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Spectrophotometric determination of metoclopramide hydrochloride using Co_3O_4 nanoparticle synthesised from the extract of rosemary

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Abstract

Background: A simple, sensitive and economical spectrophotometric method was proposed for the determination of Metoclopramide hydrochloride in its pure form and its pharmaceutical formulation Meclodin using Cobalt oxide nanoparticles prepared by extracting of rosemary. Measurements were made at Tikrit University, College of Science, during the period from 2024/3/1 to 2023/11/25.

Results: Spectroscopic measurements gave the highest absorption value at the wavelength of 275 nm for the mixture of nano solution and drug, and the linear relationship followed the Beer-Lambert law in the concentration range (2-26 $\mu\text{g/mL}$) with a good correlation coefficient, where its value reached $R = 0.9988$, which indicates good linearity. The molar absorption coefficient value = $1.6900 \times 10^4 \text{ L/mol.cm}$, and the Sandell's significance value = $0.0209 \mu\text{g/cm}^2$. The proposed method was validated statistically and quantitatively, with a detection limit value = $0.1257 \mu\text{g/mL}$ and a quantitative limit value = $0.4192 \mu\text{g/mL}$.

Conclusion: concluded from this study the success of the method used in the production of nanomaterials from green sources, and thus the trend towards green synthesis methods became more desirable because it is characterized by ease of preparation, low cost and no need to use materials harmful to the environment, and it was also concluded that when the drug Metoclopramide hydrochloride was associated with $\text{Co}_3\text{O}_4\text{NPs}$ increased The wavelength value ranged from 270 nm (for $\text{Co}_3\text{O}_4\text{NPs}$) to 275 nm when adding the drug to the particle solution (taking into account ideal conditions) as evidence of the association between these particles and the drug solution.

Keywords: Metoclopramide, $\text{Co}_3\text{O}_4\text{NPs}$, spectroscopy, extracting of rosemary, green synthesis

Introduction

Green chemistry is a modern field focused on developing environmentally friendly materials, making it an ideal way to reduce environmental pollution ^[1]. In addition to reducing the use of substances that are harmful to humans and the environment ^[2]. One branch of green technology is green nanotechnology, which uses the concepts of green chemistry and green plants. The products, processing and application of nanotechnology aim to make a significant contribution to the protection of the environment and climate, saving raw materials, energy and water, reducing greenhouse gas emissions, global warming and pollutants that turn into nanomaterials in the range of 1 to 100 nanometers ^[3]. Nanotechnology has helped change the rules of medicine used in preventing, diagnosing and treating diseases, as it provides new ways for nano-medicine carriers that can target different cells to enter the body ^[4], and the role of phytochemicals in the overall structure, architecture, and other properties of attractive nanoparticles. It is more than that, because it provides the necessary balance between plant science and nanotechnology, and this balance guides progress in nanotechnology ^[5]. The main reason for using plant extracts in the production of nanomaterials is that they are easy to obtain, safe and do not cause toxic effects on the body like chemical preparations. Toxic chemicals are absorbed from the surface and cause serious side effects when used in medicine ^[6]. The main reaction that occurs when using plant extracts is the oxidation-reduction reaction ^[7]. The size of the material class is (1-100) nanometers, and the small size of these materials makes their properties different from existing materials of their size (more

