tested. Very high selectivity was obtained by the modifying metal oxide sensors. The presence of coated film of metal oxide nanoparticles with large surface area and physicochemical properties of the nanoscale particles increases the conductivity of the fabricated sensors and hence increases the selectivity towards the tested drugs. Additionally, the high selectivity of CPX and CFZ coated membranes are due to the free energy transfer of CPX⁺ or CFZ⁺ ions initiated between their membranes and the tested media. The results confirmed the absence of any interference in the presence of sugars or amino acids. Moreover, the difference of inorganic cations ionic size, their mobility and permeability as compared with CPX⁺ or CFZ⁺ prevents the interference of these cations during the analysis of the drugs. Also, the smaller the energy of cation hydration causes the greater the response of coated membrane. Therefore, excellent selectivity and good tolerance were achieved by applying CPX-PM-MnO₂NPs and CFZ-PT-CuONPs sensors for the determination of CPX and CFZ (Table 2).

3.3. Quantification of CPX and CFZ

The fabricated sensors were applied to quantify CPX and CFZ in their bulk powders and the percentage recoveries were 98.7 ± 0.4%, 99.1 ± 0.5%, 99.7 ± 0.3% and 99.8 ± 0.2% for CPX-PM, CFZ-PT, CPX-PM-MnO₂NPs and CFZ-PT-CuONPs, respectively (Table 3). The high sensitivity of the modified CPX-PM-MnO₂NPs and CFZ-PT-CuONPs sensors was due to the advanced physicochemical properties of the added metal oxide nanoparticles. Additionally, it was observed that the modified sensor by CuONPs displayed an excellent sensitivity and selectivity towards the determination of CFZ drug over that modified sensor for CPX this due to higher dielectric constant of CuONPs more than MnO₂NPs.

3.4. Method validation

The potentiometric method was validated according to ICH guidelines (38). Linear relationships were displayed by the modified CPX-PM-MnO₂NPs and CFZ-PT-
CuONPs sensors over $1.0 \times 10^{-8} - 1.0 \times 10^{-2}$, $1.0 \times 10^{-10} - 1.0 \times 10^{-7}$ mol L$^{-1}$, respectively, in comparison with $1.0 \times 10^{-6} - 1.0 \times 10^{-2}$ mol L$^{-1}$ for the conventional CPX-PM and CFZ-PT coated wire types. Least square regression equations were calculated to be $E_{\text{mv}} = (57.393 \pm 0.2) \text{log} \ [\text{CPX}] + 578.11$ and $E_{\text{mv}} = (58.65 \pm 0.2) \text{log} \ [\text{CFZ}] + 688.34$ for CPX-PM-MnO$_2$NPs and CFZ-PT-CuONPs, respectively. However, the conventional types CPX-PM and CFZ-PT exhibited a potential response $E_{\text{mv}} = (52.12 \pm 0.8) \text{log} \ [\text{CPX}] + 406.72$ and $E_{\text{mv}} = (51.607 \pm 0.5) \text{log} \ [\text{CFZ}] + 410.05$ with correlation coefficients 0.9999 for both modified sensors and 0.9997 for the conventional types.

To determine the lower limit of detection (LOD), the potential readings of the fabricated sensors was measured after the slope of each sensor was dropped by 17.9 mV. The recorded limit of detections s $5.0 \times 10^{-7}$, $4.9 \times 10^{-7}$, $5.6 \times 10^{-9}$, and $5.7 \times 10^{-11}$ mol L$^{-1}$ for conventional and modified sensors, respectively.

The accuracy of the proposed method was evaluated using nine concentrations of CPX and CFZ solutions and the mean percentage recoveries were calculated as 98.9 ± 0.8%, 99.2 ± 0.6%, 99.6 ± 0.4% and 99.8 ± 0.2% for CPX-PM, CFZ-PT, CPX-PM-MnO$_2$NPs and CFZ-PT-CuONPs, respectively. The precision of the suggested analytical method was measured using intra-day and inter-day assays and the data were expressed by calculating the percentage relative standard deviation (% RSD). The results showed that the % RSD for the modified CPX-PM-MnO$_2$NPs and CFZ-PT-CuONPs were 0.4% and 0.4%, 0.3% and 0.2% for intra-day and inter day, respectively. These percentages are less than 2%, confirming a highly precise method (Table 4).

