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## CHARACTERIZATION AND APPLICATION OF NANOMATERIALS

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## Emerging frontiers: Harnessing the power of CNT/GO-based biosensors for early disease biomarker detection

by Amirul Islam Saddam, Md. Rakibul Islam, Razu Shahazi, Md. Kawsar Mahamud, Mohammed Muzibur Rahman, Md. Mahmud Alam

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# Characterization and Application of Nanomaterials

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### **Characterization and Application of Nanomaterials**

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#### Article

### Advanced tungsten-containing materials manufacturing from its scrap

### Levan Chkhartishvili<sup>1,2,\*</sup>, Natia Barbakadze<sup>3</sup>, Otar Tsagareishvili<sup>2</sup>, Archil Mikeladze<sup>2</sup>, Tamaz Batsikadze<sup>4</sup>, Manana Buzariashvili<sup>3</sup>, Tamar Dgebuadze<sup>3</sup>, Roin Chedia<sup>2,3</sup>

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Abstract: We develop a relatively cheap technology of processing a scrap in the form of already used tungsten-containing products (spirals, plates, wires, rods, etc.), as well not conditional tungsten powders. The main stages of the proposed W-scrap recycling method are its dispersing and subsequent dissolution under controlled conditions in hydrogen peroxide aqueous solution resulting in the PTA (PeroxpolyTungstic Acid) formation. The filtered solution, as well as the solid acid obtained by its evaporation, are used to synthesize various tungsten compounds and composites. Good solubility of PTA in water and some other solvents allows preparing homogeneous liquid charges, heat treatment of which yield WC and WC-Co in form of ultradispersed powders. GO (Graphene Oxide) and PTA composite is obtained and its phase transition in vacuum and reducing atmosphere  $(H_2)$  is studied. By vacuum-thermal exfoliation of GO-PTA composite at 170-500 °C the rGO (reduced GO) and WO<sub>2.9</sub> tungsten oxide are obtained, and at 700 °C-rGO-WO<sub>2</sub> composite. WC, W<sub>2</sub>C and WC-Co are obtained from PTA at high temperature (900–1000 °C). By reducing PTA in a hydrogen atmosphere, metallic tungsten powder is obtained, which was used to obtain sandwich composites with boron carbide B<sub>4</sub>C, W/B<sub>4</sub>C, and W/(B<sub>4</sub>C-W), as neutron shield materials. Composites of sandwich morphology are formed by SPS (Spark-Plasma Sintering) method.

**Keywords:** tungsten scrap; hydrogen peroxide; peroxpolytungstic acid; graphene oxides; composites; vacuum-thermal exfoliation; tungsten carbides and alloys; spark-plasma sintering; tungsten–boron carbide sandwich composites

#### 1. Introduction

Modern technologies widely use the tungsten-containing alloys, compounds and composites to produce hard materials, cutting tools, drills, heating elements, weapons, electronics, catalysts, sensors, coatings, abrasives, dry lubricants, colorants, etc. This results in permanent increasing the demand for such class of materials. Tungsten W is a rare metal (it makes up just a miniscule of the Earth's crust). Usually, it is found in the form of ferberite and huebnerite minerals. The main industrial applications have scheelite and wolframite. Currently, China controlling 80% of tungsten world production partially restricts the export due to which the price of tungsten (as well as its compounds) on the world market has increased significantly. For example, metallic tungsten is separated from ore by turning it into ammonium paratungstante, the price of which increased 9 times from 2003 to 2011. At present, the development of economical and efficient technologies for the mining and processing of ores or scraps

is of great importance [1,2]. Unconditioned powders, plates, spirals, rods and other products of tungsten and its alloys are collected in various technological processes, which can be processed by various methods. Tungsten has a high melting temperature (3410 °C), so it is impossible to separate metallic tungsten from scrap by melting. For this purpose, chemical processes, which include several steps, are widely used. One commonly used method (in simplified scheme) is to obtain a tungsten compound from scrap, mainly WO<sub>3</sub>. Its reducing with hydrogen to metallic tungsten, adding other components, and sintering yield the final product. Therefore, the recycling and utilization of tungsten and its compounds from used materials, machine parts, or tools is of great importance [3–7]. In particular, cobalt-cemented tungsten carbide WC–Co is produced in large quantities and, therefore, a large amount of scrap is collected. Its processing methods (so-called direct and chemical recycling and melting metallurgical processes) are quite well optimized [1,8,9].

In the paper [10], the recycling of industrial scrap (i.e., new scrap) and used products (i.e. old scrap) was discussed. Because of tungsten's diverse uses, numerous types of scrap were available for recycling by a wide variety of processes. In 2000, around 46% of US tungsten supply was derived from scrap. The percentage ratio of tungsten consumed from new scrap to that consumed from old scrap was estimated to be of 20:80. Of all the tungsten in old scrap available for recycling, around 66% was either consumed in the US or exported to be recycled.

For last decades, to remove it from tool scrap and utilize by making the new hard instruments a number industrial technologies of tungsten extracting from tungstencontaining scrap have been developed. The methods implemented so far usually are characterized both by some examples of strengths and weaknesses. Generally, when selecting ways to recycle a tungsten waste, it is important to take into account technological process' simplicity, productivity, energy costs, and environmental friendliness [11–14].

The description of currently available ways of processing of tungsten-containing hard materials has been given in paper [15]. Here we list the main methods used to recycle such kind waste in the production of tungsten-containing hard alloys: (i) dispersion of sintered waste first with a crusher and then product grinding into fine fractions; (ii) waste decomposition by chemical-metallurgical methods with strong oxidizers, product pouring, crushing and leaching; (iii) waste chlorination in the presence of carbon dioxide to obtain tungsten chloride, product purification, conversion into tungsten oxides and reducing; (iv) waste heating to high temperature, product oxidizing in air and reducing WO<sub>3</sub>; (v) first waste oxidizing and then product chlorinating to trap the tungsten chloride; (vi) electrochemical processing of waste solution in ammonia, alkaline or salts; (vii) hydro- or pyrometallurgical processing of sawdust; (viii) fine-grained grinding, quenching and crushing the forged mass; (ix) dissolution with sodium hydroxide, precipitation in hydrochloric acid, precipitation and purification of ammonium paratungstate with ammonia, and reduction to tungsten with hydrogen; (x) thermal regeneration in oxidation-reduction-carbidization process; etc.

As mentioned, tungsten carbide–cobalt WC–Co hard alloy is widely used tool material. It is why frequently, tungsten-containing waste contains cobalt as well. Presence of cobalt makes a problem because forming the cobalt tungstate hampers the

complete removal of tungsten itself. Analysis of studies on the tungsten waste regeneration from hard alloys containing cobalt showed that selective extraction of cobalt could be done by chemical (chlorine and zinc) and thermochemical and hydroand pyrometallurgical methods, as well as a technology based on explosive energy consumption.

Development in such industrial technologies solves the tungsten-containing superhard alloys and scrap materials recycling problem and, in this way, helps in their rehabilitation and, respectively, savings of these expensive raw materials. The regeneration process of hard alloys under the influence of shock waves is also processed. Through the direct regeneration of secondary raw materials, this highly efficient production technology allows, without thermochemical and metallurgical processes, obtaining the powders of hard alloys useful to create the tools. This technology differs from the existing ones in terms of high technical and economic indicators, high performance, low energy consumption and environmental friendliness. The recovery of the tungsten-containing mixture is carried out under conditions of high-pressure gradients and delivery velocities in cylindrical reaction ampoules subjected to the impact caused by the detonation of an axially symmetric explosive charge.

In our opinion, the processing of unconditioned tungsten powders by using spirals, plates and other products into tungsten compounds is best done by a relatively simple environmentally friendly technology, which involves obtaining of PTA (PeroxpolyTungstic Acid) from scrap metal by reacting it with hydrogen peroxide. Unlike other methods, only oxygen is released in this process, which is not a harmful substance for the environment. By crushing tungsten spirals and dissolving the obtained powder in hydrogen peroxide solution (30%), PTA was obtained in [16]. The optimum dissolving temperature is 60 °C. The ability of W and Mo as well to dissolve in  $H_2O_2$  solution was used to remove and separate them [17]. Investigation of thermal decomposition of peroxotungstic and peroxomolybdic acids confirmed that peroxomolybdic acid showed a preferable stability compared with PTA. This thermal stability difference can serve for the basic principle of the separation of W and Mo.

Method of dissolving tungsten in a solution of hydrogen peroxide and converting it into PTA is often used to deposit tungsten on various surfaces to obtain tungsten oxides. WO<sub>3</sub> obtained by this method has many applications in modern technologies as photocatalyst in water splitting, electrode materials for lithium-ion batteries, photochromic films and electrochromic displays [18–20].

During the manufacturing the penetrators from fine powder of tungsten and some other metals (nickel, iron, cobalt, chromium, aluminum, etc.) three types of scraps are generated: compaction scrap (powder), machining scrap (turnings) and defective products (penetrators on form of solid rods), which may contain up to 90% W. Methods for the extraction of tungsten from this scrap developed in [21] include electrical leaching of turnings from solid rods, soda annealing and leaching of turnings/powder, impurity removal from powder scrap by acid leaching and physical enrichment of powder scrap. Copper was effectively removed from W–Cu scrap with increasing FeCl<sub>3</sub> concentration in dissolver. A weight ratio of FeCl<sub>3</sub> to scrap of 2:1 at room temperature for 24 h resulted in 97% copper removal and 75% tungsten recovery.

