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Eco-Friendly Fabrication of CaO and ZnO Nanoparticle-Based Sensors for Electrochemical Determination of Cyproheptadine Hydrochloride in Pure and Pharmaceutical Formulations

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Abstract:

This research aims to develop selective electrodes based on green chemistry techniques to analyze of cyproheptadine hydrochloride. (CPH) In its pure form, it is used in pharmaceutical preparations. Nanoparticles of calcium and zinc oxides were prepared using plant extracts (lavender and chia seeds) as an environmentally friendly reducing agent. The nanomaterials were characterized using X-ray diffraction (XRD), scanning electron microscopy (SEM), and energy-dispersive spectroscopy (EDX), which confirmed the successful preparation and the presence of a nanocrystalline structure with a particle size in the 20-30 nm range. Graphite electrodes coated with nano-layers were fabricated from CaONPs and ZnONPs prepared by using a green method, they were used as electrochemical sensors for drug quantification. These electrodes demonstrated a sensitive and rapid electrochemical response over a wide concentration range (10^{-2} - 10^{-8} M), with a response time ranging from 2–38 seconds depending on the concentration. The performance of the fabricated electrodes was evaluated in terms of compatibility, accuracy, and quantitative limit. (LOQ), limit of detection (LOD), and temporal stability The results showed that these sensors have high selectivity towards CPH with minimal interference from interfering ions. The electrodes have also been shown to maintain their excellent performance for up to 38-32 one day, almost before anynoticeable deterioration in their response occurs. Practical applications for analyzing various pharmaceutical samples demonstrated high agreement between the results obtained using these electrodes and reference methods, enhancing their reliability as environmentally friendly analytical tools. This research represents an important step toward developing sustainable electrochemical sensors with high efficiency in pharmaceutical analysis, paving the way for the widespread use of this technology in environmental and medical applications.

التصنيع الصديق للبيئة لمتحسسات مستندة على جسيمات نانوية من أوكسيد الكالسيوم وأوكسيد الزنك لتقدير هيدروكلوريد السايبروهيبتادين كهربائياً في أشكاله النقية والصيدلانية

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مستخلص:

يهدف هذا البحث إلى تطوير أقطاب كهربائية انتقائية حيث تعتمد على تقنيات الكيمياء الخضراء لتحليل سيبروهيبتادين هيدروكلوريد (CPH) في شكله النقي، يتم استخدامه في المستحضرات الصيدلانية. تم تحضير جسيمات نانوية من أكاسيد الكالسيوم والزنك باستخدام المستخلصات النباتية (اللافندر وبذور الشيا) كعامل اختزال صديق للبيئة. تم تشخيص المواد النانوية باستخدام حيود الأشعة السينية (XRD)، والمجهر الإلكتروني الماسح (SEM)، والتحليل الطيفي المشتت للطاقة (EDX)، مما أكد التحضير الناجح ووجود بنية بلورية نانوية بحجم جسيم في نطاق 30–20 نانومتر. تم تصنيع أقطاب الجرافيت المطلية بطبقات نانوية من أكاسيد الكالسيوم والزنك النانوية وتم تحضيرها بطريقة خضراء، وتم استخدامها كأجهزة استشعار كهروكيميائية لتقدير كمية الدواء. أظهرت هذه الأقطاب الكهربائية استجابة كهروكيميائية حساسة وسريعة على نطاق تركيز واسع (10^{-2} - 10^{-8} M)، مع وقت استجابة يتراوح من 2–38 ثانية اعتمادًا على التركيز. تم تقييم أداء الأقطاب الكهربائية المصنعة من حيث التوافق والدقة والحد الكمي (LOQ)، حد الكشف (LOD)، والاستقرار الزمني، أظهرت النتائج أن هذه المستشعرات تتمتع بانتقائية عالية اتجاه دواء CPH مع الحد الأدنى من التداخل من الأيونات المتداخلة. وقد ثبت أيضًا أن الأقطاب الكهربائية تحافظ على أدائها الممتاز لمدة تصل إلى 38–23 يومًا تقريبًا قبل حدوث أي تدهور ملحوظ في استجابتها. أظهرت التطبيقات العملية لتحليل العينات الصيدلانية المختلفة توافقًا عاليًا بين النتائج التي تم الحصول عليها باستخدام هذه الأقطاب الكهربائية والطرق المرجعية، مما يعزز موثوقيتها كأدوات تحليلية صديقة للبيئة. يمثل هذا البحث خطوة مهمة نحو تطوير أجهزة استشعار كهروكيميائية مستدامة ذات كفاءة عالية في التحليل الصيدلاني، مما يمهد الطريق لاستخدام هذه التكنولوجيا على نطاق واسع في التطبيقات البيئية والطبية.

1- Introduction

Nanotechnology is concerned with the production of materials with nanoscale dimensions ranging from1 and 100 nm. Due to their small size, chemical composition, and surface structure, these nanoparticles possess unique properties. In recent years, green chemistry and nanotechnology have become closely linked. This enables the reduction of the negative effects caused by the production and use of nanomaterials, while alleviating concerns about problems associated with other methods. Green nanomaterial construction is the preferred option because it is safe and environmentally friendly[1]. The importance of these nanomaterials lies primarily in their high surface-to-volume ratio due to their extremely small size, which enhances surface contact with other objects[2,3]. Green chemistry is defined as methods that prevent pollution by utilizing chemicals used in specific fields, such as environmentally friendly analytical chemistry and analytical methodologies in their clean and green forms. Therefore, green synthesis is a viable approach to the production of nanoparticles because it complies with environmental standards and is biocompatible[4,5]. The goal of green nanotechnology is to produce nanomaterials and products that do not cause any harm to the environment or human health, and also to provide solutions to environmental problems through the resulting products. This technology relies on the principles of green chemistry and green engineering to produce novel nanomaterials[6]. Green nanotechnology methods provide new innovative approaches using plant extracts to synthesize novel nanoparticles with specific properties that are highly desired and desirable for the development of biosensors, biomedical devices, cosmetics, and electrochemical nanotechnology[7]. Ion-selective membrane electrodes are an automated classification and are known as electro-analytical sensors that selectively analyze the desired substances through chemical reactions occurring between them[8]. The scientist (Qstwald) discovered this type of electrode, ion-selective membrane electrodes, in 1890[9]. Nanopharmacology is based on the use of nanotechnology to explore and develop new methods for releasing medical substances and drugs by reducing their sizes to na-

noscale, which improves the properties of pharmaceuticals, especially those used in the treatment of diseases[10]. This technology has multiple advantages in the field of medicine, the most prominent of which are[11]: delivering drugs to targeted sites within the body, enhancing the solubility of poorly soluble drugs, ensuring the maintenance of therapeutic efficacy and effectiveness, protecting drugs from degradation, and reducing treatment costs, as nanopharmaceutical products are more economical compared to alternatives to conventional products. Nanoparticles are important for several applications, including sensors, as well as structural materials, electronics, drug delivery systems, and cancer diagnosis[12].

The complex Cyproheptadine HCl (CPH) has the formula shown in Figure 1. This drug is an antihistamine, commonly used to relieve symptoms caused by allergies such as runny nose, watery eyes, itching, and sneezing. CPH works by blocking a natural substance called histamine, which is produced by the body during an allergic reaction. CPH is used to treat several hormonal disorders and can also be used to treat and alleviate the side effects of antidepressants[(13)]. Ion-selective potential measurement is another tool that can be applied to analyze CPH-containing materials. Ion-selective electrodes with latent membranes have been used in the analysis of biological and pharmaceutical fluids for decades[14,15].$C_{21}H_{22}ClN.1½H_2O$, (As shown in **FIGURE 1**).

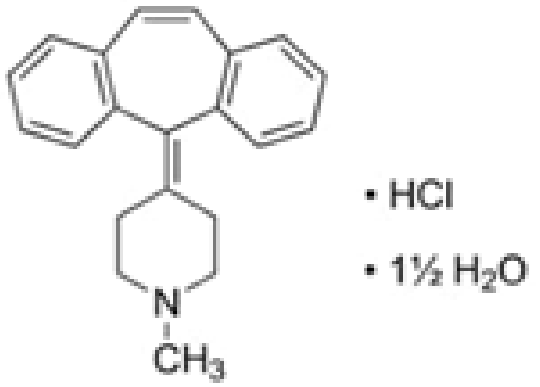


FIGURE 1. Chemical structure of cyproheptadine HCl $C_{21}H_{22}ClN.1½H_2O$ and its molecular weight is 350.9 g/mol.

2- Experimental

2-1 Chemicals

The chemicals used in this study include:

Organic and inorganic solvents such as acetone, tetrahydrofuran (THF), and tert-butyl phosphate (TBP as plastisizer). Active pharmaceutical ingredients

and excipients include cyproheptadine hydrochloride ($C_{21}H_{22}ClN \cdot 1.5H_2O$), glucose, maltose, methylcellulose, cross carmellose, and magnesium stearate. Salts and reagents such as , hydrated calcium nitrate ($Ca(NO_3)_2 \cdot 4H_2O$), zinc sulphate ($ZnSO_4 \cdot 7H_2O$), sodium hydroxide (NaOH), and hydrochloric acid (HCl). Polymers and matrix materials including polyvinyl chloride (PVC) and titanium dioxide (TiO_2). Precipitating agents such as phosphotungstic acid (PTA, $H_3O_4PW_6$), ammonium reineckate ($NH_4[Cr(NCS)_4(NH_3)_2] \cdot H_2O$)distilled water were also utilized.