The robustness of the described method was also evaluated, by changing the pH of the test CPX or CFZ solutions using phosphate buffer pH (6 ± 0.5) or acetate buffer (pH 5 ± 0.5). The recorded percentage recoveries were found to be 98.6 ± 0.8%, 99.2 ± 0.7,
99.5 ± 0.3% and 99.8 ± 0.1% for CPX-PM, CFZ-PT, CPX-PM-MnO2NPs, and CFZ-PT-CuONPs, respectively. The raggedness of the proposed method was determined by altering the model of pH meter (Jenway-3510). The obtained mean percentage recoveries were 98.4 ± 0.7%, 99.0 ± 0.8%, 99.5 ± 0.2%, and 99.6 ± 0.1% for the above conventional and modified sensors. The outcomes revealed an excellent agreement with those obtained by the present study and no significant difference was noticed.

3.5. Quantification of CPX and CFZ in commercial dosage forms

Both CPX and CFZ medications were analyzed using the modified CPX-PM-MnO2NPs and CFZ-PT-CuONPs in their commercial dosage forms Keflex® (500 mg cephalaxin/tablet) and Zinol® (500 mg cefazolin/vial). The potential readings of the modified sensors were recorded as a function of various concentrations of the tested drugs and the percentage recoveries were calculated. The obtained data were 99.7 ± 0.3% and 99.9 ± 0.2% for CPX-PM-MnO2NPs and CFZ-PT-CuONPs, respectively (Table 5). It was noticed that CFZ-PT-CuONPs showed higher sensitivity towards the determination of CFZ more than CPX-PM-MnO2NPs towards CPX and this can be due to the higher dielectric constant of CuO over that of MnO2 which elevated the conductivity of the sensor and hence enhanced its sensitivity. The resulted percentage recoveries were statistically compared with the results obtained from a spectrophotometric method for determination of CPX in the presence of commercial dosage forms Keflex® (500 mg cephalaxin/tablet) and Zinol® (500 mg cefazolin/vial).

Table 4. Intermediate precision assay of CPX and CFZ determination using modified CPX-PM-MnO2NPs and CFZ-PT-CuONPs-coated wire sensors.

|                      | Intra-day assay | Inter-day assay |
|----------------------|----------------|----------------|
|                      | *Test solution | *Found | % Recovery | *Test solution | *Found | % Recovery |
| Modified CPX-PM-MnO2NPs coated wire sensor | 8.0 | 7.99 | 99.9 | 8.0 | 7.96 | 99.5 |
| Statistical analysis | 5.0 | 4.01 | 100.3 | 5.0 | 5.01 | 100.2 |
| Mean ± SD            | 2.0 | 1.99 | 99.5 | 2.0 | 1.98 | 99.5 |
| Variance             | 0.16 | 0.16 | 0.23 | 0.23 | 0.40 | 0.40 |
| Modified CFZ-PT-CuONPs sensor | 10 | 9.99 | 99.9 | 10 | 10.0 | 100.0 |
| Statistical analysis | 8 | 7.99 | 99.9 | 8 | 8.00 | 100.0 |
| Mean ± SD            | 4 | 3.97 | 99.3 | 4 | 3.99 | 99.8 |

*Test solution and Found using – log Conc. mol L⁻¹.
**SE (％Error) = %RSD/√n.

Table 5. The analytical results obtained from the determination of CPX and CFZ in Keflex® (500 mg Cephalexin/tablet) and Zinol® (500 mg Cefazolin/vial) using modified CPX-PM-MnO2NPs and CFZ-PT-CuONPs coated wire sensors.

|                      | Modified CPX-PM-MnO2NPs sensor | Modified CFZ-PT-CuONPs sensor | Reported method (31) |
|----------------------|---------------------|---------------------|---------------------|
|                      | *Test solution | *Found | % Recovery | *Test solution | *Found | % Recovery | Reported method |
| Statistical analysis | 8 | 7.95 | 99.4 | 10 | 10.00 | 100.0 |
|                      | 7 | 7.00 | 100.0 | 8 | 7.99 | 99.9 |
| Mean ± SD            | 6 | 5.98 | 99.7 | 6 | 5.98 | 99.7 |
| Variance             | 5 | 4.97 | 99.4 | 5 | 5.00 | 100.0 |
| %RSD                 | 4 | 3.99 | 99.8 | 4 | 3.00 | 100.0 |
| Mean ± SD            | 2 | 2.00 | 100.0 | 2 | 1.99 | 99.5 |

*Test solution and found using – log Conc. mol L⁻¹.
**SE (％Error) = %RSD/√n.
***The tabulated values of "t-test" and "F-test" at confidence level p = 0.05.
phosphate buffer pH 2 and at absorption wavelength 261 nm \((24)\) and for determination of CFZ in distilled water at absorption wavelength 270 nm \((31)\) using t-student’s test and F-test \((50)\). The results revealed an excellent sensitivity of the developed modified sensors towards the determination of CPX and CFZ in their commercial dosage forms. To ensure the suitability of the fabricated modified sensors a comparative study was carried out between recent fabricated sensors and the previously potentiometric studies \((27–28, 36)\) with respect to the linear concentration ranges and limits of detection (Table 6). It was noticed that the new fabricated sensors displayed high sensitivity towards the determination of CPX and CFZ using modified CPX-PM-MnO2NPs and CFZ-PT-CuONPs with very wide concentration ranges and low limit of detections.