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than 100 nanometers) [4, 8], Nanoparticles contain more surface atoms than fine particles, which leads to increased performance, and this difference has led to their use in many applications. Fields such as medicine, catalysis, sensors, optoelectronics, food industry, textile industry and agriculture [9], Cobalt particles were selected for this study based on their magnetic characteristics. Because of their potential impact in a variety of technical applications, including data storage, magnetic fields, information storage devices, and sensing devices, cobalt oxide nanoparticles are essential oxides for scientific research [10]. Nowadays, instead of being used as antibacterial agents, cobalt nanoparticles are usually treated as magnetic nanoparticles, with very little [11] investigations examining the antibacterial properties of cobalt oxide at the nanoscale [12]. However, they share a high surface area to volume ratio with other nanoparticles, which increases their chemical reactivity and renders nano-sized cobalt oxide potentially effective as antibacterial agents in biomedical applications [13]. The hydrothermal approach is one of the popular synthesis techniques for producing cobalt oxide particles that have been documented in the literature [14, 15], solvothermal decomposition [16], laser deposition [17], chemical vapor deposition [18], spray pyrolysis [19], plasma sputtering [20], solid phase thermal decomposition [21], mechano-chemical processing [22], gamma-radiolysis [23] and so on.

Metoclopramide hydrochloride (MCP-HCl), 4-amino-5-chloro-2-methoxy-en-(2-2-diethylamine-ethyl)benzamide, is often used in patients with gastrointestinal disturbances and is therefore used to treat nausea Vomiting and also for the treatment of patients suffering from migraines as appear in Fig. 1 and is 354.3 g/mol that molecular weight of MCP, it is a white crystalline powder, soluble in water easy but soluble in alcohol freely, 183 °C that melting point of MCP drug in Fig. 1 and is 354.3 g/mol that molecular weight of MCP, it is a white crystalline powder, soluble in water easy but soluble in alcohol freely, 183 °C that melting point of MCP drug [11].

It is a medication used to treat nausea and vomiting and is usually administered orally or by injection. It works by stimulating intestinal motility and accelerating the passage of food from the stomach to the intestines. It is also used to treat gastrointestinal motility disorders and constipation [24].

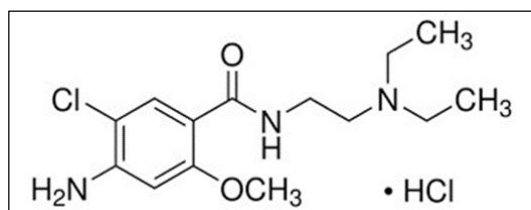


Fig 1: Chemical Structure of metoclopramide hydrochloride

Materials and Methods

Instruments

- UV-VIS spectrophotometric - Shimadzu 1800 a double beam with a pair of 1 cm matched quartz cell, Japan.
- A sensitive balance - Sartorius-Entris224-1S.
- pH scale - JENWAY PH-meter 3310
- Burning furnace - Sci Finetech-Muffle furnace-FTMF-705
- FT-IR spectrometer - Shimadzu FTIR_8400s
- Hot plate & magnetic stirrer - Lab Tech
- Dissolution apparatus - Rigg Etec -Germany

- Drying oven - Memmert-Modell 100-800
- water bath - Faithful - China
- X-ray diffraction apparatus - Iran / XRD Lab-
- Scanning electron microscope - Iran / XRD Lab-

Chemical materials

- Metoclopramide hydrochloride drug solution at a concentration of 100 µg/ml was prepared from 0.0100 g of metoclopramide hydrochloride powder in a small amount of non-ionic water with thorough stirring, then the volume was completed to the mark using a 100 ml volumetric flask and the remaining concentrations were prepared by dilution.
- The pharmaceutical preparation of metoclopramide hydrochloride 10mg from local pharmacies was prepared at a concentration of 100 µg /ml by grinding 5 tablets with a total weight of 0.8782g to obtain 0.1796g of the active substance. Then, 0.01g of the powder was dissolved in a small amount of deionized water with thorough stirring, and the volume was completed to the mark using a 100ml volumetric flask, and the remaining concentrations were prepared by dilution.
- Aqueous cobalt chloride (CoCl₂·6H₂O) was provided from the inorganic chemistry laboratory at Tikrit University by taking 2.7 g of it and dissolving it in a small amount of deionized water, then completing the volume to the mark in a 100ml volumetric flask to obtain a concentration of 0.1M.
- The HCl solution was prepared by taking 0.83 mL of its concentrated solution and diluting it with nonionic water using a 100 mL volumetric vial to obtain a concentration of 0.1 M
- The sodium hydroxide solution was prepared by dissolving 0.4 g of sodium hydroxide in an amount of nonionic water using a 100 mL volumetric bottle, then the volume was completed to the mark with the same solvent De-ionized water as a solvent.