2.2. Tools and Devices

A variety of analytical and laboratory instruments were employed throughout the experimental procedures to ensure the accuracyand reliability of the results. A precision balance (KERN ABS, Germany) was used for accurate weighing of chemicals and reagents. A calomel electrode (Me-SC900, England) served as the reference electrode in electrochemical measurements. For high-temperature treatments and thermal decomposition, an electric muffle furnace was utilized. Functional group characterization was conducted using a Fourier Transform Infrared Spectroscopy (FTIR) instrument (Shimadzu, Japan). The Jenway pH Meter 3310 was used to measure and adjust the pH of various solutions. Mixing and heating processes were performed using a magnetic stirrer with a hot plate (FTH-PM-10, Korea). Sample drying and heating were carried out in a laboratory oven (KAROL, Korea). Distilled water was prepared using a Puridest PD 12 R water distillation unit, which operates on single distillation technology. Finally, Whatman filter paper No. 1 was used for filtration purposes during the sample preparation stages.

3. Preparation of Lavender Leaf Extract

It was milled 10 grams of lavender leaves were ground using a nano-grinder, then the ground quantity was dissolved in 150 ml of pure distilled water. The mixture was left to boil for half an hour at 80°C, then the solution was cooled. The mixture was filtered through filter paper to remove suspended particles. The extract was light brown. (As shown in **FIGURE 2**)

FIGURE 2. Lavender leaf extract.

4. Green Synthesis of Calcium Oxide Nanoparticles (CaONPS)

Mixed25 ml of 0.1 M aqueous calcium nitrate prepared using ultrapure distilled water and a 25 ml solution of lavender extract was heated for 30 min at 70°C. Drops of 1 M NaOH solution were then added. A precipitate began to form. The mixture was filtered using filter paper and the precipitate was washed several times with pure distilled water to remove any remaining extract. The mixture was dried in an air oven at 80°C for 30 minutes. The nano-precipitate was then fired in an oven at 500°C for three hours. This yielded white-gray calcium oxide nanoparticles. (As shown in **FIGURE 3**).

FIGURE 3. Calcium oxide Nanoparticles (CaONPS).

5. Chia Seed Extract Preparation

It was milled10 grams of chia seeds were ground using a nano-mill, then the ground quantity was dissolved in 150 ml of pure distilled water. The mixture was left to boil for half an hour at 80 degrees Celsius, then the solution was cooled and then filtered using filter paper to remove any suspended particles. (As shown in **FIGURE 4**).

FIGURE 4. Chia seed extract

6. Green Synthesis of Zinc Oxide Nanoparticles (ZnONPS)

Prepared50 ml of 0.2 M hydrated zinc sulfate was prepared using ultra-pure distilled water. This solution was then mixed with 10 ml of chia seed extract and heated for half an hour at 60°C. The mixture was then heated for 2 hours at 80°C under continuous stirring (750 rpm) for 30 minutes. The mixture was filtered using filter paper and washed with pure distilled water three times to remove any remaining extract. The mixture was then dried in an air oven at 100°C for 30 minutes. This resulted in white zinc oxide nanoparticles. (As shown in **FIGURE 5**).

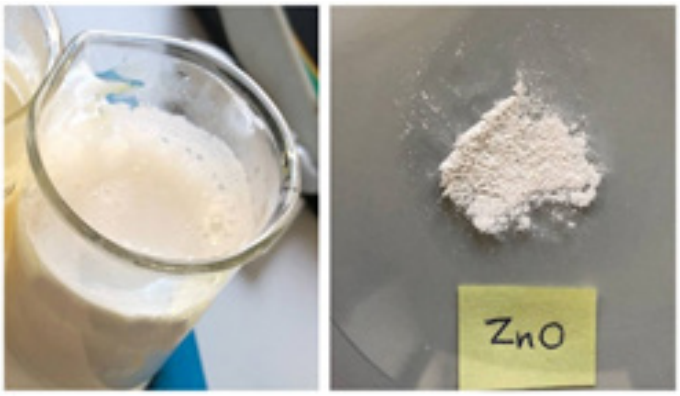


FIGURE 5. Zinc oxide Nanoparticles (ZnONPS)

7. Preparation of a Standard Solution of Cyproheptadine Hydrochloride (0.01M)

It is prepared by dissolving 0.3509 g of CPH pharmaceutical powder in a 100 ml volumetric flask and top up with distilled water to the mark. A series of solutions ranging from (10^{-2} to 10^{-8}) are then prepared by dilution.

8. Preparation Of the Ion Pair (CPH_AR)

The ion pair is prepared. (CPH_AR) By adding 50ml of the precipitating agent AR to 50ml of CPH drug at the same concentrations (10^{2}) M in a 100ml beaker. After a few minutes we observed the formation of a pink precipitate. Then we left it for 24 hours and filtered the solution and let the filtrate dry. At laboratory temperature for 72 hours. To obtain the desired precipitate. (As shown in **FIGURE 6**)

FIGURE 6. Ion pair (CPH_AR)

9. Preparation of the Ion Pair (CPH_PTA)

The ion pair is prepared. (CPH_PTA) By adding 50ml of the precipitating agent PTA to 50ml of CPH drug at the same concentrations (10^{2}) M in a 100ml beaker. After a few minutes we observed the formation of a light brown precipitate. Then we left it for 24 hours and filtered the solution and let the filtrate dry. At laboratory temperature for 72 hours. To obtain the desired precipitate. (As shown in **FIGURE 7**).

FIGURE 7. Ion pair (CPH_PTA)

10. Membrane Composition and Electrode Fabrication

a- To form a nano-coated graphite electrode (CPH_AR_TBP_CaONPs_ ZnONPs) (I) 0.19 g of PVC was mixed with 0.01 g of CPH_AR, 0.005 g of nano zinc oxide, and 0.005 g of nano calcium oxide, prepared using green methods, in a 10 ml beaker and dissolved in 5 ml of THF. 0.35 ml of (Tributyl phosphate) TBP was added and mixed well with a glass stirrer. A 6 cm long graphite electrode was then taken. It was thoroughly washed with acetone and pure distilled water and allowed to dry. It was then placed in a plastic tube. One end of the electrode was left connected to a potentiometer. The other end was immersed several times in the above mixture to form a thick film layer and allowed to dry for a few minutes. The process was repeated several times until a thick film layer was formed. To form the electrode of the nanoparticle-coated electrode membrane (CPH_AR_TBP_CaONPs_ ZnONPs) (I) After that, we immerse the electrode in the CPH drug solution with a concentration of (10^2) M for a whole day until the electrode is ready for study and application. (As shown in **FIGURE 8**).

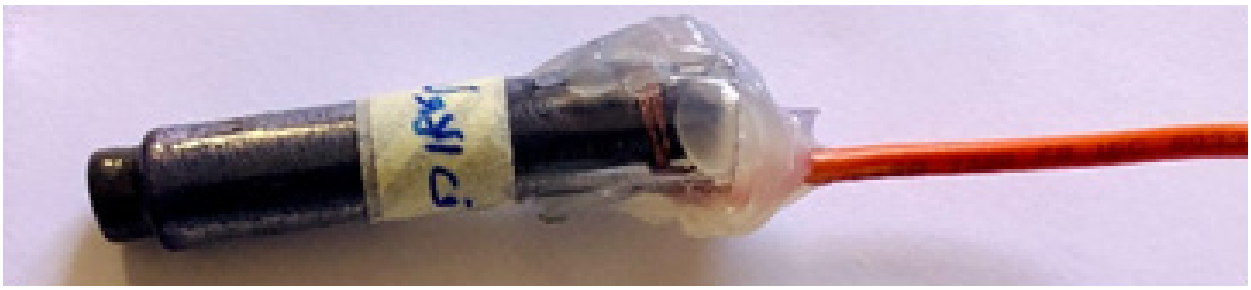


FIGURE 8. Electrode (I)

b- To form a nano-coated graphite electrode (CPH_PTA_TBP_CaONPs_ ZnONPs) (I) 0.19 g of PVC was mixed with 0.01 g of CPH_PTA, 0.005 g of each of nano-zinc oxide, and 0.005 g of nano-calcium oxide, prepared using green methods, in a 10 ml beaker and dissolved in 5 ml of THF. 0.35 ml of (Tributyl phosphate) TBP was added and mixed well with a glass stirrer. Next, a 6 cm long graphite electrode was taken. It was thoroughly washed with acetone and pure distilled water and allowed to dry. It was then placed in a plastic tube. One end of the electrode was left to connect to a potentiometer. The other end was immersed several times in the above mixture to form a thick film layer and allowed to dry for a few minutes. The process was repeated several times until a thick film layer was formed. To form the electrode of the nanoparticle-coated electrode membrane (CPH_PTA _TBP_ CaONPs_ZnONPs) (II) after that, we immerse the electrode in the CPH drug solution with a concentration of (10^2) M for a whole day until the electrode is ready for study and application. (As shown in **FIGURE 9**).