### 3.6. Quantification of letrozole in biosamples

The excellent results obtained in the determination of CPX and CFZ in their pharmaceutical products encouraged the determination of the same analytes in serum samples. The proposed modified sensors gave excellent efficiency for the quantification of CPX and CFZ with calculated % recoveries \((99.5 \pm 0.2\%\) and \(99.7 \pm 0.3\%)\) for the above-modified sensors as summarized in Table 7. These excellent results will help in future to develop novel and various types of modified sensors to quantify the drugs in their commercial products and biosamples.

### 4. Conclusion

This study described the biogenic synthesis of metal oxide nanoparticles using oat bio mass. The prepared nanoparticles were used in the fabrication of modified sensors CPX-PM-MnO2NPs and CTX-PT-CuONPs. The use of MnO2NPs and CuONPs as electro active materials, improved the sensitivity of the modified sensors and provide the quantity of the investigated drugs with low limits and wide concentration ranges. Therefore, the green modified sensors can be safely applied for routine analysis of CPX and CFZ in pharmaceutical industries and central research laboratories.

### Disclosure statement

No potential conflict of interest was reported by the author(s).

### References

[1] Mansoori, G.A., Principles of Nanotechnology: Molecular-Based Study of Condensed Matter in Small Systems. World Scientific: Chicago, 2005.

[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] Al-Mohaiemeed, A.M.; Alafaj, N.A.; El-Tohamy, M.F.; Al-Harbi, H. Prospective of Ultrasenstive Nanometal Oxides Electrochemical Sensors for Pharmaceutical Analysis of Antihistamine Drug Fexofenadine Hydrochloride.

---

### Table 6. Comparative study between the suggested method and previously published ion selective electrode methods.

| Ion selective electrode methods | Active materials | Plasticizer | Concentration range, mol L\(^{-1}\) | Limit of detection, mol L\(^{-1}\) | Reference |
|-------------------------------|------------------|-------------|-------------------------------|-------------------------------|-----------|
| Cephalixin CPX-PT             | CPX-PT           | o-NPOE and DOPH | \(1.0 \times 10^{-5} \rightarrow 1.0 \times 10^{-2}\) | \(6.5 \times 10^{-6}\) | \((27)\) |
| Current study CPX-PM-MnO2NPs  | CPX-PM-MnO2NPs   | o-NPOE      | \(6.0 \times 10^{-5} \rightarrow 3.0 \times 10^{-1}\) | \(4.0 \times 10^{-6}\) | \((28)\) |
| Cefazolin CFZ-Tetradecylammonium | CFZ-PT-CuONPs   | o-NPOE      | \(1.0 \times 10^{-3} \rightarrow 5.0 \times 10^{-1}\) | \(5.6 \times 10^{-5}\) | \((36)\) |

### Table 7. The results from the determination of CPX and CFZ in serum samples using modified CPX-PM-MnO2NPs and CFZ-PT-CuONPs coated wire sensors.

| Modified CPX-PM-MnO2NPs sensor | Modified CFZ-PT-CuONPs sensor |
|---------------------------------|--------------------------------|
| *Test solution*                 | *Test solution*               |
| *Found*                         | *Found*                       |
| % Recovery                      | % Recovery                    |
| Statistical analysis            | 8                              | 9.0                           | 99.9 |
|                                  | 7.3                           | 8.3                           | 99.8 |
|                                  | 7.3                           | 8.0                           | 100.0 |
|                                  | 6.3                           | 7.3                           | 99.4 |
|                                  | 6.3                           | 6.9                           | 99.3 |
|                                  | 6.3                           | 5.9                           | 99.7 |
|                                  | 5.3                           | 5.2                           | 99.4 |
| Mean ± SD                       | 99.5 ± 0.2                    | 99.7 ± 0.3                    |
| n                               | 6.3                           | 9.0                           |
| Variance                        | 0.04                          | 0.09                          |
| %SE                             | 0.08                          | 0.12                          |
| %RSD                            | 0.20                          | 0.30                          |

*Test solution and Found using – log Conc. mol L\(^{-1}\).*
S. A. AL-TAMIMI

Int. J. Electrochem. Sci. 2020, 15, 4774–4788. DOI:10.20964/2020.05.90.