Application of the methodology part

Preparation of herbal extract

The rosemary leaves that were gathered from the home garden were used to make the herbal extract. After gathering the leaves, they were cleaned with tap water to get rid of any dirt, and then they were repeatedly rinsed with distilled water. They were allowed to dry in the shade, then processed into a powder using an electric grinder, sieved, and put in a container for storage.

Weighing out 5 g of the powdered rosemary leaves, we put them in a glass beaker. Using a magnetic stirrer, 100 milliliters of deionized water was added and continually stirred. After 30 minutes of boiling at 80 °C, the mixture was allowed to cool to room temperature. Filter paper was then used to filter it.

Preparation of cobalt oxide nanoparticles

After weighing and thoroughly mixing 2.7 g of CoCl₂·6H₂O in 100 ml of deionized water, the solution was completely dissolved. Next, 50 ml of the produced extract was added using a pipette, dropwise, and constant stirring at 20 °C. The solution was then brought to 80 °C and left on a heater for four hours. The mixture's pH was brought to 8 by adding 0.1M sodium hydroxide solution.

The fluid turned brown and a precipitate formed at the bottom when the magnetic stirring operation was finished.

After a 12-hour incubation period at room temperature, the precipitate was filtered through filter paper and deionized water was used to eliminate any remaining contaminants. After being dried for six hours at 80 °C, the precipitate was put into a calcination furnace and heated to 400 °C for two hours. After being calcined, the produced material was gathered, and 0.1 g of it was immersed in an ultrasonic bath at 60 °C for 15 minutes together with a little amount of deionized water in a container. After that, the volume was filled to the brim in a 100 ml volumetric flask to create a Co_3O_4 solution for use in later tests.

In a 10-milliliter volumetric flask, 1 milliliter of methoclopramide hydrochloride solution (concentration:

100 $\mu\text{g}/\text{ml}$) is added to 5 milliliters of $\text{Co}_3\text{O}_4\text{NPS}$ solution. The mixture is then diluted with deionized water and its absorption spectrum is measured. It was discovered that the absorbance at 275 nm was the highest. Multiple spectrum measurements were used to change the reaction conditions in order to assess the impact of different elements, such as the addition of hydrochloric acid, the ideal amount of acid to add to the solution, and the ideal volume of the nanomaterial solution.

Using a 10 ml volumetric flask, the following measurements were made. The findings were as follows: Figure (2) illustrates how hydrochloric acid produced a distinct effect by increasing absorbance.