FIGURE 9. Electrode (II)

11. Characterization of Nanoparticles

11.1 Infrared Spectrometry Technology (FTIR)

FTIR (Fourier Transform Infrared Spectroscopy) is an analytical technique used to identify chemical compounds by measuring infrared absorption in a given range of frequencies. The technique detects chemical bonds in the substance by recording its interaction with infrared light, resulting in a spectrum containing distinctive peaks expressing the molecular vibrations of chemical bonds.

Spectrum analysis FTIR for calcium oxide:

•Top at 711.76 cm-1 shows vibration of the bonds between calcium and oxygen (Ca-O), indicating the formation of calcium oxide. (As shown in **FIGURE 10**)

FTIR Spectrum Analysis for Zinc Oxide:

Top at 445.57 cm-1 confirms the• presence of Zn-O vibrations, indicat-As) .ing the formation of zinc oxide .(shown in **FIGURE 11**

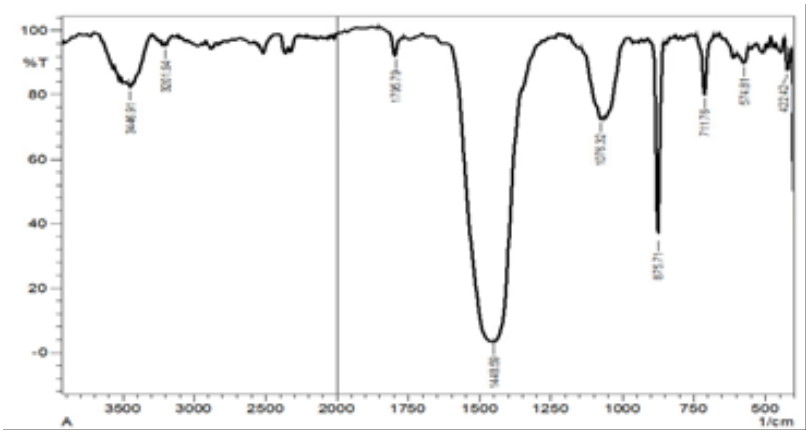


FIGURE 10. FTIR for Calcium Oxide Nanoparticles (CaONPS)

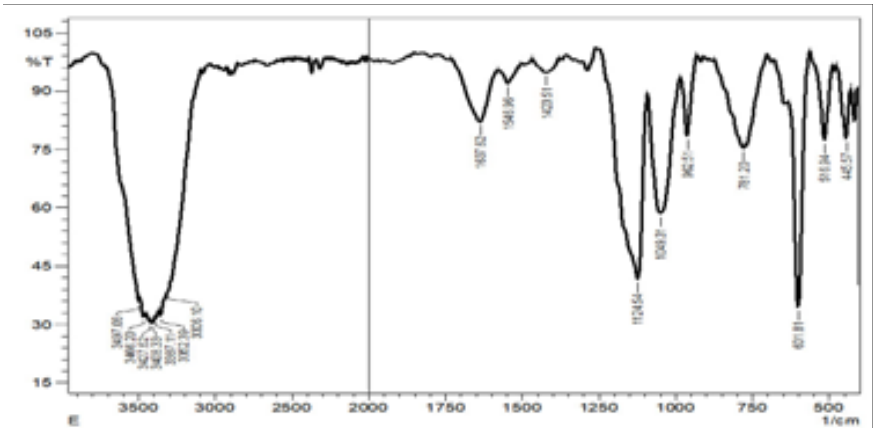


FIGURE 11. FTIR for Zinc Oxide Nanoparticles (ZnONPS)

11-2. X-ray diffraction spectrum

A- X-ray diffraction spectrum of CaONPs prepared by plant extracts.

TABLE 1. SHOWS THE MOST IMPORTANT BANDS AND DATA OBTAINED FROM X-RAY DIFFRACTION SPECTRUM OF CAONPS.

material	2θ	Miller indexes	Intensity	FWHM	d spacing	D (nm)	Avg. D (nm)
A	13.8574	100	136.80	0.2362	6.39071	35.39619	32.46809
	19.1654	110	72.40	0.4723	4.63106	17.82124	
	20.3284	110	233.68	0.1181	4.36865	71.39587	
	23.0984	111	45.94	0.9446	3.85065	8.967854	
	28.1150	200	69.81	0.4723	3.17395	18.11507	
	29.4828	200	1426.91	0.1968	3.02974	43.60776	
	31.9091	210	36.25	0.9446	2.80468	9.138289	
	34.8990	211	64.62	0.2362	2.57095	36.83267	
	35.6279	211	312.93	0.2755	2.52001	31.64241	
	36.0905	211	130.70	0.1968	2.48876	44.35405	
	39.5324	220	165.96	0.2362	2.27965	37.33761	
	41.3259	221	58.51	0.2362	2.18476	37.55341	
	43.2816	300	207.09	0.1574	2.09047	56.72734	
	43.8378	310	225.13	0.2362	2.06523	37.8756	
	47.5667	311	220.15	0.1968	1.91167	46.08615	
	48.5999	222	225.91	0.1968	1.87342	46.27189	
	50.7194	320	67.44	0.6298	1.80000	14.58333	
	57.5205	400	108.62	0.3149	1.60230	30.06484	
	60.8405	411	57.96	0.4723	1.52257	20.37789	
	65.1284	420	12.17	1.8893	1.43232	5.212348	

Analysis showed XRD of the samples shows crystalline structures based on the high-intensity bands that appeared in the spectra of the measured compounds. Table (1) shows the most important bands and data obtained from diffraction analysis, in addition to the Miller coefficients calculated according to the Bragg equation, as well as the particle sizes calculated according to the Scherrer equation. (As shown in **FIGURE 12**).

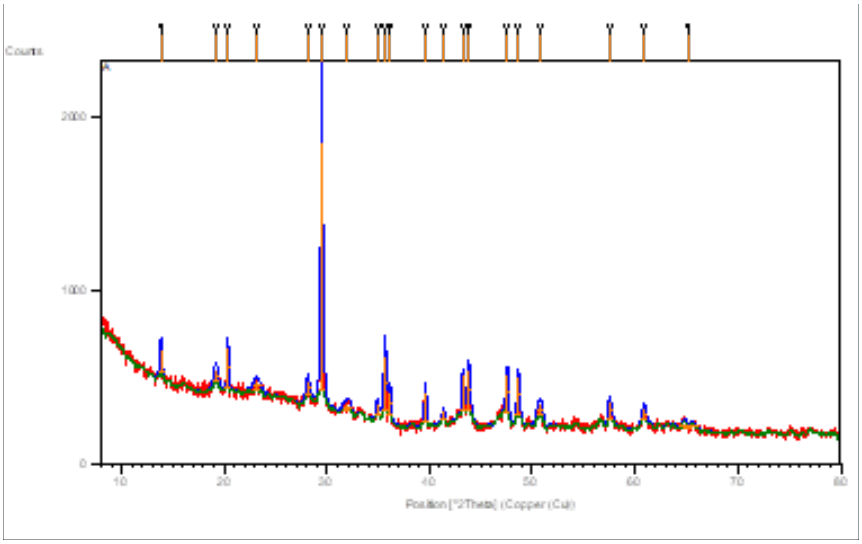


FIGURE 12. XRD analysis of CaONPs

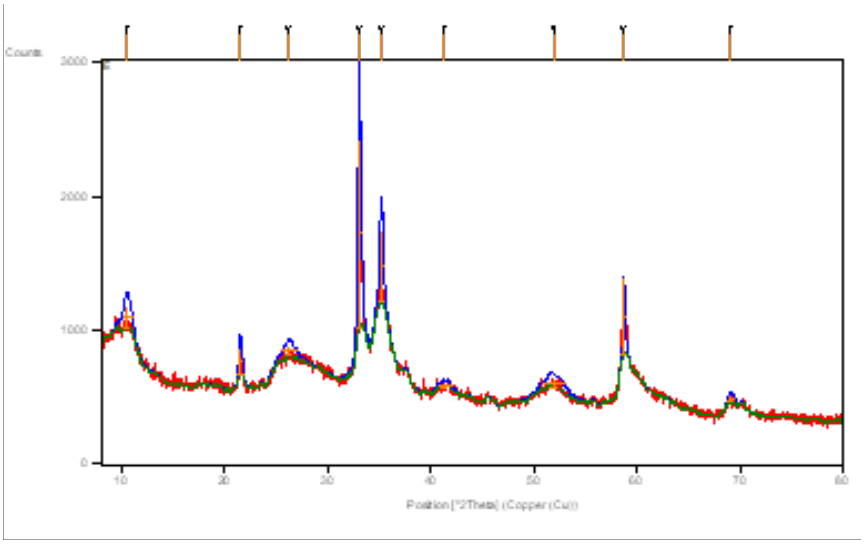
B- X-ray diffraction spectrum of ZnONPs prepared by plant extracts:

As shown in Figure 11. X-ray diffraction (XRD) patterns indicated other unspecified diffraction peaks attributable to impurities. The size of nickel oxide nanoparticles ZnONPs was calculated using the Shearer equation and the results are shown in **TABLE 2** below. And (As shown in **FIGURE 13**).