Complete removal of copper occurred at increased temperatures and acidic conditions, however, at the efficiency of direct tungsten reduction dropped to 50% [22].

On the one hand, metalperoxy compounds have the ability to form complex compounds with many organic compounds. For example, in work [23] is discussed synthesis of peroxotungstate (VI) complexes containing benzene core carboxylic, benzoic, 2-chlorobenzoic and 3-aminobenzoic acids. As GO (Graphene Oxide) may contain many oxygen functional groups (carboxyl, carbonyl, hydroxyl, peroxy groups, etc.), it can be considered as a macroligand and has to form complexes with metal compounds. On the second hand, the properties of hydrophilicity and hydrophobicity are combined in GO, therefore they will affect the adsorption ability of these composite materials toward both inorganic and organic species [24]. These properties can used to obtain GO and PTA composites.

It is confirmed, that the oxide semiconductors can be strongly coupled with the GO sheets to form hybrid composites, which have to be promising platforms for the design of electronic devices. In particular, competition between the growth of tungsten oxide nanowires and the reduction of GO sheets leads to the formation of sandwich-structured tungsten oxide–rGO (reduced GO) composite [25,26]. G (Graphene) and its derivatives such as GO and chemically obtained rGO composites are promising materials for photocatalysis, making lithium battery electrodes, sensors, photocurrent generation, etc. In the paper solvothermal process simultaneously enables [27] the reduction of GO and the formation of tungsten oxide of composition  $W_{18}O_{49}$  making it suitable for the preparation of other G-based composites. A systematic investigation on the incorporation of WO<sub>3</sub> nanorods and G for high-efficiency visible-light-driven photocatalysis and NO<sub>2</sub> gas sensing was given in paper [28].

Thus, by obtaining PTA from tungsten scrap it is possible to produce many tungsten compounds and composites that are now used in different fields. Among them, the composites of GO–PTA type are especially promising materials for modern developments in science and technology.

#### 2. Experimental

#### 2.1. Materials

Graphite flake (natural, 325 mesh, 99.98 % metals basis) used to obtain graphene oxide, reduced graphene oxide and graphene itself, and boron carbide powder (1–7  $\mu$ m) were purchased from Alfa Aesar and used without prior purification. Reagents such as KMnO<sub>4</sub>, H<sub>2</sub>SO<sub>4</sub> (98%) and HCl (37%) were purchased from Sigma Aldrich and used without prior purification.

Organic compounds and polymers (carbohydrates, glucose, sucrose, cellulose, polyvinyl alcohol, polyvinylpyrrolidone, etc.) were used as a carbon source (for carbidization and as a reducing agent), which pyrolysis produces activated amorphous carbon, so-called carbon black. The purity of chemical reagents and solvents used for synthesis reached 99.00–99.99% purity.

Inert environment in the reaction area was created using nitrogen (99.95%) or argon (99.95%) gases. Hydrogen gas with purity of 99.95% was used to reduce the tungsten oxide and obtain WC–Co.

Tungsten scrap (unconditioned powders, plates, spirals, rods, etc.) was collected from the Ferdinand Tavadze Metallurgy and Materials Science Institute (Tbilisi, Georgia). It was crushed in a steel ball mill and sieved in a vibrating screen. For PTA syntheses, powders  $< 250 \,\mu\text{m}$  in size, as well powders with as larger grain sizes of 1– 3 mm, were used.

#### 2.2. Equipment

To grind the powders there was used planetary mill Pulverisette 7 Premium Line with grinding cup and balls made from WC–Co hard alloy. For the ultrasound treatment and homogenization of suspensions it was used an ultrasonic cleaner (45 kHz) and JY92–IIDN Touch Screen Ultrasonic Homogenizer (20–25 kHz, 900 W).

Thermal treatment (< 1500 °C) of samples was conducted in the high-temperature vacuum furnace Kejia. In the same furnace, metal oxides deposited on boron nitride were reduced in hydrogen flow. To obtain WC–Co, tungsten oxide also was reduced in the Kengo digital generator. Compaction of powder samples or simultaneous synthesis and compaction were carried out by using the SPS (Spark-Plasma Sintering) facility operating in DC (Direct Current), pulsed DC and pulsed AC (Alternating Current) modes, which was designed at the Georgian Technical University (Tbilisi, Georgia).

The morphology and microstructure of the powders were studied with SEM (Scanning Electron Microscope) JEOL–JSM 6510 LV equipped with energy dispersive analyzer: Dispersive Micro-X-ray Spectral Analyzer X-MaxN (Oxford Instruments). An EDS (Energy-Dispersive Spectrometer) and tabletop SEM TM3030 Plus (Hitachi) were be used to determine the samples elemental composition. XRD (X-Ray Diffraction) patterns were obtained with DRON–3M (Cu K<sub>a</sub>, Ni filter, 2°/min) and XZG–4 (Cu K<sub>a</sub>,  $\lambda = 1.5418$  Å) diffractometers.

The powder particle sizes were determined by the Scherrer method. Particle sizes were also analyzed by photon correlation nanoparticle size analyzer Winner 802 DLS and Malvern Instruments Mastersizer. The powder specific surface area was measured on Micromeritics Gemini VII Instrument.

Samples FTIR (Fourier Transform InfraRed) spectra were recorded on Agilent Cary 630 Spectrometer (at 350–5000 cm<sup>-1</sup>).

#### 2.3. Chemical synthesis methods

The synthesis methods used in this study were previously used by authors to solve some other research tasks and are described in the papers [29–32]. Below are described their versions modified to fit the task of producing tungsten compounds and composites from its scrap.

Method 1: Synthesis of PTA

5.0 g of tungsten powder is slowly dissolved in 40 ml of 20%-25% H<sub>2</sub>O<sub>2</sub>. The H<sub>2</sub>O<sub>2</sub> solution is added to the tungsten powder in three portions during 2 h (Note that the reaction is very exothermic!). Then 15 ml of hydrogen peroxide solution is again added to the reaction mixture and stirred at room temperature for 5 h. The solution is left for 12 h and then filtered. A yellowish transparent solution is obtained. Excess H<sub>2</sub>O<sub>2</sub> is decomposed using a platinum spiral and the solution is evaporated under

vacuum. An orange crystalline substance containing 85.4% WO<sub>3</sub> is obtained (at 600 °C for 4 h).

Method 2: Preparing PTA solution

To obtain different composite materials, it is convenient to use PTA solutions of a certain concentration. The production of PTA is carried out by the process described above with the difference that after filtering the obtained solution is diluted with distilled water and a solution with a W concentration of 50–100 mg/ml is prepared.

Method 3: Synthesis of GO

40 ml of 98% sulfuric acid and 1 g graphite powder (325 mesh) is added into a glass reactor. The mixture is stirred at 30-40 °C for 0.5 h and 3 g of KMnO<sub>4</sub> is added at 40–45 °C under 1 h (the temperature can reach 50 °C). The mixture is stirred for 3 h. A gray viscous mass is obtained, which is cooled to 10 °C and 100 ml of ice water is added to the reactor. The mixture is diluted to 500 ml and 2 ml of 30% of  $H_2O_2$ solution is added. A yellowish suspension of graphite oxide is obtained. During the washing of the sediment, its color gradually changes to dark brown. 20 min later solution is removed by decantation. This process is repeated twice. For the rapid precipitation of graphite oxide from the suspension, a 5% solution of hydrochloric acid (500 ml) is added. Decantation is repeated 3 times in 10 min intervals. An aqueous gel-like mass is obtained. Washing of this precipitate is continued until the pH of the solution reached a value of 5-6. GO is separated from the obtained suspension by centrifugation and dried in a vacuum at 60 °C for 4 h. In many cases, to obtain composites containing PTA, it is more convenient to use GO suspension without separation from the reaction mixture. GO suspension with a GO concentration of 12 mg/ml is used in this process.

Method 4: Vacuum-thermal exfoliation of GO and obtaining of rGO

Vacuum exfoliation of GO temperature depends on its synthesis method, chemical composition, preparation time, heating rate and pressure. The vacuum exfoliation temperature range of GO obtained by methods known in the literature is of 150-250 °C. 0.5 g GO plates are cut into small pieces (2–4 mm) and placed in 1 l glass flask. After vacuuming the flask, it is heated at rate of 5 °C/min to 160–170 °C. In this temperature range, a volumetric exfoliation of the GO plates takes place and a fluffy black powder is formed. Vacuuming is continued for 1 h and then the flask is cooled under vacuum. The bulk density of the obtained powder reaches 20–30 mg/ml.