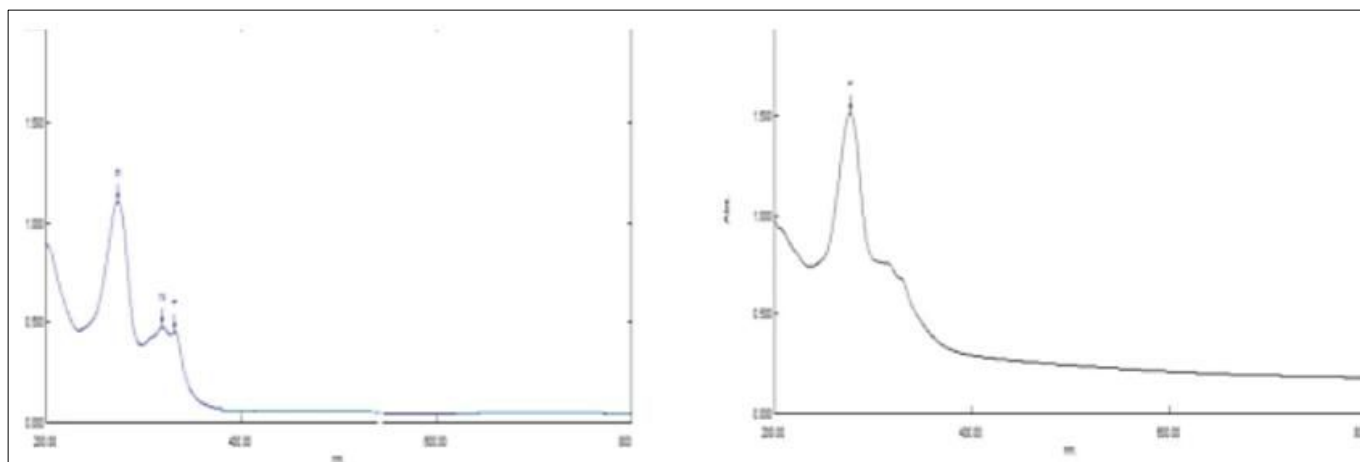


Fig 2: (A) MCP+ $\text{Co}_3\text{O}_4\text{NPS}$, (B) MCP+ $\text{Co}_3\text{O}_4\text{NPS}+\text{HCl}$

The best volume of hydrochloric acid that was mixture of the nano solution and the drug (mix ratio 1:5 ml) is 1.5 ml as show in in Figure 3.

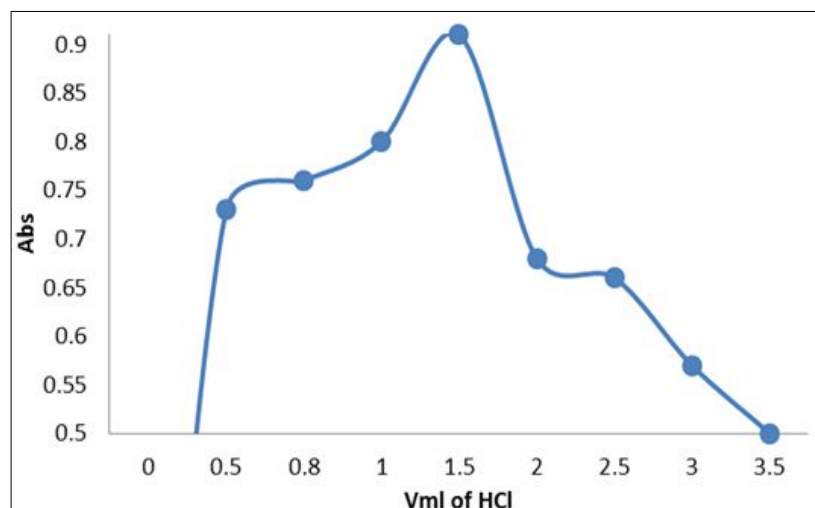


Fig 3: Volume of the optimal acid

And the best volume of $\text{Co}_3\text{O}_4\text{NPs}$ solution is 3ml as show in in Fig (4).