TABLE 2. SHOWS THE MOST IMPORTANT BANDS AND DATA OBTAINED FROM X-RAY DIFFRACTION SPECTRUM OF ZNONPS

material	2θ	Miller indexes	Intensity	FWHM	d spacing	D (nm)	Avg. D (nm)
E	10.5118	100	172.37	0.9446	8.41593	8.823381	19.60627
	21.5083	200	205.23	0.3149	4.13160	26.82723	
	26.2021	211	80.47	1.5744	3.40116	5.412422	
	33.0125	310	1419.87	0.3149	2.71342	27.48891	
	35.1479	311	544.12	0.3936	2.55331	22.1185	
	41.2912	321	32.68	1.5744	2.18652	5.633323	
	51.8863	332	64.47	2.5190	1.76223	3.663995	
	58.6960	520	584.06	0.1574	1.57298	60.49254	
	69.0610	611	60.24	0.6298	1.36005	15.99616	

FIGURE 13. XRD analysis of ZnONPs.



12. SEM Microscopy of Nanopatricles

A- CaONPs

Scanning electron microscope (SEM) measurements were performed. SEM) was used to study the surface morphology of the prepared samples using a scanning electron microscope (Thermoscientific Quattro S). Figure (3-18) shows SEM images taken at two different scales (1 micrometer, 200 nm) of the prepared calcium oxide nanoparticles. It was observed that the nanoparticles CaONPs The obtained particles have a disordered-like shape with different dimensions and average particle size ((29.37 nm), SEM results clearly demonstrated that this method significantly affects the shape and dimensions of CaONPs, each of which has different shapes, widths, and lengths. (As shown in **FIGURE 14**).

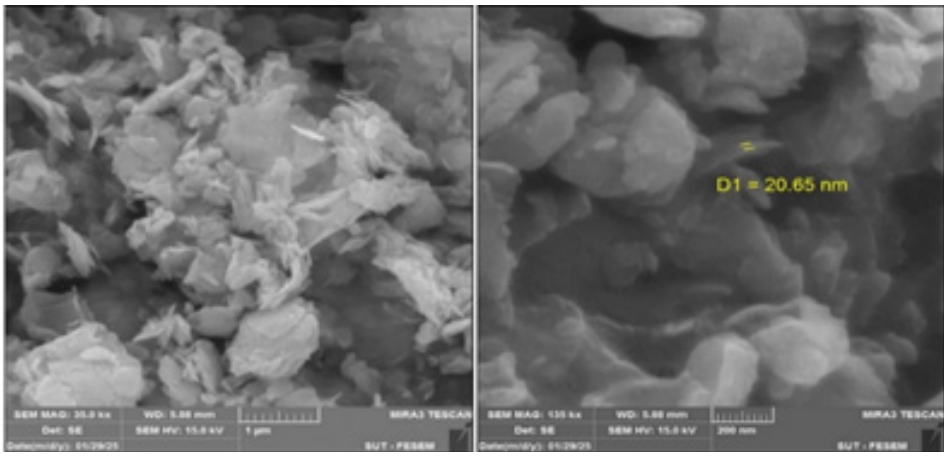


FIGURE 14. SEM Microscopy of CaONPs

B- ZnONPs

Scanning electron microscope (SEM) measurements were performed. (SEM) was used to study the surface morphology of the prepared samples using a scanning electron microscope (Thermoscientific Quattro S). **FIGURE 15** shows SEM images taken at two different scales (1 micrometer, 200 nm) of the prepared zinc oxide nanoparticles. It was observed that the nanoparticles ZnONPs The obtained particles have a disordered-like shape with different dimensions and average particle size (20.65 nm), SEM results clearly demonstrated that this method significantly affects the shape and dimensions of ZnONPs, each of which has different shapes

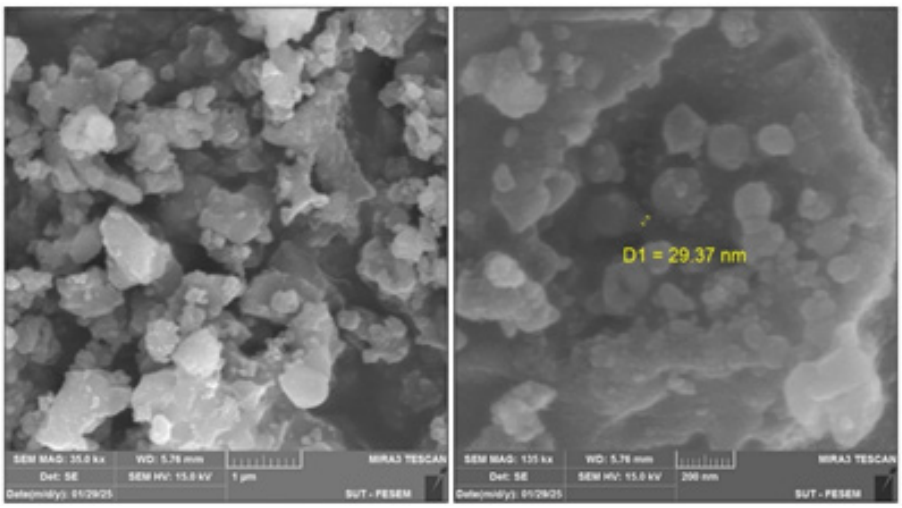


FIGURE 15. SEM Microscopy of ZnONPs

13- Energy dispersive X-ray spectroscopy (EDX)

Energy-dispersive X-ray spectroscopy (EDX) is a reliable and widely used technique for chemical characterization and visualization. Using EDX, various strong signals were detected, verifying the formation of calcium oxide nanoparticles (CaONPs). Peaks appear at optical absorption values of 3.8 keV for calcium atoms. A strong peak was observed at 0.6 keV for oxygen atoms. This confirms the presence of calcium oxide nanoparticles. Table 2 shows a calcium content of 22.21% and an oxygen content of 43.16%. In addition, low levels of sodium, magnesium, potassium, and aluminum, result-

ing from the lavender extract, which is rich in organic acids and bioactive molecules such as phenols and flavonoids, effectively contributed to the reduction of calcium and the synthesis of calcium nanoparticles. As shown in **FIGURE 16** and **TABLE 3**.

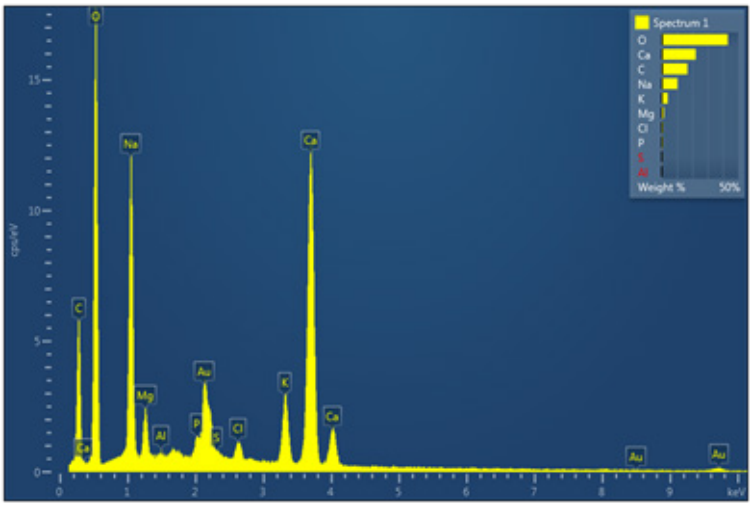


FIGURE 16. Energy dispersive X-ray spectroscopy (EDX) of CaONPs

TABLE 3. SHOWS THE MOST IMPORTANT BANDS AND DATA OBTAINED FROM (EDX) OF CAONPS.

Element	Line Type	Apparent Concentration	k Ratio	Wt%	Wt% Sigma	Atomic %	Standard Label	Factory Standard
C	K series	0.78	0.00784	16.87	0.41	26.35	C Vit	Yes
O	K series	4.40	0.01480	43.16	0.35	50.63	SiO2	Yes
Na	K series	1.89	0.00796	10.35	0.13	8.45	Albite	Yes
Mg	K series	0.21	0.00136	1.46	0.06	1.13	MgO	Yes
Al	K series	0.02	0.00011	0.10	0.04	0.07	Al2O3	Yes
P	K series	0.17	0.00096	0.71	0.07	0.43	GaP	Yes
S	K series	0.06	0.00054	0.39	0.06	0.23	FeS2	Yes
Cl	K series	0.13	0.00111	0.80	0.05	0.42	NaCl	Yes
K	K series	0.69	0.00588	3.93	0.09	1.89	KBr	Yes
Ca	K series	3.64	0.03254	22.21	0.21	10.40	Wollastonite	Yes
Total:				100.00		100.00		

14. Energy dispersive X-ray spectroscopy (EDX)

After applying the technology EDX to verify the formation of ZnONPs (zinc oxide nanoparticles) showed some signals. Some peaks appeared at 1 keV for zinc atoms. A strong peak was observed at 0.6 keV for oxygen atoms. This confirmed the presence of zinc oxide nanoparticles. Table 2 shows the zinc content of 59.14% and the oxygen content of 34.72%, with some small amounts of sulfur, resulting from the chia extract, which is rich in organic acids and bioactive molecules. as shown in **FIGURE 17** and **TABLE 4**.