Method 5: Obtaining of GO-PTA composite

40 ml suspension containing 480 mg GO is sonicated for 1 h and placed in a 100 ml flask. The suspension is heated to 50 °C and 1ml solution of PTA (50 mg W/ml) is added. The resulting suspension is stirred for 1 h at 50 °C. The obtained suspension is dried in air at 100 °C (3 h). Black plates (0.645 g) are obtained. It is kept in a desiccator. Carbon black–PTA composite can be obtained in a similar procedure.

Method 6: Vacuum-thermal exfoliation of GO-PTA composite

0.315 g of GO–PTA composite is placed in a quartz flask. After vacuuming the flask, it is heated at a rate of 5 °C/min to 170–175 °C. In this temperature range, volumetric exfoliation of the composite powder takes place. Material heating at this temperature is continued for 1 h and then it is cooled in argon. The powder volume increases in 50–70 times. Black 164 mg composite – 1st Sample is formed: powder rGO–PTA-170. The 2nd Sample of the composite obtained by this method is heated at

 $500 \,^{\circ}$ C in vacuum for 1 h and cooled to room temperature under argon: powder rGO–PTA-500.

Method 7: Reduction of powder rGO–PTA-170 with  $H_2$  at 700 °C and obtaining of rGO–W composite

0.5 g of rGO–PTA-170 composite powder is placed in a quartz boat-like vessel and put in high temperature vacuum furnace. The sample is heated in argon flow at rate of 10 °C/min. At 400 °C, argon is replaced by hydrogen and the temperature is raised to 700 °C and kept under for 2 h. After that, the furnace is turned off and cooled in argon stream. To prevent oxidation of metallic tungsten, the sample is kept in an argon desiccator. As a result, the rGO–W composite is obtained.

Method 8: Obtaining of rGO–WO<sub>2</sub> composite

0.5 g of rGO–PTA-170 composite powder is placed in a quartz boat-like vessel and put in high temperature vacuum furnace. The sample is heated to 700 °C in an argon stream at a rate of 10 °C/min and kept for 2 h. After that, the furnace is turned off and cooled in argon stream. The sample is stored in an argon desiccator. rGO–WO<sub>2</sub> composite is obtained.

Method 9: Obtaining WC–W<sub>2</sub>C composite from carbon black–PTA and rGO– PTA-170

WC–W<sub>2</sub>C tungsten carbides are obtained by the interaction of acetylene carbon black and PTA solution, drying the obtained paste to 180–200 °C and sintering the obtained powder at 1000 °C in a hydrogen atmosphere for 1 h. WC–W<sub>2</sub>C composite was obtained from rGO–PTA-170 powder in similar way.

Method 10: Obtaining WC–Co from  $PTA-Co(CH_3COO)_2 \cdot 4H_2O-C_{12}H_{22}O_{11}$  (sucrose).

A mixture of 2.65 g PTA, 2.1 g Co(CH<sub>3</sub>COO)<sub>2</sub>·4H<sub>2</sub>O and 4 g C<sub>12</sub>H<sub>22</sub>O<sub>11</sub> (sucrose) is dissolved in 50 ml of water. The obtained solution is evaporated and the paste is dried at 180–200 °C for 2 h. The obtained black mass is ground, placed in a quartz tube and heated at 600 °C in an argon flow (30 ml/min) for 2 h. The obtained material is milled in nanomill. Then the pre-ceramic precursor powder is transferred into a quartz boat-like vessel, placed in muffle furnace tube, and thermally treated in H<sub>2</sub> flow (heating rate of 10 °C/min, holding time of 2 h at 1000 °C). The obtained powder of WC–Co is of a gray color.

Method 11: Preparation W-B<sub>4</sub>C powder composite

1 g PTA is dissolved in 20 ml of 1% hydroxyl ethyl cellulose (HES 30000) aqueous solution, containing 5 ml of ethylene glycol. 6 g of boron carbide  $B_4C$  powder are added to the obtained solution. The suspension is evaporated under stirring and the obtained mass is burned in a high temperature furnace at 600 °C for 1 h in argon. The resulting WO<sub>3</sub>/B<sub>4</sub>C composite is reduced at 700 °C in H<sub>2</sub> flow for 2 h. A powder composite W/B<sub>4</sub>C containing 9%–10% metallic tungsten is formed.

Method 12: Obtaining of sandwich-like W/(W-B4C) composite by SPS method

12 mm diameter graphite press-form lined with graphite foil is placed together with a certain amount of W wet powder, which was obtained by heating PTA at 600 °C and then by the reduction of WO<sub>3</sub> at 700 °C in a H<sub>2</sub> stream for 2 h. Poured tungsten powder is pressed and wet W–B<sub>4</sub>C powder obtained by the method described above is also poured on top. This surface is covered with graphite foil and a graphite punch is placed on top. The press form is placed in the SPS facility, and after vacuuming its chamber, the powder is pressed at 30–50 MPa (holding at 1500–1700 °C for 10 min. Pulsed AC mode with pulse duration of 5  $\mu$ s and pause of 1  $\mu$ s is used to sinter these ceramics. The sample heating rate reaches 100–200 °C/min. The samples are cooled in vacuum. W/(W–B<sub>4</sub>C) sandwich-like composite is obtained similarly.

#### 3. Results and discussion

Tungsten scrap is a fragile material and it breaks easily under mechanical impact. In laboratory practice, it is possible to obtain powder from scrap (spirals, plates) using a steel mortal, and a steel ball mill was used to crush rods with large diameter. A fine fraction with a particle size of  $< 250 \,\mu\text{m}$  and a relatively large fraction of 1–3 mm were obtained from the scrap. The interaction of the powders with the hydrogen peroxide solution takes place energetically resulting in the formation of a weak yellowish solution.

As a result of solution evaporation, an orange crystalline substance is obtained, the EDS analysis of which shows that it consists of tungsten and oxygen and does not contain other metals as impurities (**Figure 1**). For example, from <sup>74</sup>W L- and <sup>8</sup>O K-series analysis in a point there are obtained: 21.16at.%W and 78.84at.%O.



Figure 1. EDS spectrum of PTA obtained from tungsten scrap.

The main processes of scrap recycling are given in **Figure 2**. Obtaining PTA from tungsten scrap by this method is advantageous for several reasons. The simplicity of the method and the synthesis of a water-soluble substance, from which many promising and scarce materials or substances can be obtained are remarkable. For example, it is possible to obtain tungsten oxides (WO<sub>x</sub>), metallic tungsten powder, carbides, borides, composites for various functional purposes, radiation-resistant metal ceramics, catalysts, metallized coatings, sensor materials and others.



**Figure 2.** General scheme of technological route of obtaining PTA from tungsten scrap.

#### 3.1. Phase transitions in GO-PTA composite

It is very promising to obtain composites containing tungsten compounds from G and its oxides—GOs. This needs studying the phase transitions in GO–PTA composite due to the interaction of GO with PTA in different environments and temperature regimes. Corresponding results are summarized in **Figure 3**.



Figure 3. Scheme of obtaining different materials from GO-PTA composite.

At the initial stage, GO–PTA composite was obtained. The formation of this composite is easy because the components consist of many oxygen-containing functional groups, which interact with each other and form a stable homogeneous suspension, by drying of which, the polymer films are obtained. They are flexible and can be used to coat various surfaces with tungsten oxides.

We aimed to study the effect of temperature increase on the synthesized composite under vacuum, inert and reducing atmospheres. It should be noted that the process of vacuum-thermal exfoliation of composites GO–Me compounds was previously studied by authors and in this way, it was obtained rGO–Me (Me = Ag, Pt and Pd) and rGO–Me<sub>x</sub>O<sub>y</sub> (Me<sub>x</sub>O<sub>y</sub> = CuO, Cu<sub>2</sub>O, TiO<sub>2</sub>, Fe<sub>2</sub>O<sub>3</sub>, Fe<sub>3</sub>O<sub>4</sub>, CoO, etc.)

composites. Their biocidal (rGO–Ag, rGO–CuO, rGO–TiO<sub>2</sub>, rGO–Fe<sub>2</sub>O<sub>3</sub>) and magnetic properties, as well as effects of G on morphology, fracture toughness and electrical conductivity of titanium dioxide composite (G–TiO<sub>2</sub>), were studied [32–35].

The developed methods were used for vacuum-thermal exfoliation of GO–PTA composite. It is determined that the exfoliation temperature of the composite, when using newly synthesized GO, is 170-175 °C and practically coincides with the temperature of vacuum exfoliation of GO (160-170 °C). Because of exfoliation, a fluffy powder is obtained, the volume of which is in 200–300 times greater, than the volume of the initial composite. For comparison, we present the corresponding images in **Figure 4**.



**Figure 4. (a)** GO–PTA composite; **(b)** and **(c)** composite rGO–PTA-170 obtained from it by vacuum-thermal method.

It is confirmed that the volume of the rGO–PTA-170 powder composite depends on several factors. For example, if the drying temperature of the initial rGO–PTA composite is increased to 150 °C, the volume of the obtained powder decreases by 5– 7 times. Also, the volume of the rGO–PTA-170 powder composite depends on the GO: PTA mass ratio. The maximum volume of powdered rGO–PTA-170 is obtained when the amount of PTA in the GO–PTA composite is in the range of 8–20% of GO.