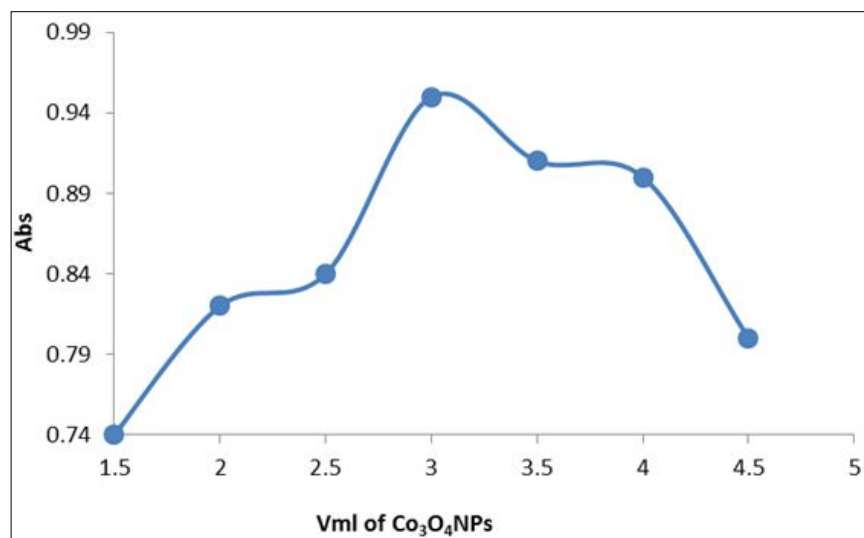


Fig 4: The optimal volume of Co₃O₄NPs

Following these modifications, a 10 mL volumetric flask containing escalating doses of the medication was filled with 3 mL of Co₃O₄ NPs, 1.5 mL of hydrochloric acid at pH 1.2, and deionized water to create the calibration curve for metoclopramide hydrochloride.

At a wavelength of 275 nm, the absorbance of the solutions was measured. Figure 5 displays the outcome of the calibration curve. And the correlation coefficient $R = 0.9988$, the Sandel significance of $0.0209 \mu\text{g}/\text{cm}^2$, and the molar absorption coefficient of $1.6900 \times 10^4 \text{ L}/\text{mol}\cdot\text{cm}$ were all determined.

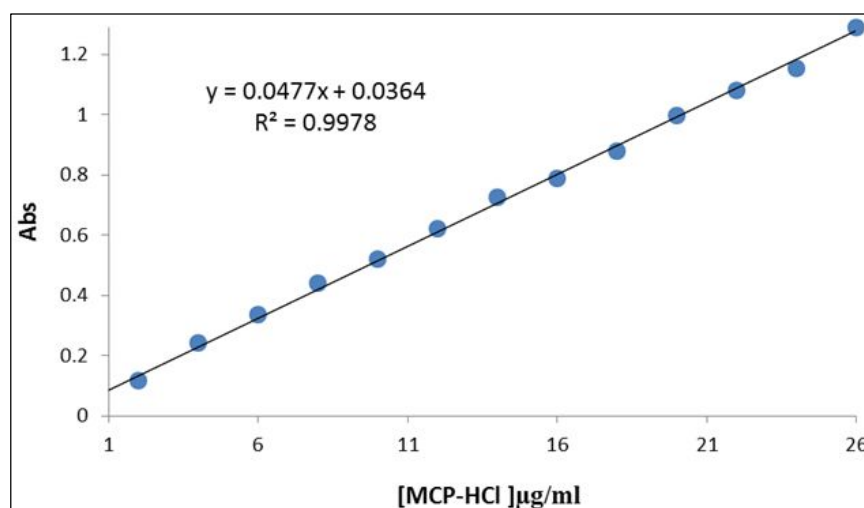


Fig 5: Calibration curve

Accuracy and precision

Three different concentrations of metoclopramide hydrochloride solution were taken within the limits of Fanon Beer-Lambert in the calibration curve, at a rate of three readings for each concentration, and from the results of the

calculations of the recovery rate (Rec.%) and deviation. These conditions were used to carry out the accuracy and precision test for this study.

Table (1) illustrates the high accuracy and good precision of the relative standard (RSD %) approach.

Table 1: Accuracy and precision

Taken MCP-HCl $\mu\text{g}/\text{ml}$	Found MCP-HCl $\mu\text{g}/\text{ml}$	% Recovery	Average of % Recovery	% R.S.D
6	5.74	95.66	97.42	0.29
10	9.81	98.1		0.47
14	13.8	98.5		0.13

The Limit of Detection (LOD) and the Limit of Quantity (LOQ) were calculated using the following mathematical relationship

$3\delta/S$ is the LOD.

$10\delta/S$ is the value of LOQ.