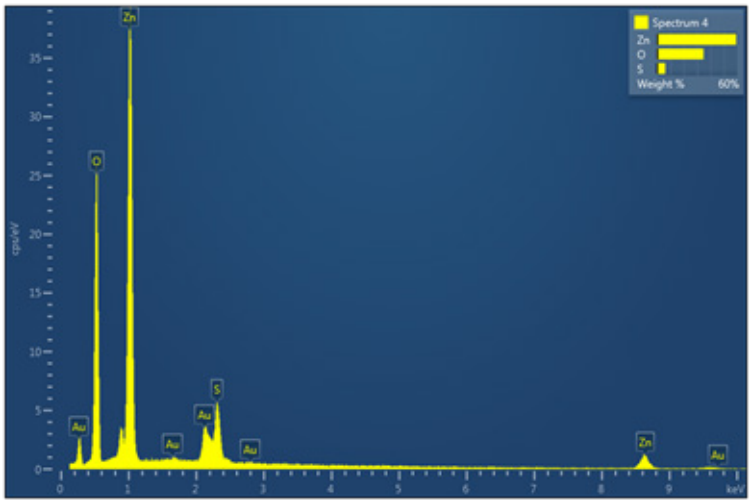


FIGURE 17. Energy dispersive X-ray spectroscopy (EDX) of ZnONPs

TABLE 4. SHOWS THE MOST IMPORTANT BANDS AND DATA OBTAINED FROM (EDX) OF ZNONPS.

Element	Line Type	Apparent Concentration	k Ratio	Wt%	Wt% Sigma	Atomic %	Standard Label	Factory Standard	Standard Calibration Date
O	K series	6:30	0.02121	34.72	0.36	66.44	SiO2	Yes	
S	K series	0.79	0.00685	6.13	0.18	5.86	FeS2	Yes	
Zn	L series	5.36	0.05359	59.14	0.37	27.70	Zn	Yes	
Total:				100.00		100.00			

15. RESULT AND DISCUSSION:

To study the quality of the produced electrode, its detection limits, and its comparison with previous work, as well as to determine the strength, durability, and electrode conditions, and to review the properties of this nanosensor, tests were conducted by varying the solution conditions and concentrations after fabrication to determine the electrode response, linear concentration range, slope value, correlation coefficient, lifetime, detection limit, and other tests.

15.1. Effect of Temperature:

The effect of temperature on the response of the manufactured electrodes can be known by taking 20 ml of the drug solution prepared at concentrations of (10^2,10^4) molar were prepared separately in a (25 mL) beaker. The fabricated electrodes (I, II) were immersed, respectively, with the calomel electrode in the CPH drug solution. Then, the potential was measured after changing the temperature of the two solutions (10^2,10^4) molar from (20-55) degrees Celsius. Then, the relationship was drawn. In the Excel program between the potential difference and temperature, and through the results it was shown that the electrodes give better results by about (20-40°C) A decrease in the potential value of electrodes manufactured at high temperatures is observed. The decrease in the potential value of electrodes with increasing temperatures is explained by the fact that high temperatures lead to the expansion of the pores of the electrode membrane, which means an increase in the surface area of the membrane. Also, high temperatures accelerate the movement of the drug molecules in question; that is, the collisions of the molecules within the drug with each other increase, which leads to irregular ion exchange between the drug in question and the electrode membrane. As a result of these reasons, the potential decreases, as shown in **FIGURES (18,19).**

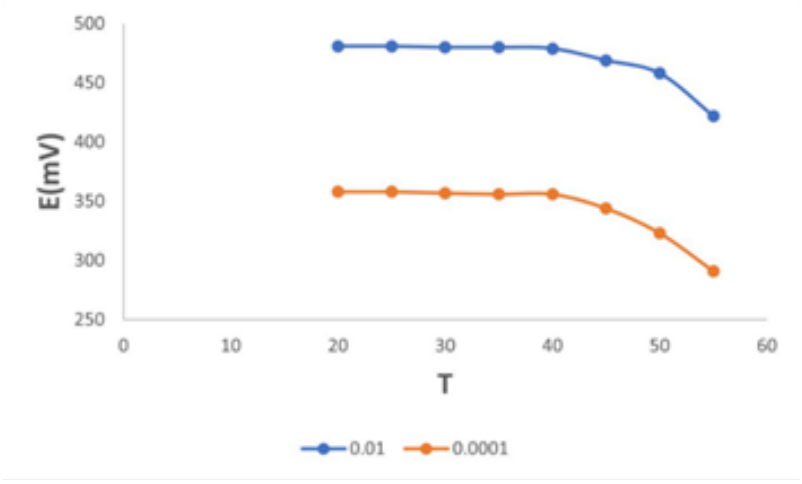


FIGURE 18. Effect of Temperature value on electrode (I)

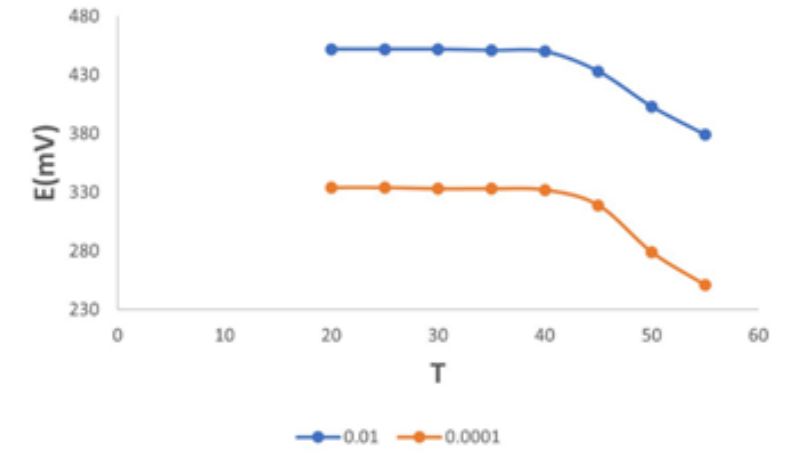


FIGURE 19. Effect of Temperature value on electrode (II)

15-2. Effect of pH:

In order to Know the effect of the acid function on the response of the electrodes that were manufactured, several glass cups with a capacity of 20 ml containing CPH drug and the fabricated electrodes (I,II) were immersed respectively with the calomel electrode in the drug solution at concentrations of (10^2,10^4) M respectively and separately

Then the potential difference was measured with the pH value changing within the range.(2-12) Using a 0.1 molar hydrochloric acid solution and a 0.1 molar sodium hydroxide solution, after each measurement the electrodes were cleaned with distilled water and dried, then the relationship was drawn. in Excel program Between the potential difference and the acidity function, and the results shown in the two **FIG-**

URES (20,21) The acidity function indicates that the response of the two electrodes operates in the range (3-8), that the potential value of the electrodes will decrease when the solution is basic or acidic due to the formation of a white precipitate of the drug or as a result of the formation of the salt of the drug substance when the solution in question becomes cloudy. This is due to the increase in the concentration of hydroxyl in the basic medium and thus will lead to the flocculation of the electrode membrane. However, when the acidity function is low in the acidic medium, we also find a decrease in the potential and the explanation for this is the increase in the hydrogen ion as a result of adding HCl and thus a proton ion doublet will be formed with a weak response to the drug ions.