When obtaining similar powders by vacuum-thermal exfoliation, the preparation time of the GO suspension sample should be taken into account. In the case of using a suspension made 3 months earlier or more, powders of a significantly smaller volume are obtained from the GO–PTA composite. A similar result was obtained when obtaining composites of compounds of other elements, with the difference that the vacuum exfoliation of the composite of GO–metal nitrates actually takes place by explosion. This is caused by the presence of nitrate ions in the system, which with any organic compound produces explosive materials. Exfoliation of non-nitrate systems is safe and easy to do even in glassware.

We note here that the separation of the matrix (GO) is caused by the decomposition of the oxygen-containing functional groups contained in it, the generation of gases (CO<sub>2</sub>,  $H_2O$  and vapors of organic compounds) and the

development of a certain pressure between the layers of GO, which causes the exfoliation of the layers. Without vacuum, i.e. in air or any gas flow the films of GO itself or its composites do not change their geometric shape and remain in the form of plates. Thus, the method of vacuum-thermal exfoliation can be considered as a new method for obtaining composites of tungsten compounds and GOs.

Further heating of the rGO–PTA-170 composite up to 500 °C literally does not change the phase composition and the rGO–WO<sub>2.9</sub> composite is obtained, which transforms into the rGO–WO<sub>2</sub> composite at 700 °C (**Figures 5** and **6**).



**Figure 5.** XRD patterns of rGO (green) and composites rGO–(rGO–WO<sub>2.9</sub>-170) (blue) and rGO–(rGO–WO<sub>2.9</sub>-500) (red).



Figure 6. XRD patterns of rGO–WO<sub>2</sub>-700 composite (green) and WO<sub>2</sub> phase (red).

Comparing these diffractograms, it can be concluded that in the rGO–WO<sub>2.9</sub>-170 and rGO–(rGO–WO<sub>2.9</sub>-500) composites, the WO<sub>2.9</sub> phase is not fully formed, while in the rGO–WO<sub>2</sub>-700 composite, the WO<sub>2</sub> phase is well defined (**Figure 6**). In general, PTA gradually undergoes dehydration and deoxygenation during heat treatment, and at 600 °C the WO<sub>3</sub> phase is obtained and metallic tungsten is obtained in hydrogen environment [18–20]. It is also known that in a reducing environment WO<sub>3</sub> reduces to metallic W. In our case, rGO–PTA-170, as well as rGO–WO<sub>2.9</sub>-170 composites in a reducing atmosphere (H<sub>2</sub>) are reduced to metallic tungsten and rGO–W is obtained.

It is known [8] that in the temperature range of 700–1000 °C the W–C system produces tungsten carbides. Different types of organic compounds are often used for carbon sources, which, when the temperature rises, produce active carbon, both carbonizing and reducing agent in the carbonizing process. Using organic reagents, we have obtained nanopowders of many metal carbides and multicomponent metal-ceramics – see the earlier papers [36–38]. In general, the GO–PTA composite is a W–C type system containing a tungsten compound and a carbonizing agent (carbon source) in the form of GO. By their heating to 900 °C in hydrogen (or argon) flow tungsten carbides WC and  $W_2C$  are obtained (**Figure 7**).



Figure 8. XRD patterns of WC and W<sub>2</sub>C phases obtained from carbon black–PTA mixture at 900 °C in H<sub>2</sub> flow.

For comparison, we carried out carbon black–PTA mixture carbonization at 900 °C in  $H_2$  flow. As can be seen from the XRD patterns, as it was expected WC and  $W_2C$  phases are also obtained in this case (**Figure 8**). The diffractogram also shows the peak of excess carbon. In the case of GO–PTA, a carbon low intensity peak is visible. Such a difference is due to the fact that GO forms G with a defective structure at high temperature (a chemical method of graphene synthesis) because the oxygen-containing groups are removed from it. Therefore, the carbon present in GO is spent

both on carbonization and formation of low-molecular carbon-containing compounds. In the case of carbon black, the oxygen content is low (1%–3%), while the oxygen content in GO is in the range of 20%–34%. These results are presented in our previous works [33,35,39].

#### 3.2. Preparation WC–Co from PTA

With the proposed method, it is possible to transform tungsten scrap into WC– Co, which is an important metal-ceramic in metalworking technology (drills, cutters, abrasives, coatings, etc.). Carbothermic process is mainly used to obtain the mentioned material, which involves the carbonization of a mixture of tungsten powder, cobalt and carbonaceous material (amorphous coal, black carbon obtained by various methods) in a hydrogen environment at 900–1000 °C. The technological process requires dispersed tungsten powder, which is obtained by long grinding in mills, due to which the target product is contaminated with wear materials of the mill and balls. Besides, the grain size of the WC–Co powder obtained by the traditional method is several micrometers.

Currently, much attention is being paid to the technologies that lead to obtaining ultradisperse (nanosize) powders of hard materials [36,40]. Using traditional methods, it is impossible to achieve the goal, because it is practically impossible to grind the components of the starting material down to the nanosize. One of the ways to solve this problem is to obtain pre-ceramic precursors from liquid charge, where the components are broken down into molecules and ions [37,38,41].



**Figure 9.** XRD pattern of WC–Co obtained from PTA–Co(CH<sub>3</sub>COO)<sub>2</sub>(4H<sub>2</sub>O–  $C_{12}H_{22}O_{11}$  (sucrose) precursors at 1000 °C in H<sub>2</sub> flow.

To obtain WC–Co, we selected the system PTA–Co(CH<sub>3</sub>COO)<sub>2</sub>·4H<sub>2</sub>O–C<sub>12</sub>H<sub>22</sub>O<sub>11</sub> (sucrose), which contains water-soluble components. Specifically, PTA is an ideal precursor candidate for obtaining WC–Co as it is highly soluble in water and can be obtained as a solution up to 50%. Cobalt acetate (or cobalt nitrate and chloride) is also soluble in water. It is possible to use water-soluble synthetic and natural polymers, carbohydrates, alcohols and other organic compounds as carbonizing agents. By mixing the component solutions and drying them by vaporization at 300–400 °C, a preceramic precursor is obtained, in which tungsten, cobalt and carbon compounds are

homogeneously distributed, and WC–Co is obtained by their carbonization in a hydrogen atmosphere. This technology does not require scarce metal powders: the target product is obtained from available reagents. The WC–Co diffractogram obtained by heating the preceramic precursor obtained from PTA–Co(CH<sub>3</sub>COO)<sub>2</sub>·4H<sub>2</sub>O–C<sub>12</sub>H<sub>22</sub>O<sub>11</sub> (sucrose) at 1000 °C in the hydrogen environment is shown in **Figure 9**.

## **3.3.** Obtaining of radiation resistant sandwich-like composites W/B<sub>4</sub>C and W/(W–B<sub>4</sub>C)

Boron carbide–tungsten B<sub>4</sub>C–W thin-layered sandwich structures are known as effective shield composite materials, in which low- and high-Z atoms (Z is the atomic number), B and W, serve as effective absorbers for, respectively, (epi)thermal neutrons and secondary gamma-quanta accompanying the neutrons capture by <sup>10</sup>B nuclei [42–44]. To obtain them, first note that WO<sub>3</sub> is obtained from tungsten scrap by heating of PTA, which is reduced above > 500 °C to metallic tungsten in H<sub>2</sub> flow [19,45,46]. PTA solutions are also used for tungstenizig (metallizing with tungsten) of various surfaces [47,48].

We obtained both metallic tungsten powder and powder of composite W–B<sub>4</sub>C containing 8–10% tungsten from PTA using a similar method. The obtained powders were used to obtain W/B<sub>4</sub>C and W/(W–B<sub>4</sub>C) sandwiches. It is known that boron carbide reacts with metals at high temperatures and forms borides, which are also binding (cement) phases of composites. Many composites were obtained by this method, which found use in obtaining radiation resistant materials [49]. Thus, the W–B<sub>4</sub>C powder composite obtained by us from PTA is a promising material for making radiation-resistant sandwiches. Sintered composites of WC–WB–W<sub>2</sub>B were prepared from B<sub>4</sub>C–W–WC powders using a reactive energization hot-pressing technique that initiated a solid state reaction between B<sub>4</sub>C and W [50]. It is established that the resulting sandwiches do not undergo exfoliation because at the contact boundary between the metal and boron carbide, a transitional bonding phase W<sub>2</sub>B<sub>5</sub> is formed, which is also the best neutron absorber compound [51].

When tungsten and boron carbide powders are sintered by SPS method, actually a three-layer sandwich  $W/W_2B_5/B_4C$  is formed. If we selectively remove the tungsten layer with a hydrogen peroxide solution, the sandwich  $W_2B_5/B_4C$  will remain. XRD analysis of such composition detects both  $W_2B_5$  phase and  $B_4C$ . For XRD analysis, half the surface of the  $W_2B_5/B_4C$  cylindrical sample was peeled off at an angle of approximately 40–45 degrees to expose the  $B_4C$  layer [31].  $W/B_4C$  and  $W/(W-B_4C)$ sandwiches were made by SPS method, in which tungsten powder was obtained by reduction of PTA separated from scrap (in  $H_2$  flow at 700 °C). In this case, the sintering method was partially changed. In the SEM image of the  $W/B_4C$  sample fragment, the separation boundary between tungsten and boron carbide is clearly seen in **Figure 10**. It seems that there is a mutual diffusion of tungsten and boron carbide, as a result of which the  $W_2B_5$  phase is formed, whose irregular layer is well separated between the white and black layers. **Figure 11** shows the EDX (Energy Dispersive X-ray) mapping images and distributions of each element in the sandwich structure.  $W/(W-B_4C)$ sandwiches were obtained by a similar method.