The value of b , or δ , the relative deviation of the intersection resulting from the straight line equation ($Y=aX+b$), is found using a five-time calibration curve. The slope value of the calibration curve, represented by S , is $0.4192 \mu\text{g}/\text{mL}$ for the quantitative limit and $0.1257 \mu\text{g}/\text{mL}$ for the detection limit.

Metchlopramide HCl was subjected to the direct technique. pharmaceutical preparation (Meclodin 5 mg), where three different concentrations of the preparation solution were taken, which are 4,8,12 $\mu\text{g/mL}$, the solution was treated with the same steps for preparing a calibration curve for a pure

solution of Metchlopramide HCl, and measuring its absorption at a wavelength of 275 nm, as well as calculating the recovery rate and its relative standard deviation, as in Table (2).

Table 2: Direct method to the pharmaceutical preparation

Taken MCP-HCl $\mu\text{g/mL}$	Found MCP-HCL $\mu\text{g/mL}$	% Recovery	Average of % recovery	%R.SD
14	13.37	95.5	97.37	0.43
16	15.94	99.37		0.10
18	17.47	97		0.32

Diagnosis of nanoparticles

Diagnosis of nano-cobalt oxide by FTIR

The present investigation recorded the infrared spectra of hydrated cobalt chloride salt ($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$) prior to the cobalt oxide nanoparticle creation reaction, as depicted in Figure (6) following the preparation of the particles as potassium bromide (KBr) discs within the (4000-400) cm^{-1} range. The identification of the absorption bands was followed by an attempt to interpret them using the literature, taking note of the variations in these bands' positions and intensities. Absorption bands were visible in the spectra of the hydrated cobalt chloride salt at (640, 808, 1643, 3404

cm^{-1}). The vibration of the hydroxyl group (O-H) is represented by the absorption band at (1643 cm^{-1}). The vibrations of (Cl-Co-Cl) correspond to the absorption band at 808 cm^{-1} , and the vibrations of (Co-Cl) correspond to the band at 640 cm^{-1} .

The synthesized cobalt oxide nanoparticles exhibit novel absorption bands at 671 and 578 cm^{-1} in their infrared spectra. The vibrations of (O-Co-O) correspond to the absorption band at 671 cm^{-1} , while the vibrations of (O-Co) are represented by the band at 578 cm^{-1} , which is devoid of any other bands. According to Figure (7).