FIGURE 20. Effect of pH value on electrode (I)

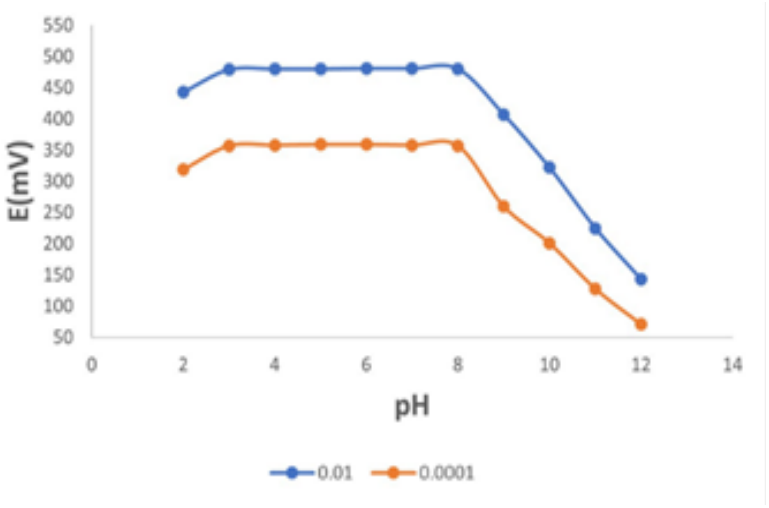
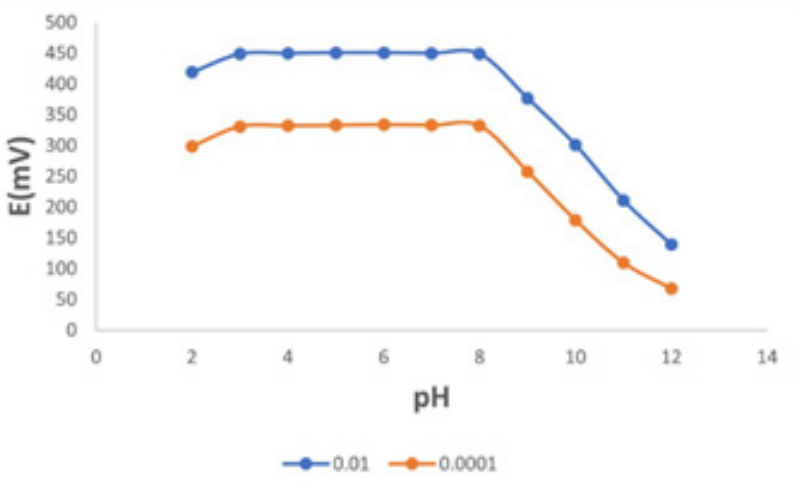


FIGURE 21. Effect of pH value on electrode (II)



15-3 Response Time

After determining the best conditions for the electrode in terms of pH and temperature, the response time of the electrodes was studied (I,II) by taking a 25 ml glass beaker containing 20 ml of the medicine CPH . And at concentrations (10^{-2}_10^{-8}) Molarity was measured separately for the two electrodes (I, II) and the electrodes were immersed with the calomel electrode in the drug solution. Then the voltage was measured. After each measurement, all electrodes were cleaned with distilled water and then dried. Then the relationship was drawn. In the Excel program between response time and voltage, it was found that the lowest response time at which the electrode works(I) 31 seconds for a concentration of 10^8 and for a concentration of 10^2 it is 2 seconds. As for electrode (II), the minimum response time at which the electrode works is 38 seconds for a concentration of 10^8, while for a concentration of 10^2 it is 3 seconds. **FIGURES (22,23)** Below they explain that,

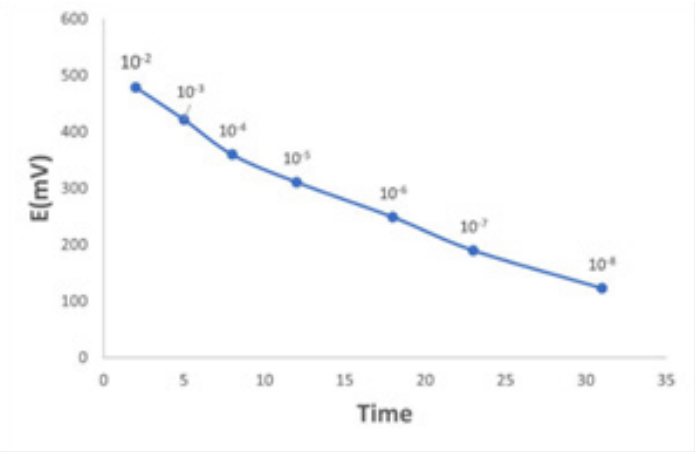


FIGURE 22. Effect of Response Time value on electrode (I)

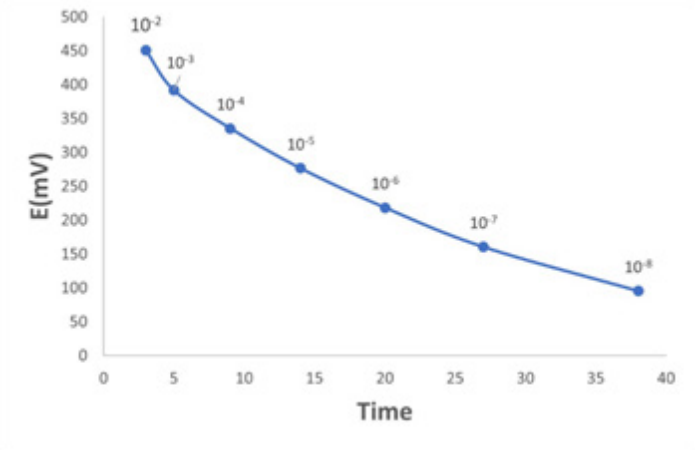


FIGURE 23. Effect of Response Time value on electrode (II)

15-4 The lifespan of the electrode

The lifetime of the electrodes (I,II) must be known. By measuring the potential difference of the drug solution CPH Focused 10^2 molar when a 25 ml beaker is taken and 20 ml of the drug solution is placed in it and the voltage is measured once every two days for of 50 days. The age of the electrode was determined by measuring the voltage over a period of 50 days using the drug solution. The results showed that the measured voltage remained stable during this period. The electrode's lifetime was estimated at 45 days. That is, after this period, the recorded voltage began to decrease. Figures (24,25) below they explain that.

FIGURE 24.
The lifespan of electrode (I)

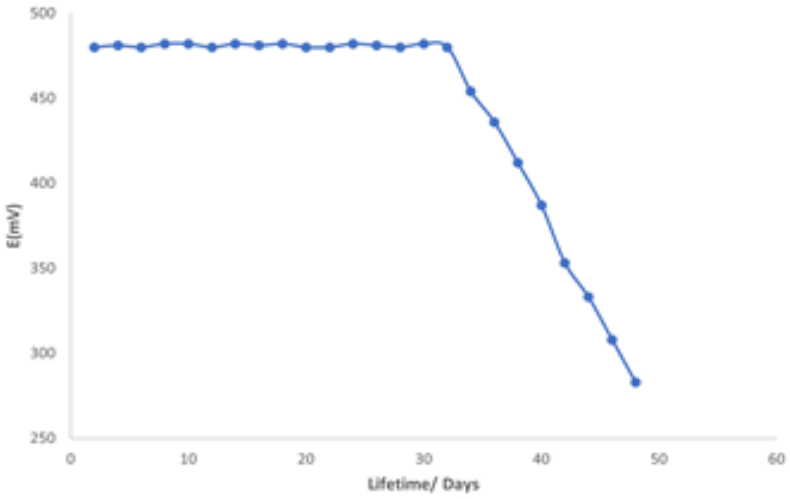
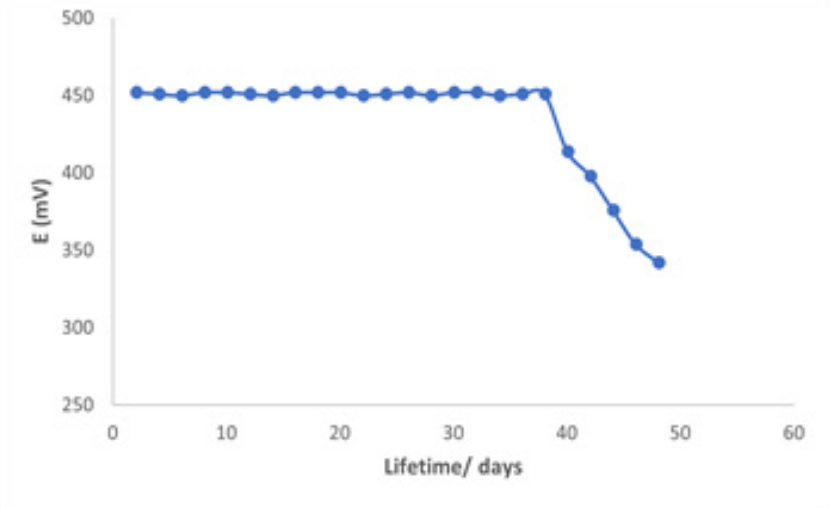


FIGURE 25.
The lifespan of electrode (II)



15-5. Calibration curve

After the electrode test Graphite nanoparticles, a series of different concentrations of the drug solution Cyproheptadine hydrochloride (CPH) were prepared and measured under selected optimum conditions. A calibration curve representing the relationship between the voltage change (mV) and the concentration change (expressed as -log[CPH]) was drawn, as shown **FIGURES (26,27).**