**Figure 10.** SEM images of composite  $B_4C-W$  obtained by SPS from  $B_4C$  and W powders at 1500 °C: fracture surfaces with different magnifications. (a) × 90; (b) × 10,000.



Figure 11. EDX mapping of all elements (a) and separately B (b) C (c) and W (d) distributions in  $B_4C$  and W phases contact regions.

If we consider these processes, it can be concluded that the  $W_2B_5$  phase, which is a powder binder, is formed on the contact surface of the W–B<sub>4</sub>C composite powder particles. This is important because it allows pressure-free sintering of pressed composites (green products) at relatively low temperatures (1400–1500 °C). Thus, PTA is a necessary component for obtaining  $W-B_4C$  powder composites, so it's obtaining from tungsten scrap is a promising direction.

#### 4. Conclusions

Methods for obtaining solution and crystalline PTA from tungsten scrap are developed. By mechanically crushing tungsten scrap and dissolving the resulting powder in hydrogen peroxide solution, a PTA solution is obtained. In addition, by its evaporating a crystalline PTA is formed. They are used in the preparation of metallic tungsten W powder; tungsten–boron carbide composite W–B<sub>4</sub>C powder, GOs containing composites GO–PTA, rGO–WO<sub>2.9</sub>, rGO–WO<sub>2</sub>, and rGO–W; tungsten carbides W<sub>2</sub>C, WC, and WC–Co; and sandwich composites W/B<sub>4</sub>C and W/(W–B<sub>4</sub>C). It is established that by thermal treatment of PTA in the hydrogen environment at 600–700 °C, metallic tungsten W powder is obtained, which has many applications.

Phase transitions of GO–PTA composite in vacuum and hydrogen atmosphere at 170–900 °C is studied. By the interaction of PTA solution and GO suspension, an amorphous GO–PTA composite is obtained. In addition, rGO–WO<sub>2.9</sub> composite powder is formed by their vacuum thermal explosion at 170–500 °C. It is determined that WO<sub>2.9</sub> phase transforms into WO<sub>2</sub> at 700 °C and rGO–WO<sub>2</sub> composite is formed. By reduction the latter in a hydrogen atmosphere (700 °C), rGO–W composite containing metallic tungsten is obtained.

Using the PTA solution, a liquid charge containing the PTA– Co(CH<sub>3</sub>COO)<sub>2</sub>·4H<sub>2</sub>O–C<sub>12</sub>H<sub>22</sub>O<sub>11</sub> (sucrose) system is prepared. A preceramic precursor powder is obtained from this charge. It is determined by XRD analysis that through carbonization in hydrogen atmosphere at 1000 °C WC–Co is obtained, in which cobalt content reaches 6–20wt.%.

Obtaining possibilities of sandwich composites containing boron carbide and metallic tungsten layer using metallic tungsten powder obtained from PTA also are studied. It is confirmed that by SPS process it is possible to obtain sandwich-like W/B<sub>4</sub>C and W/(W–B<sub>4</sub>C) composites at 1500–1700 °C. On the contacting surface of tungsten and boron carbide, formation of the  $W_2B_5$  intermediate phase is detected, which serves for an additional binder phase.

Thus, from the point of view of implementing environmentally friendly technologies, replacing commercial tungsten powder with tungsten scrap obtained from PTA and processing with appropriate methods, it is possible to obtain many scarce and widely used tungsten-containing composites and materials. We note here that when tungsten scrap is dissolved in an aqueous solution of hydrogen peroxide, oxygen is formed as a by-product, which is not an environmental pollutant.

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#### Article

### Polymeric nanoparticles for protein and peptide delivery

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Copyright © 2024 by author(s). *Characterization and Application of Nanomaterialst* is published by EnPress Publisher, LLC. This work is licensed under the Creative Commons Attribution (CC BY) license. https://creativecommons.org/licenses/ by/4.0/ Abstract: Protein- and peptide-based medications are recognized for their effectiveness and lower toxicity compared to chemical-based drugs, making them promising therapeutic agents. However, their application has been limited by numerous delivery challenges. Polymeric nanostructures have emerged as effective tools for protein delivery due to their versatility and customizability. Polymers' inherent adaptability makes them ideal for meeting the specific demands of protein-delivery systems. Various strategies have been employed, such as enzyme inhibitors, absorption enhancers, mucoadhesive polymers, and chemical modifications of proteins or peptides. This study explores the hurdles associated with protein and peptide transport, the use of polymeric nanocarriers (both natural and synthetic) to overcome these challenges, and the techniques for fabricating and characterizing nanoparticles.

Keywords: drug delivery; nanoparticles (NPs); protein delivery; therapeutic effect

#### **1. Introduction**

Protein is derived from the Greek word "PROTOS", meaning the first or the supreme. Proteins are large organic molecules composed of amino acids linked together in a linear chain by peptide bonds, with proteins typically containing more than 50 amino acids. Peptides are short polymers formed by the linkage of amino acids in a specific order (a peptide contains < 50 amino acids). Proteins exhibit various structural forms: the primary structure, which is the sequence of amino acids; the secondary structure, consisting of regularly repeating local structures stabilized by hydrogen bonds; the tertiary structure, representing the three-dimensional configuration of the polypeptide; and the quaternary structure, formed by the assembly of multiple protein molecules (polypeptide chains) [1]. Proteins and peptides can be classified into different types, including polypeptides, oligopeptides, fibrous proteins, globular proteins, and oligomeric proteins, based on the number of amino acids present.

Proteins are essential to the body as they participate in various biological roles in the form of enzymes that catalyze virtually all chemical reactions (e.g., 6GDH), help in the transport of hemoglobin of erythrocytes, contract muscles (actin and myosin), maintain the structure of the body (collagen in bones), provide defensive activity (immunoglobulins and antibodies), regulate secretions (insulin), provide nutrition and storage in the body (ovalbumin), generate and transmit nerve impulses, provide immune protection through antibodies, and control growth.

Bioapplications of proteins and peptides include the use of erythropoietin to stimulate red blood cell production, tissue plasminogen activator for treating heart attacks and strokes, oxytocin to manage labor pain, bradykinins to enhance peripheral circulation, somatostatin to reduce bleeding in gastric ulcers, gonadotropin to induce ovulation, and insulin to regulate blood sugar levels. Although proteins and peptides offer many benefits, their delivery poses challenges due to their large size and instability. Their structures are maintained by weak noncovalent forces, making them susceptible to degradation under mild storage conditions and gastric juices [2–4].

#### 2. Problems with protein and peptide

The primary challenges in delivering proteins and peptides are proteolysis by exo/endo proteases, small-size proteins getting filtered out by kidneys very easily, causing elimination of B and T cells, and may show unwanted allergic reactions (even toxicity), and less therapeutic activity of proteins due to insolubility/adsorption [5].

#### **3.** Barriers to protein and peptide delivery

#### **3.1. Enzymatic barriers**

Proteins and peptides can be degraded by enzymes in two distinct ways. One method involves the hydrolytic breaking of peptide bonds by enzymes that degrade insulin, convert angiotensin, and renin. Since proteolysis is an irreversible event, it may harm medications that include proteins and peptides. Others include chemical modification of proteins by oxidizing them using glucose oxidase or xanthine oxidase or phosphorylating them with kinases [6].

#### 3.2. Intestinal epithelial barrier

It prevents protein medications from passing through the intestinal epithelium. Transport of protein and peptide medicines across the intestinal epithelium is accomplished by several processes, including paracellular movements, endocytosis, transcytosis, passive transport, and carrier-mediated transport. Dipeptides and tripeptides from the small intestine are extensively absorbed through active transport. Proteins and peptides that are too large to be absorbed through carrier-mediated transport can be taken up via endocytosis, which is one of the processes by which cellular internalization of proteins and peptides occurs that include pinocytosis (cell drinking) and phagocytosis (cell eating). Paracellular migration and persorption are the two mechanisms involved in drug absorption. The epithelial mucosa of the small intestine serves as a barrier against macromolecule penetration [7].

#### 3.3. Capillary endothelial barrier

Proteins and peptides must either cross the endothelial cells themselves or move between the cells to pass through the capillary endothelium. Cytoplasmic enzymes can alter or metabolize solutes that pass through endothelial cell membranes. Therefore, the endothelial passage presents an enzymatic or metabolic barrier to the passage of the proteins and peptides [8].