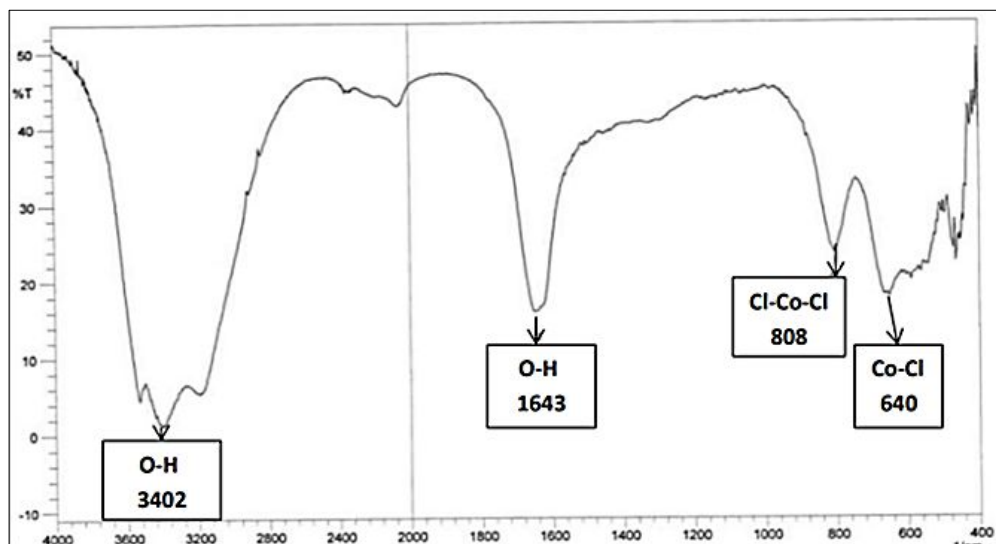


Fig 6: Shows the infrared spectrum of aqueous cobalt chloride

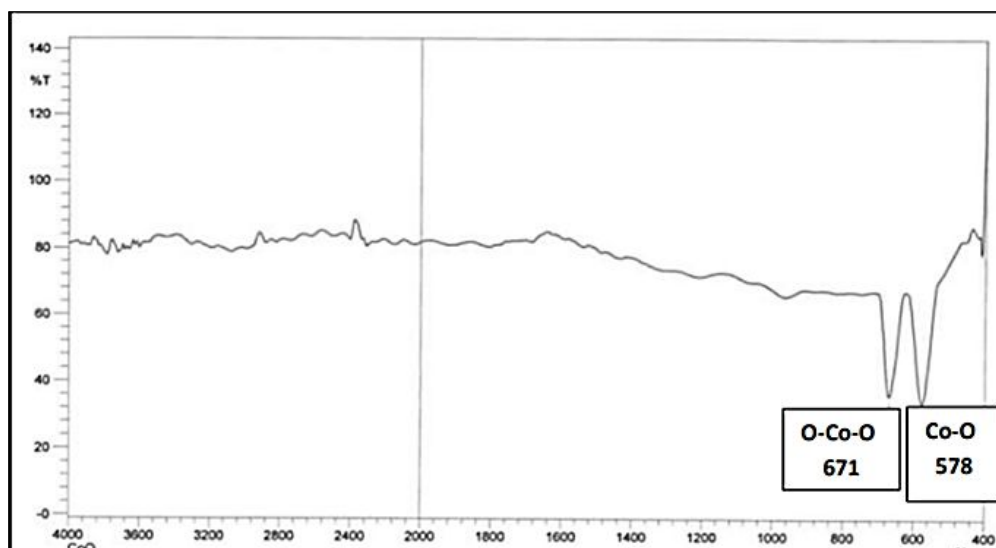


Fig 7: Shows the infrared spectrum of cobalt oxide nanoparticles

Diagnosis of nano- cobalt oxide by SEM

Using a scanning electron microscope, the morphological and structural characteristics of cobalt oxide nanoparticles were examined. The nanoparticles were generated in the nanoscale range, as Figure 8 demonstrates. The SEM pictures showed that while most of the nanoparticles are present in an agglomerated form, some of them are well separated from one another. In addition to the impact of aqueous suspension, electrostatic factors also contribute to this agglomeration, which is consistent with earlier research.

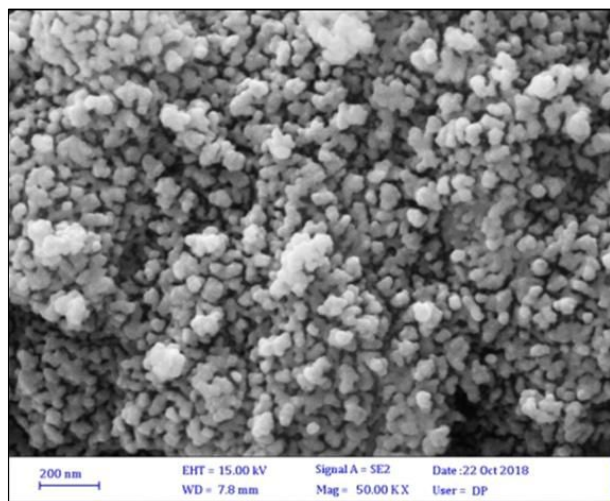


Fig 8: Scanning Electron Microscope (SEM) image of cobalt oxide nanoparticles

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