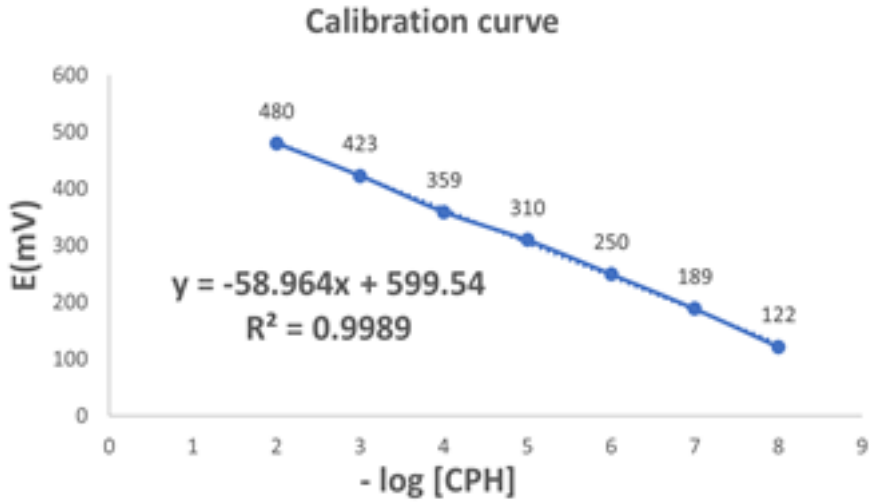


FIGURE 26 Calibration diagram of the nanoelectrode (I)

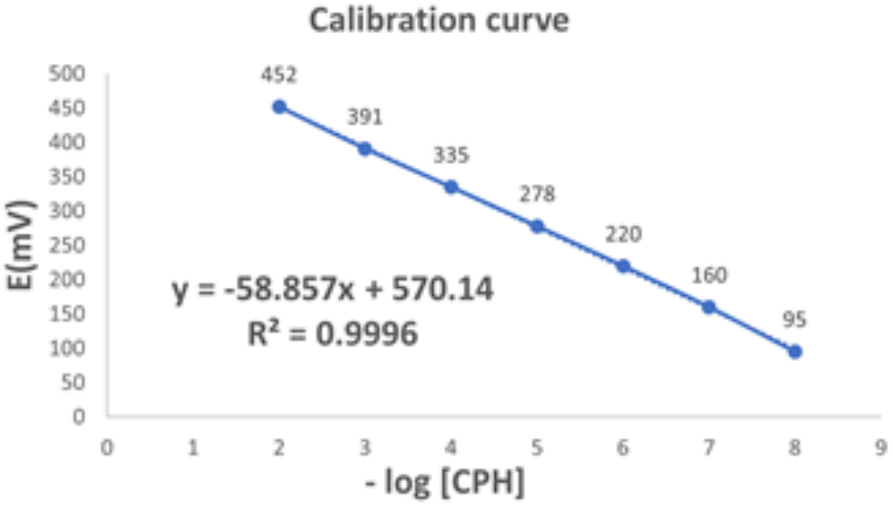


FIGURE 27 Calibration diagram of the nanoelectrode (II)

TABLE 5. SHOWS THE STATISTICAL TREATMENT OF THE CALIBRATION CURVE FOR ELECTRODES (I,II)

Samples	The second electrode			The first electrode		
	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
Pure drug	2.0	2.007	100.35	2.0	2.010	100.50
	3.0	2.993	99.77	3.0	2.994	99.80
	4.0	3.995	99.88	4.0	3.978	99.45
	5.0	4.964	99.28	5.0	5.012	100.24
	6.0	5.949	99.15	6.0	6.013	100.22
	7.0	6.968	99.54	7.0	6.963	99.47
	8.0	8.073	100.91	8.0	8.065	100.81
%mean	99.840.618			100.070.517		
variance	0.382			0.267		
N	7			7		
%SE	0.234			0.195		
%RSD	0.619			0.516		

15-6. Accuracy and Precision:

After the optimum conditions (pH, temperature) were established, the accuracy and compatibility of the fabricated electrodes were calculated (I,II) When the potential was measured for concentrations (10^2,10^4,10^6) molar of the CPH drug solution and located within the linear range through six readings for each concentration used, then the recovery and standard deviation were calculated, where the agreement depends on the standard deviation and the accuracy depends on the recovery results or the relative error. as shown in **TABLE (6)**.

TABLE 6. CALCULATIONS THE ACCURACY AND COMPATIBILITY OF THE FABRICATED ELECTRODES (I,II)

Variance	Recovery %	RSD%	Found -Log conc. mol. L^{1-}	Taken -Log conc. mol. L^{1-}	Electrodes
0.217	100.08	0.465	2.001	2.0	The first electrode
0.199	100.09	0.445	4.003	4.0	
0.161	99.65	0.402	5.979	6.0	
0.217	99.93	0.466	1.999	2.0	The second electrode
0.482	99.73	0.696	3.989	4.0	
0.281	100.14	0.529	6.009	6.0	

From the results shown in Table (6), we note that the recovery values were:(100.08,100.09,99.65)% for electrode I nano coated and was(99.93,99.73,100.14)%For the nano-coated electrode II for the prepared concentrations which were selected from the calibration curve and the highest standard deviation value was for the coated electrode I (0.465) . And the highest standard deviation of the electrode coated was II (0.696) from the results shown above, it is clear that the modified nanoelectrodes (II,I) They highly accurate for this drug.

15-7. Selectivity

The optimum conditions (pH, temperature) were established and the selectivity of the fabricated electrodes was measured (I,II).First, the potential of the standard solution of the studied drug is measured by taking the capacity of the Becker 25 ml contains 10 ml of a drug solution with a concentration of 10^2 M. This potential is symbolized by the symbol Ei. Then, the potential of the interfering substance is measured when 10 ml of it is mixed with 10 ml of the drug at the same concentration that was previously taken from the drug. This potential is symbolized by the symbol Ej. After each measurement, the electrodes must be cleaned with distilled water and then dried. From the results in the table below, we note that the electrodes (I, II) have high accuracy for the drug. The ions that were added, such as (TiO2, Glucose, Maltose, Cross Carmellose, Methyl Cellulose, Magnesium Stearate) do not cause any interaction with the drug CPH. The evidence for this is that the selectivity coefficient value for each ion was less than unity for these electrodes. The results were as shown in **Table (7)**.

TABLE 7. CALCULATIONS THE SELECTIVITY OF THE FABRICATED ELECTRODES (I,II)

Selectivity coefficient		**ion Interfering**
Electrodes		
Electrode II	Electrode I	
0.817	0.791	TiO_2
0.641	0.676	Glucose
0.592	0.650	Maltose
0.785	0.703	Cross Carmellose
0.592	0.731	Methyl Cellulose
0.429	0.535	Magnesium Setrate

15-8. Limit of Detection (LOD) and Limit of Quantity (LOQ)

After the optimal conditions (pH, temperature) are established, the detection limit and the quantum limit of the fabricated electrodes are calculated (I,II) the results were as shown in **Table (8)**.

TABLE 8. CALCULATIONS THE (LOD) AND (LOQ) OF THE FABRICATED ELECTRODES (I,II)

LOQ	LOD	Electrode type
4.01 x 10^9	1.20 x 10^9	The first electrode
11.86 x 10^8	3.55 x 10^8	The second electrode

16. Applications

A- direct method

The property has been assessed Cyproheptadine HCl (CPH) is administered by taking a 25 ml beaker containing 20 ml of the pharmaceutical preparation solution containing the studied drug in five concentrations ranging between (10^3,10^4,10^5,10^6,10^7) molarity separately for solutions prepared for pharmaceutical companies used (Cyproheptadine HCl 2mg/5ml syrup - iraq, Cyproheptadine HCl 2mg/5ml syrup - Egypt, Cyproheptadine HCl PB 4mg Tablets -India ,Cyproheptadine HCl 4mg Tablets - Iraq) Then the manufactured electrodes are immersed (I,II) in series with the calomel electrode in the solutions prepared for measuring the potential. After each measurement, all electrodes must be cleaned with distilled water and then dried. Then, the relationship is drawn. in the Excel program between the negative logarithm of the concentration and the potential to obtain a calibration curve Standard to know the drug concentration directly by applying the straight-line equation. Results shown in (**TABLE9) .**

TABLE 9. APPLICATION RESULTS OBTAINED BY THE DIRECT METHOD USING ELECTRODES (I,II)

pharmaceutical preparation	The second electrode			The first electrode		
	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
CPH 2mg/5ml syrup - iraq	3.0	2.979	99.30	3.0	3.011	100.37
	4.0	4.012	100.30	4.0	4.029	100.73
	5.0	5.015	100.30	5.0	4.995	99.90
	6.0	6.034	100.57	6.0	5.996	99.93
	7.0	6.985	99.79	7.0	7.013	100.19
%mean	100.050.506			100.220.340		
variance	0.256			0.116		
N	7			5		
%SE	0.226			0.152		
%RSD	0.506			0.339		
	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
CPH 2mg/5ml syrup - Egypt	3.0	3.027	100.90	3.0	2.994	99.80
	4.0	3.978	99.45	4.0	3.978	99.45
	5.0	4.998	99.96	5.0	5.012	100.24
	6.0	5.983	99.72	6.0	6.013	100.22
	7.0	7.019	100.27	7.0	6.946	99.23
%mean	100.060.559			99.790.451		
variance	0.313			0.204		
N	5			5		
%SE	0.250			0.202		
%RSD	0.559			0.452		
	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
CPH PB 4mg Tablets -India	3.0	3.01	100.33	3.0	3.028	100.93
	4.0	4.012	100.30	4.0	4.012	100.30
	5.0	5.032	100.64	5.0	4.978	99.56
	6.0	5.966	99.43	6.0	5.9797	99.65
	7.0	6.951	99.30	7.0	7.030	100.43

pharmaceutical preparation	The second electrode			The first electrode		
%mean variance N %SE %RSD	100.000.596 0.355 5 0.267 0.596			100.170.572 0.327 5 0.256 0.571		
CPH 4mg Tablets - Iraq	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
	3.0 4.0 5.0 6.0 7.0	2.993 3.961 5.015 6.000 6.934	99.77 99.03 100.30 100.00 99.06	3.0 4.0 5.0 6.0 7.0	2.977 4.029 4.995 5.962 6.963	99.23 100.73 99.90 99.37 99.47
%mean variance N %SE %RSD	99.630.570 0.325 5 0.255 0.572			99.740.605 0.366 5 0.271 0.607		