#### 3.4. Blood-brain barrier

One of the main barriers to protein delivery to the brain compartment is the bloodbrain barrier (BBB). It is made up of the blood-cerebrospinal fluid barrier and the vascular BBB. BBB is made up of a monolayer of cells at both locations that are joined by tight junctions and contain additional mechanisms to prevent or slow the flow of plasma into the central nervous system, permitting only the passage of uncharged, tiny, lipophilic molecules and gases. Proteins and other large molecules cannot cross the BBB [9].

Different barriers to protein and peptide drug delivery are illustrated in a visual format in **Figure 1**.



Figure 1. Intestinal barrier, capillary endothelial barrier and blood brain barrier for protein and peptide delivery.

#### 4. Polymeric nanocarriers for protein and peptide delivery

Polymeric nanoparticles (NPs), which are solid colloidal carriers ranging from 10 to 100 nm in size, can be formulated with synthetic, semi-synthetic, or natural polymers. The choice of materials used to synthesize these NPs affects their drug delivery performance and therapeutic effects. Proteins can be chemically attached, adsorbed, or encapsulated on the surface of polymeric NPs [10,11].

#### 4.1. Natural polymers

Therapeutic proteins can be delivered to specific sites for distinctive benefits with natural polymers. The natural polymers may be of plant, animal, and marine origin and are generally inexpensive. The existence of reactive sites in natural polymers is significant in drug delivery systems because it facilitates ligand conjugation, crosslinking, and other modifications that make the polymers perfect drug carriers for a variety of therapeutic proteins. However, natural polymers are more susceptible to processing parameters.

#### 4.1.1. Polysaccharide-based natural polymers

Polysaccharides exhibit structural and functional diversity because of their vast number of reactive groups, wide range of molecular weights, and varied chemical composition. Being naturally occurring biomaterials, polysaccharides are safe, nontoxic, and biodegradable and exhibit remarkable stability in biological fluids. Polysaccharides are also known as mucoadhesive polymers because of their mucoadhesive qualities (polysaccharides, which are hydrophilic in nature, create noncovalent connections with biological tissues) due to the presence of many derivable groups on the molecular structure, such as hydroxyl, carboxyl, and amino groups. Mucoadhesive polysaccharide-based NPs have been demonstrated to improve the residence and absorbance time of integrated therapeutic protein. Various polysaccharides used for the transport of proteins and peptides are represented in **Table 1**.

| Polysaccharide polymers | Properties  | Role of polymers in transportation of Protein and Peptides   | Reference |
|-------------------------|---|--|-----------|
| Chitosan                | Biocompatible,<br>Non-toxic   | Aid in facilitating the intestinal epithelial mucosal absorption of therapeutic proteins with high molecular weight.   | [12,13]   |
| Cyclodextrins           | Utilized as potential carriers in pharmaceutical biotechnology and non-toxic  | Improve the bioavailability of the protein molecule by delivering it directly to the barrier membrane  | [14,15]   |
| Alginates               | Excellent mucoadhesive qualities,<br>Biocompatibility,<br>biodegradability,<br>High degree of flexibility and non-<br>toxic | Helps in transport of therapeutic proteins that are heat<br>sensitive.<br>Alginate also transports labile proteins and peptides safely to<br>the colon while shielding them from the stomach<br>environment. | [16,17]   |
| Pectins                 | Mucoadhesive activity<br>Inert for physiological fluids and<br>non-toxic  | Stops integrated proteins from being broken down by gastric<br>enzymes and greatly boosts the intestinal absorption by its<br>unique mucoadhesive activity on the intestinal epithelium.                     | [18,19]   |
| Xanthan Gum             | Biocompatible,<br>Non-toxic,<br>biodegradable and bioadhesive<br>properties   | Preserves the integrity of the therapeutic protein and extends its sustained release   | [20,21]   |

Table 1. List of various polysaccharide polymers for proteins and peptide drug delivery.

#### 4.1.2. Protein-based polymers

Amidst natural polymers, protein-based polymers have garnered significant attention because of their attributes such as abundance, accessibility, minimal toxicity, modifiability due to their intricate heterogeneity, and adaptability in delivery methods as depicted in **Table 2**. There is still more work to be done to make protein-based polymers stable enough to be used as the perfect therapeutic polymers.

| Protein polymers | Properties   | Role of polymers in transportation of Protein and Peptides  | Reference |
|------------------|--|---|-----------|
| Lectins          | Sugar-binding proteins   | Ability to improve the active transport of therapeutic proteins with large molecular weights from the intestinal epithelium | [22]      |
| Albumin          | Non-toxic, Biocompatible   | Deliver therapeutic proteins across the blood-brain barrier and nuclear membrane  | [23]      |
| Collagen         | Biocompatible<br>Easily modifiable and available<br>Synergic with bioactive components | Facilitates the delivery of therapeutic proteins and extends the sustained release of the incorporated proteins.            | [24]      |
| Gelatin          | Biocompatible<br>Biodegradable   | Thermo-reversible properties are utilized for delivering therapeutic molecules through targeted drug delivery systems       | [25]      |

Table 2. List of various protein polymers for proteins and peptide drug delivery.

#### 4.2. Synthetic polymers

Formulators are focusing on synthetic polymers for the delivery of therapeutic proteins and peptides. It has been demonstrated that these polymers lengthen the pharmacokinetic and circulation periods of integrated medicinal compounds. Drug carriers made of synthetic polymers frequently serve a passive purpose as tabulated in **Tables 3** and **4**.

**Table 3.** List of various synthetic biodegradable polymers with their properties and transport of proteins and peptide drug delivery.

| Synthetic polymers                 | Properties   | Role in transportation of Protein and Peptides   | Reference |
|------------------------------------|--|--|-----------|
| Polyethylene Glycol                | Non-immunogenic, Nontoxic, Highly soluble in water                                     | PEGylation of therapeutic proteins protects them from<br>enzymatic degradation and reduces immunogenicity, thereby<br>extending their residence time in the body, enhancing<br>stability, and modifying pharmacokinetics by altering various<br>physicochemical properties | [26,27]   |
| Polaxomers                         | Thermosensitive<br>Inert and stable  | Helps to sustain the stability of incorporated therapeutic<br>proteins and peptides more effectively than other prolonged<br>release drug delivery systems   | [28,29]   |
| Poly (lactic-co-<br>glycolic acid) | Biocompatible and Biodegradable  | Several types of PLGA-PEG block copolymers have been developed for the proteins and peptides sustained delivery  | [30,31]   |
| Pluronic F127                      | Non-irritant<br>Biocompatibility<br>Good mechanical strength<br>Bioadhesive properties | Ensures greater stability of incorporated therapeutic proteins<br>and peptides compared to other prolonged release drug<br>delivery systems  | [32]      |

| Synthetic polymers Properties                                   | Role in transportation of Protein and Pentides | Reference |
|---|--|-----------|
| peptide drug delivery.  |  |           |
| Table 4. List of various synthetic non-biodegradable polymers w | ith their properties and transport of protein  | is and    |

| Synthetic polymers | Properties  | Role in transportation of Protein and Peptides  | Reference |
|--------------------|---|---|-----------|
| Silicons           | High loading capacity, surface functionalization,<br>biocompatibility, physicochemical and thermal<br>stability | Protection of proteins from degradation, increase<br>the half-life of protein, targetted delivery, ability<br>to functionalize their surfaces | [33]      |
| Polyacrylate       | Versatile, non-toxic, mucoadhesive  | Safe delivery of protein, controlled and sustained release of proteins and peptides   | [34]      |

#### 4.2.1. Synthetic biodegradable polymers

Biodegradable polymers offer significant advantages in biomedical applications, especially for drug delivery. Their capacity to break down into smaller, absorbable molecules eliminates the need for surgical removal, improving patient comfort and compliance. Moreover, their biocompatibility and non-toxicity make them ideal for use in a range of medical devices and treatments, reducing the risk of adverse reactions and promoting better integration within the body. This makes them a favored option for many cutting-edge therapeutic solutions [35,36].

#### 4.2.2. Synthetic non-biodegradable polymers

Non-biodegradable polymers present considerable challenges in medical applications, as they require surgical removal once the medication, they deliver is exhausted. This limitation confines their use to cases where the implant can be easily retrieved. On the other hand, biodegradable polymers naturally break down within the body, providing a more convenient and less invasive alternative for drug delivery systems. This distinction highlights the importance of choosing the appropriate polymer type based on the specific medical requirements and desired treatment outcomes.

#### 5. Method of preparation of nanocarriers

Typically, two primary approaches are utilized, which are the dispersion of prefabricated polymers or the polymerization of monomers. The lists of commonly used techniques are presented in **Figures 2** and **3**.



Figure 2. Methods of preparation of NPs.



Figure 3. Preparation of NPs.

#### 5.1. Solvent evaporation method

An emulsion is prepared by dissolving the polymer in an organic solvent like chloroform, acetone, or ethyl acetate using polyvinyl alcohol as a stabilizer. If the homogenization procedure is carried out for a long enough duration, it can help to evaporate the organic solvent [37]. Ultracentrifugation is used to gather the NPs at the end of the homogenization process. The desired particle size and other characteristics can be attained by modifying process variables, including the ratio of polymer to organic solvent, the type of organic solvent, and the speed and duration of homogenization [38].