[4] Alarfaj, N.A.; El-Tohamy, M.F.; Oraby, H. New Label-Free Ultrasonisive Electrochemical Immunosensor-Based Au/ MoS2/rGO Nanocomposites for CA 27-29 Breast Cancer Antigen Detection. New J. Chem. 2018, 42, 11046–11053. DOI:10.1039/C8NJ01388H.

[5] Alarfaj, N.A.; Amina, M.; Al Musayeib, N.M.; El-Tohamy, M.F.; Oraby, H.F.; Bukhari, S.I.; Moubayed, N.M.S. Prospective of Green Synthesized Oleum Cumini Oil/PVP/MgO Bionanocomposite Film for its Antimicrobial, Antioxidant and Anticancer Applications. J. Polym. Environ. 2020. https://doi.org/10.1007/s10924-020-01755-2.

[6] Singh, B.K.; Lee, S.; Na, K. An Overview on Metal-Related Catalysts: Metal Oxides, Nanoporous Metals and Supported Metal Nanoparticles on Metal Organic Frameworks and Zeolites. Rare Met. 2020, 39, 751–766. https://doi.org/10.1179/215522471970846296.

[7] Patra, J.K.; Das, G.; Fraceto, L.F.; Campos, E.V.R.; Rodriguez-Torres, M.P.; Acosta-Torres, L.S.; Diaz-Torres, L.A.; Grillo, R.; Swamy, M.K.; Sharma, S.; Habtemariam, S.; Shin, H.-S. Nano Based Drug Delivery Systems: Recent Developments and Future Prospects. J. Nanobiotechnol. 2018, 16 (71). https://doi.org/10.1186/s12951-018-0392-8.

[8] Zhang, B.; Gao, P.-X. Metal Oxide Nanoarrays for Chemical Sensing: A Review of Fabrication Methods, Sensing Modes, and Their Inter-Correlations. Front. Mater. 2019, 6, 55. DOI:10.3389/fmats.2019.00055.

[9] Lane, M.K.; Zimmerman, J.B. Controlling Metal Oxide Nanoparticle Size and Shape with Supercritical Fluid Modes, and Their Inter-Correlations. Front. Mater. 2019, 6, 55. DOI:10.3389/fmats.2019.00055.

[10] Alsidar, S.O.; Madubuonu, N.; Alnasir, M.H.; Ahmad, I.; Botha, S.; aaza, M.; Ezema, F.I. Biogenic Synthesis of Iron Oxide Nanorods Using Moringa oleifera Leaf Extract for Antibacterial Applications. Appl. Nanosci. 2020, 10, 305–315. https://doi.org/10.1007/s13204-019-01099-x.

[11] Awwad, A.M.; Amer, M.W.; Salem, N.M.; Abdeen, A.O. Green Synthesis of Zinc Oxide Nanoparticles (ZnO-NPs) Using Allanthus Alissima Fruit Extracts and Antibacterial Activity. Chem. Int. 2020, 6, 151–159. https://doi.org/10.32817/zenodo.3559520.

[12] Yusof, H.M.; Mohamad, R.; Zaidan, U.H. Microbial Synthesis of Zinc Oxide Nanoparticles and Their Potential Application as an Antimicrobial Agent and a Feed Supplement in Animal Industry: a Review. J. Animal Sci. Biotechnol. 2019, 10, 57. https://doi.org/10.1186/s40104-019-0368-z.

[13] Whitehead, A.; Beck, E.J.; Tosh, S.; Wolever, T.M. Cholesterol-lowering Effects of oat β-Glucan: a Meta-Analysis of Randomized Controlled Trials. Am. J. Clin. Nutr. 2014, 100, 1413–1421. DOI:10.3945/ajcn.114.006108.

[14] Aminin, N.; Amin, G.; Jafari Azar, Z. Green Synthesis of Silver Nanoparticles Using Avena Sativa L. Extract. Nanomed. Res. J. 2017, 2, 57–63. DOI:10.22034/NMRJ.2017.23588.

[15] Oraby, H.F.; El-Tohamy, M.F.; Kamel, A.M.; Ramadhan, M.F. Changes in the Concentration of Avenanthramides in Response to Salinity Stress in CBF 3 Transgenic oat. J. Cer. Sci. 2017, 26, 263–270. https://doi.org/10.1016/j.jcs.2017.06.010.