B- Standard addition method

The property has been assessed Cyproheptadine HCl (CPH) by the standard addition method, by taking a 25 ml beaker containing 20 ml of the pharmaceutical preparation solution containing the studied drug at five concentrations ranging between (10^3,10^4,10^5,10^6,10^7) molars separately for the solutions prepared for the pharmaceutical companies used (Cyproheptadine HCl 2mg/5ml syrup - iraq, Cyproheptadine HCl 2mg/5ml syrup - Egypt, Cyproheptadine HCl PB 4mg Tablets -India ,Cyproheptadine HCl 4mg Tablets - Iraq) Then the manufactured electrodes were immersed (I,II) are placed in series with the calomel electrode in the solutions prepared for measuring the potential. After each measurement, the electrodes (I,II) must be cleaned with distilled water and then dried. This potential is called E1. After that, 0.1 ml of the standard drug solution is added with the same concentrations used for all companies studied separately. After adding, the potential is measured. This potential is called E2. After that, the change in the potential is measured for all companies studied separately through the law $\Delta E = E2 - E1$. Results shown in **(TABLE10) .**

TABLE 10. APPLICATION RESULTS OBTAINED BY THE STANDARD ADDITION METHOD USING ELECTRODES (I,II)

pharmaceutical preparation	The second electrode			The first electrode		
	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
CPH 2mg/5ml syrup - iraq	3.0	3.027	100.90	3.0	3.028	100.93
	4.0	4.029	100.73	4.0	3.995	99.88
	5.0	4.981	99.62	5.0	4.978	99.56
	6.0	5.949	99.15	6.0	6.013	100.22
	7.0	7.002	100.03	7.0	7.030	100.43
%mean	100.080.736			100.200.526		
variance	0.542			0.276		
N	5			5		
%SE	0.329			0.235		
%RSD	0.735			0.525		
CPH 2mg/5ml syrup - Egypt	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
	3.0	2.967	99.20	3.0	2.977	99.23
	4.0	3.978	99.45	4.0	4.012	100.30
	5.0	5.032	100.64	5.0	4.961	99.22
	6.0	6.017	100.28	6.0	5.949	99.15
	7.0	6.968	99.54	7.0	7.013	100.19
%mean	99.820.609			99.620.573		
variance	0.371			0.328		
N	5			5		
%SE	0.273			0.256		
%RSD	0.610			0.575		

pharmaceutical preparation	The second electrode			The first electrode		
CPH PB 4mg Tablets -India	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
	3.0	3.010	100.33	3.0	2.994	99.80
	4.0	3.995	99.88	4.0	4.012	100.30
	5.0	4.981	99.62	5.0	4.961	99.22
	6.0	6.034	100.57	6.0	5.979	99.65
	7.0	7.019	100.27	7.0	6.964	99.49
%mean	100.130.380			99.690.403		
variance	0.144			0.162		
N	5			5		
%SE	0.170			0.180		
%RSD	0.379			0.404		
CPH 4mg Tablets - Iraq	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %	Taken -Log conc. mol. L^{1-}	Found -Log conc. mol. L^{1-}	Recovery %
	3.0	2.993	99.77	3.0	3.011	100.37
	4.0	4.012	100.30	4.0	3.978	99.45
	5.0	5.015	100.30	5.0	5.012	100.24
	6.0	5.966	99.43	6.0	5.996	99.93
	7.0	6.934	99.06	7.0	6.963	99.47
%mean	99.770.544			99.890.424		
variance	0.296			0.180		
N	5			5		
%SE	0.243			0.190		
%RSD	0.545			0.425		

CONCLUSIONS

In this research, green chemistry methods were used because they are safe, cheap, easy to use, non-hazardous, do not use chemicals, and rely on electrochemistry. We studied the potential difference after manufacturing nanoelectrodes, made of calcium and zinc, which represent nanomaterial-coated graphite electrodes for drug testing in its pure form and in its pharmaceutical formulations. Through this study, the results showed that the electrodes coated with nano oxides have high selectivity and sensitivity, in addition to a faster response time and stable results. This is due to the properties of nanoparticles in the electrophoresis process, which have a larger surface area and smaller volume, making them more sensitive and selective. These properties enabled us to study the drug (CPH) with wide concentration ranges and low thresholds. The high sensitivity of nanoparticle-coated electrodes is due to the rapid movement of drug ions toward the coating, a result of the excellent physical and chemical properties of these particles. These nanoparticle-coated electrodes can be relied upon for CPH detection in pharmaceutical and research facilities.

REFERENCES

1. Patel K, Abhale Y, Oza R, Lin KYA, Larios AP, Ghotekar S. Green Silver Nanoparticles for Nanoremediation. In: Green Nanoremediation. Cham: Springer International Publishing; 2023. p. 253–74.

2. Abida A, Almutairi MH, Mushtaq N, Ahmed M, Sher N, Fozia F, et al. Revolutionizing Nanotechnology with Filago desertorum Extracts: Biogenic Synthesis of Silver Nanoparticles Exhibiting Potent Antioxidant and Antibacterial Activities. ACS Omega. 2023 Sep 26;8(38):35140–51.

3. Mahendra Kumar S, Rajni Y, Sandeep Prasad T. Recent advances in nanotechnology. International Journal of Nanomaterials, Nanotechnology and Nanomedicine. 2023 Sep 15;9(2):015–23.

4. Silva Brito R, João Bebianno M, Rocha TL. Plant-based silver nanoparticles ecotoxicity: Perspectives about green technologies in the One Health context. Crit Rev Environ Sci Technol. 2024 Aug 17;54(16):1218–35.

5. Veeramani C, El Newehy AS, Aloud AA, Alsaif MA, Al-Numair KS. Nutritional plants, phytochemicals, microorganisms-derived silver nanoparticles and their diabetic managements. In: Silver Nanoparticles for Drug Delivery. Elsevier; 2024. p. 241–64.

6. Subramanian V, Peijnenburg WJGM, Vijver MG, Blanco CF, Cucurachi S, Guinée JB. Approaches to implement safe by design in early product design through combining risk assessment and Life Cycle Assessment. Chemosphere. 2023 Jan;311:137080.

7. Khan F, Shariq M, Asif M, Siddiqui MA, Malan P, Ahmad F. Green Nanotechnology: Plant-Mediated Nanoparticle Synthesis and Application. Nanomaterials. 2022 Feb 17;12(4):673.

8. Robert W. Cattrall. Chemical sensors. 1997 Nov 27;78.

9. Xu T. Ion exchange membranes: State of their development and perspective. J Memb Sci. 2005 Oct;263(1–2):1–29.

10. Chauhan MK, Sachdeva A, Ansari L, Gugulothu D. Manufacturing Process of Nanoparticles. In 2023. p. 151–72.

11. Adebayo AO, Alli YA, Bamisaye A, Adewuyi S. Nano chitosan anchored copper-ferrite: a smart magnetic nanocomposite agent for drug delivery. Emergent Mater. 2024 Feb 14;7(1):343–51.

12. Atiyah MI, Al-Samarrai SY, Al-Hayawi AY. A new spectrophotometric method for sensing promethazine hydrochloride in its pharmaceutical formulation and in biological fluids using copper nanoparticles (CuNPs). Sensors and Machine Learning Applications. 2023 Jun 29;2(2).

13. Raghu MS, Basavaiah kanakapura. Application of Ion-Association Titration for the Assay of Cyproheptadine Hydrochloride in Pharmaceuticals. ISRN Analytical Chemistry. 2012 Mar 25;2012:1–7.

14. Hussien EM, Abdel-Gawad FM, Issa YM. Ion-selective electrodes for determination of fluoxetine in capsules and in biological fluids. Biochem Eng J. 2011 Jan;53(2):210–5.

15. Ejeian F, Sadeghi S, Zargar M, Arshadi F, Noorisafa F, Razmjou A. Ion Selective Membranes. In: Encyclopedia of Materials: Electronics. Elsevier; 2023. p. 308–22.