#### 5.2. Spontaneous emulsification/solvent diffusion method

This method utilizes water-immiscible solvents such as dichloromethane or chloroform as the organic phase, while water-miscible solvents like methanol or acetone serve as the organic phase. NPs are formed when these two phases are combined, resulting in interfacial turbulence and leading to the formation of NPs. Despite producing nanosized particles, this approach has certain drawbacks, such as the existence of leftover organic solvent [39,40].

#### 5.3. Salting out/emulsion diffusion method

In the salting-out process, the polymer is first dissolved in a water-miscible organic phase, such as acetone or tetrahydrofuran, and then added to the aqueous phase containing the emulsifier [39]. The fast addition of water to the emulsion, combined with gentle stirring, decreases the ionic strength, causing the water-soluble organic solvent to migrate to the aqueous phase and resulting in the formation of polymeric nanoparticles [41].

#### 5.4. Phase separation method

This technique works with both lipophilic and hydrophilic medications. The hydrophilic medications are typically introduced to the organic phase after being dissolved in water. Conversely, the medications that are lipophilic are dissolved in polymer solutions. After the aqueous and organic phases are combined to form an emulsion, a second organic nonsolvent, such as silicone oil, is added while stirring vigorously. Silicone oil is miscible with the initial organic phase but does not dissolve the medication. Consequently, the first organic solvent is extracted, reducing the solubility of the polymer and causing phase separation, leading to the formation of a polymer coacervate. Drug-loaded nanoparticles are formed when this polymer coacervate adsorbs onto active pharmaceutical ingredients [42].

#### 5.5. Emulsion polymerization method

Emulsion polymerization is a widely used technique for synthesizing polymeric NPs. In this process, the monomer is emulsified in a continuous phase of an immiscible liquid. A polymerization reaction occurs in situ, resulting in nanospheres. The choice between water-in-oil (w/o) or oil-in-water (o/w) emulsion systems depends on the hydrophobicity of the desired monomer. Surfactants play a crucial role in stabilizing emulsions and controlling particle size. High-speed mixing, homogenization, or ultrasound sonication are common methods for carrying out this process [43].

#### 5.6. Nanoprecipitation

The nanoprecipitation technique utilizes two miscible solvents: One acts as a good solvent (usually an organic solvent such as acetone, isopropanol, or ethanol), while the other functions as a non-solvent for the polymer or lipid used to form the NPs. For instance, water can be a non-solvent. The procedure involves preparing an

organic phase and a non-solvent phase (often referred to as the aqueous phase). Both phases ensure complete solubility of all starting materials. The organic phase may include polymers, solid or liquid lipids, surfactants with low HLB values, and active compounds dissolved in organic solvents. The solubility of the active molecule in the solvent affects the drug loading capacity of the particles. Meanwhile, the non-solvent phase includes stabilizing agents dissolved in water, facilitating NP formation and ensuring system stability [44,45].

#### 5.7. Ion gelation

Ionotropic gelation is a well-studied method for preparing nanocarrier systems due to its mild conditions and straightforward procedures. In this technique, polyelectrolytes (such as chitosan, alginate, hyaluronic acid, and carrageenan) are cross-linked in the presence of counterions. The cross-linking process involves the formation of a network through ionic bridges between macromolecular chains. Typically, a charged ionic entity with a defined molecular weight serves as the crosslinking agent. Researchers frequently use this procedure to prepare NPs [46,47].

#### 6. Characterization of protein loaded NPs

#### 6.1. Size, polydispersity index (PDI), and zeta potential

Particle size characterization of protein-loaded NPs involves morphological examination by transmission electron microscopy (TEM), scanning electron microscopy (SEM), and atomic force microscopy (AFM) [46]. Transmission electron microscopy (TEM) provides direct visualization of NP size and provides detailed images of NP morphology. Dynamic light scattering (DLS) is commonly used to measure the hydrodynamic diameter and PDI of NPs [48–50].

#### 6.2. Stability and surface properties

Surface charge (zeta potential), hydrophilicity, and wettability are vital for determining the interactions between NPs and biological systems. Zeta potential measurements predict the stability of NP dispersions and can be measured by a zeta sizer. *This* measures the surface charge of NPs, which influences their stability in suspension. A higher absolute zeta potential value typically indicates better stability due to electrostatic repulsion between particles. NPs with zeta potential of more than 30 mV (+/-) have been reported to be stable in the deposit because the surface charge prevents the particles from clotting.

#### **6.3. Encapsulation efficiency**

The encapsulation efficiency is determined by measuring the amount of protein in the supernatant after centrifugation of the NPs. The protein content is quantified using methods like Lowry's assay or BCA assay. The encapsulation efficiency is calculated as:

(Total protein – Protein in supernatant)/Total protein × 100%

Release Kinetics: The drug release behaviour of NPs is evaluated in simulated biological fluids to understand how they release their therapeutic load over time. This assessment is conducted using techniques like dialysis or sample-and-separate methods.

Biodegradability and degradation rate: Gel Permeation Chromatography (GPC) and Mass Spectrometry (MS) are used to track the degradation of polymeric NPs over time.

Cellular Uptake Studies: NPs internalization by cells is measured and visualized through techniques such as confocal microscopy and flow cytometry, which help assess how effectively the NPs are delivered to target cells.

Cytotoxicity: The compatibility of NPs with cells is tested using various assays like MTT, XTT, or LIVE/DEAD assays to evaluate their potential toxicity to healthy cells.

Haemolysis and Protein Binding: Haemolysis tests determine how NPs interact with red blood cells and are analysed through SDS-PAGE or mass spectrometry that investigates how serum proteins attach to NPs and potentially affect their behaviour.

In-vivo characterization: It focuses on how polymeric NPs perform inside living organisms, providing critical information for preclinical evaluation.

- Pharmacokinetics (PK): The absorption, distribution, metabolism, and excretion (ADME) of NPs are examined using techniques such as HPLC, LC-MS, and fluorescence imaging. Prolonged circulation times of NPs are often preferred for better bioavailability.
- Biodistribution: NPs distribution across different organs or tissues is analysed using radioactive labelling or fluorescent dyes in combination with imaging technologies like MRI, PET, or bioluminescence imaging to ensure that NPs reach their target, such as tumours.
- In-vivo toxicity: The safety of NPs is evaluated by examining major organs (e.g., liver, kidneys, lungs) using histopathological analysis, blood tests, and immune response monitoring. Both acute and chronic toxicity assessments are conducted to detect any adverse effects.
- In-vivo Efficacy: These studies evaluate whether the NPs effectively deliver their therapeutic payload in animal models. Endpoints like tumour shrinkage, inflammation reduction, or changes in specific biomarkers are monitored to assess therapeutic success.
- Immunogenicity and Immune Response: NPs should not trigger harmful immune reactions. The immune response is gauged by measuring levels of cytokines, antibodies, and other immune markers using ELISA or multiplex assays.
- Targeting Efficiency: The effectiveness of targeted delivery mechanisms (e.g., ligand-receptor binding or enhanced permeability and retention (EPR) effect) is studied. Imaging techniques or tissue analysis help determine the extent of NPs accumulation at the target site [51–57].