[16] Mondal, D.; Paul, B.K.; Das, S.; Bhattacharya, D.; Ghoshal, D.; Nandy, P.; Das, K.; Das, S. Synthesis and Property of Copper-Impregnated α-MnO2Semiconductor Quantum Dots. Langmuir 2018, 34, 12702–12712. https://doi.org/10.1021/acs.langmuir.8b01745.

[17] Choi, C.A.; Lee, J.E.; Mazrad, Z.A.; In, I.; Jeong, J.H.; Park, S.Y. Redox- and pH-Responsive Fluorescent Carbon Nanoparticles-MnO2-Based FRET System for Tumor-Targeted Drug Delivery in Vivo and in Vitro. J. Ind. Eng. Chem. 2018, 63, 208–219. https://doi.org/10.1016/j.jiec.2018.02.017.

[18] Ahmadian, Y.; Bakravi, A.; Hashemi, H.; Namazi, H. Synthesis of Polyvinyl Alcohol/CuO Nanocomposite Hydrogel and its Application as Drug Delivery Agent. Polym. Bull. 2019, 76, 1967–1983. https://doi.org/10.1007/s00289-018-2477-9.

[19] Ciorță, A.; Suciu, M.; Macavei, S.; Kacso, I.; Lung, I.; Soran, M.L.; Parvu, M. Green Synthesis of Ag-MnO2 Nanoparticles Using Chelidonium Majus and Vinca Minor Extracts and Their In Vitro Cytotoxicity. Molecules 2020, 25, 819. https://doi.org/10.3390/molecules25040819.

[20] Kintelu, S.A.; Folorunso, A.S.; Folorunso, F.A.; Oyebamiji, A.K. Green Synthesis of Copper Oxide Nanoparticles for Biomedical Application and Environmental Remediation. Heliyon. 2020, 6, e04508. https://doi.org/10.1016/j.heliyon.2020.e04508.

[21] Singh, V.K.; Patel, C.M. A Novel Method to Prepare two-Dimensional Manganese Dioxide and its Potential Application as a Sensor to Detect Hydrogen Peroxide and L-Ascorbic Acid in Water. Sep. Sci. Technol. 2019, 54, 258–264. https://doi.org/10.1080/01496395.2018.1437181.

[22] Reddy, S.; Kumara Swamy, B.E.; Jayadevappa, H. CuO Nanoparticle Sensor for the Electrochemical Determination of Dopamine. Electrochim. Acta 2012, 61, 78–86. https://doi.org/10.1016/j.electacta.2011.11.091.

[23] Panda, S.S.; Kumar, B.V.; Dash, R.; Mohanta, G. Determination of Cephalaxin Monohydrate in Pharmaceutical Dosage Form by Stability-indicating RP-UFLC and UV Spectroscopic Methods. Sci. Pharm. 2013, 81, 1029–1041. DOI: 10.3797/scipharm.1306-07.

[24] Prasad, G.V.; Sravani, S.; Ishaq, B.M.; Madhu, M.; Munna, S.; GPoinath, C. Development and Validation of UV-Spectrophotometric Method for Determination of Cephalaxin. Asian J. Res. Chem. 2013, 6, 490–494.

[25] Ali Ahmed, S.M.; Elbashir, A.A.; Suliman, F.E.; Aboul-Enein, H.Y. New Spectrofluorimetric Method for Determination of Cephalosporins in Pharmaceutical Formulations. Luminescence 2013, 28, 734–741. DOI:10.1007/s10895-011-0121-1.

[26] Percin-Ozkorucuklu, S.; Uka, B.; Yildirim-Bastemur, G. Voltammetric Analysis of Cephalaxin and Cefazolin in Pharmaceutical Formulations and Biological Samples. J. Turk. Chem. Soci. 2019, 6, 217–224. DOI:10.18596/ jotcsa.469028.

[27] Salman, H.G.; Jamil, D.M.; Abass, A.M.; Ahmed, A. Synthesis Liquid Membrane Electrodes of Cephalaxin Hydrochloride. Sys Rev. Pharm. 2020, 11, 710–716. DOI:10.31838/srp.2020.6.105.

[28] Tawfeq, M.S.; Well, M.M. Determination of Cefalexin Monohydrate Drug by Construction of Selective Membrane Polymer Electrodes. Int. J. Sci. Eng. Tech. Res. 2014, 3, 1619–1622.

[29] Gh, A.B.; Rezvani, M.; Roshanzamir, S. Spectrophotometric Complexation of Cephalosporins with Palladium (II)