Each of these techniques provides insights into different aspects of protein-loaded NPs, helping to optimize their design for specific applications, such as drug delivery or therapeutic interventions (**Table 5**).
| Polymer used                                | Type of polymeric NP /method of preparation  | Route of administration   | Drug/Active agent  | Treatment   | Reference |
|---|--|---|--|---|-----------|
| Chitosan                                    | Ion crosslinking method  | Nasal   | Quercetin  | Allergic rhinitis (AR)  | [58]      |
| Chitosan                                    | CS-Au based on gold NPs and chitosan (CS)  | Intravenous   | Myricaria germania   | Immunization  | [59]      |
| Poly (β-amino<br>esters) (PBAEs)            | Encapsulation of the synthetic mRNA<br>encoding bevacizumab, an anti-VEGF<br>antibody in NPs | Intravenous   | mRNA encoding<br>bevacizumab   | Non-small cell lung cancers (NSCLCs)  | [60]      |
| Chitosan                                    | MTX was entrapped in the Chitosan NPs  | Topical application   | Methotrexate (MTX)   | Rheumatoid arthritis  | [61]      |
| Chitosan                                    | Encapsulation of AMP NRC-07 in CS-NPs by ionotropic gelation                                 | Intravenous   | antimicrobial peptide<br>NRC-07  | Antibacterial and <i>in</i><br><i>vitro</i> anticancer<br>activities                          | [62]      |
| Elastin-like<br>peptides (ELPs)             | Supramolecular NPs based on elastin-like peptides modified capsid protein                    | Intravenous   | Doxorubicin  | Murine melanoma and colorectal cancer.  | [63]      |
| Poly(N-<br>isopropylacrylami<br>de)         | Temperature-responsive Polymer NPs   | Intravenous   | Paclitaxel   | Anticancer activity   | [64]      |
| Albumin                                     | Elastin-targeted NPs   | Intravenous   | Doxycycline  | LPS-mediated lung inflammation  | [65]      |
| Polymeric and<br>lipid-based                | Levodopa-loaded NPs  | Intravenous,<br>transdermal<br>delivery and<br>intranasal<br>administration | Levodopa   | Parkinson's disease   | [66]      |
| Hydrogel                                    | pH-responsive polymeric nanocarriers   | Intravenous   | IL-12  | Immunotherapy of<br>Cancer  | [67]      |
| Chitosan                                    | Concanavalin A (ConA) coated chitosan (CS) nanocarrier                                       | Intravenous   | Short antimicrobial peptide (CM11)   | Helicobacter pylori<br>gastric infection  | [68]      |
| Glutenin                                    | Glucose-conjugated glutenin NPs  | Intravenous   | Camptothecin   | Breast cancer   | [69]      |
| Chitosan                                    | Peptides in chitosan NPs Coated with Zein  | Oral  | Antihypertensive<br>Peptides, Isoleucine-<br>Proline-Proline and<br>Leucine-Lysine-<br>Proline | Antihypertensive<br>activity  | [70]      |
| ROS-responsive<br>polymer                   | Modified emulsion approach   | Intravenous   | Dexamethasone  | Acute lung injury<br>(ALI)  | [71]      |
| Chitosan                                    | Hyaluronic acid coated chitosan NPs  | Oral  | Insulin  | Hypoglycemic<br>activity  | [72]      |
| Phenylboronic<br>ester                      | Phenylboronic ester-modified polymeric<br>NPs  | Nano vaccine  | TRP2 peptide antigen<br>delivery   | Cancer<br>immunotherapy   | [73]      |
| Poly(lactic-co-<br>glycolic) acid<br>(PLGA) | Double emulsion technique  | Oral  | Capreomycin peptide  | Impact of stress<br>conditions on peptide<br>degradation:<br>Thermal, mechanical,<br>chemical | [74]      |
| Chitosan                                    | Self-assembled chitosan NPs by ionic cross-<br>linking technique                             | Intranasal  | Recombinant protein<br>interleukin-17<br>receptor C (IL-17RC)                                  | Asthma  | [75]      |
| pH-sensitive<br>polymer                     | D-melittin polymeric NPs   | Intravenous   | D-melittin   | Anti-cancer treatment   | [76]      |
| Chitosan                                    | Cross-linked NPs   | Percutaneous<br>delivery  | Betamethason   | Contact dermatitis  | [77]      |

# Table 5. Applications.

| Polymer used   | Type of polymeric NP /method of preparation  | Route of administration Drug/Active agent |  | Treatment                                     | Reference |
|--|--|---|--|---|-----------|
| Hypoxia-<br>responsive<br>polymer PLA                              | Targeted and non- targeted self-assembled polymeric NPs  | Intravenous                               | Doxorubicin (DOX)  | Hypoxic, triple-<br>negative breast<br>tumors | [78]      |
| Chitosan   | Self-gelation method   | Oral Insulin<br>Recombinant               |  | Diabetes                                      | [79]      |
| Poly (lactic-co-<br>glycolic acid)<br>(PLGA)                       | Double emulsion modified method  | Intravenous                               | Recombinant<br>adrenomedullin-2  | Angiogenesis                                  | [80]      |
| PLGA, PEG  | S2P peptide-conjugated PLGA-Maleimide-<br>PEG NPs, modified emulsion/solvent<br>evaporation technique. | Intravenous                               | Imatinib   | Atherosclerosis                               | [81]      |
| Poly (lactide-co-<br>glycolide)-b-poly<br>(ethylene glycol)<br>NPs | Polymeric NPs functionalized with muscle-<br>homing peptides   | Intravenous                               | Phosphatase and<br>tension homology<br>inhibitor to skeletal<br>muscle | Duchenne muscular<br>dystrophy (DMD)          | [82]      |
| Human serum<br>albumin (HSA)                                       | Synthetic protein NPs (SPNP), polymerized HSA equipped with iRGD                                       | Intravenous                               | siRNA against Signal<br>Transducer                                     | Glioblastoma                                  | [83]      |

## Table 5. (Continued).

## 7. Conclusions and future prospects

Peptides and proteins are essential for numerous biological reactions and play significant roles in various pathological conditions. However, their therapeutic application in treating life-threatening disorders encounters several challenges, including instability, poor absorption, enzymatic degradation, a short biological half-life, and rapid elimination. Polymeric NPs have shown considerable potential in enhancing the absorption of macromolecules. These polymers are typically inert, biocompatible with biological fluids, biodegradable, and can be removed from the body as inert biodegradable products. The choice of polymers used to deliver therapeutic proteins and peptides significantly impacts their therapeutic efficacy. Polymeric NPs hold promise for various delivery routes, including nasal, pulmonary, oral, and ocular delivery; nonviral gene delivery; and crossing the blood-brain barrier. A versatile system that can ensure the delivery and systemic stability of various proteins and peptides would be highly beneficial in the near future.

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# Significance of ZnO nano photocatalysts in the clean hospital environment: Effective bacterial disinfection and antibiotic waste (ciprofloxacin) disposal

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Copyright © 2024 by author(s). *Characterization and Application of Nanomaterialst* is published by EnPress Publisher, LLC. This work is licensed under the Creative Commons Attribution (CC BY) license. https://creativecommons.org/licenses/ one of the essential, widely used antibiotics and is often detected in water bodies and soil. It is vital to treat these medical wastes, which urge new research towards waste management practices in hospital environments themselves. Ultimately minimizes its impact in the ecosystem and prevents the spread of antibiotic resistance. The present study highlights the decomposition of ciprofloxacin using nano-catalytic ZnO materials by reactive oxygen species (ROS) process. The most effective process to treat the residual antibiotics by the photocatalytic degradation mechanism is explored in this paper. The traditional coprecipitation method was used to prepare zinc oxide nanomaterials. The characterization methods, X-Ray diffraction analysis (XRD), Fourier Transform infrared spectroscopy (FTIR), Ulraviolet-Visible spectroscopy (UV-Vis), Scanning Electron microscopy (SEM) and X-Ray photoelectron spectroscopy (XPS) have done to improve the photocatalytic activity of ZnO materials. The mitigation of ciprofloxacin catalyzed by ZnO nanophotocatalyst was described by pseudo-first-order kinetics and chemical oxygen demand (COD) analysis. In addition, ZnO materials help to prevent bacterial species, S. aureus and E. coli, growth in the environment. This work provides some new insights towards ciprofloxacin degradation in efficient ways.

Abstract: Hospital waste containing antibiotics is toxic to the ecosystem. Ciprofloxacin is

Keywords: hospital antibiotic waste; ciprofloxacin; ZnO nanomaterials; photocatalytic degradation; bacterial control

# 1. Introduction

In recent decades, the disposal of hospital harmful wastes, such as antibiotic drugs, directly into municipal wastes has been the major concern to the environment that will affect the animals and human health [1]. The antibiotics in the environment are also a main issue of public concern, since an antibiotic-resistant was formed in exposed non-target organisms [2]. It is urging the development of new guidelines and strategies to detoxify the antibiotic contaminants in the disposal [3]. There are many techniques available for waste treatment, such as advanced oxidation processes, photocatalysis, photolysis, electrolysis, and sonolysis, that are used for the removal of antibiotic toxins [4]. Among various methods, photocatalytic degradation of antibiotic pollutants exhibits low cost and high efficiency. The nanomaterials are serving as an effective photocatalyst for the antibiotic pollutant removal and applications of disinfection in the hospital environment [5].

Nanotechnology plays a great role in the removal of the antibiotic contaminants. Zinc oxide active photocatalysts play an important role in developing environmental challenges such as hospital waste degradation. It paves the way for the efficient oxidation of contaminants under UV or visible irradiation.

Ciprofloxacin is one of the widely used antibiotic medicines to treat infections and antibacterial genes in microorganisms, chosen as a test sample in the present work [6]. The literature revealed that the ciprofloxacin concentration in wastewater treatment plants, raw drinking water, hospital wastewater, lakes, and discharges of the pharmaceutical industry has been reported as 11–99 mg/L, 0.032 mg/L, 150 mg/L, 6.5 mg/L and 31–50 mg/L, respectively. In addition, ciprofloxacin in the hospital environment leads to antibiotic-resistant bacterial formation, and as a result, antibiotic requirements will be higher doses in bacterial infections.

The antibiotic ciprofloxacin with ZnO photocatalyst was tested for finding the degradability of this pharmaceutical pollutant [7]. The present plan is to carry out the UV photocatalysis for the mitigation process, and the usage of ZnO (catalyst) with the different concentrations of antibiotics was discussed in detail [8]. The outcome of the research would meet the great demand of disposal of hospital wastes. Considering the significant detection of ciprofloxacin in hospital environments, the necessity of removing it emerges and leads the way for further large-scale practical applications.

## 2. Materials and methods

## 2.1. Synthesis of ZnO Nanoparticles

Zinc acetate (Zn (CH<sub>3</sub>COO)<sub>2</sub> (H<sub>2</sub>O)<sub>2</sub>) and ammonium hydroxide (NH<sub>4</sub>OH) were taken as precursors to prepare ZnO nanoparticles by the co-precipitation. After zinc acetate was completely dissolved in double deionized water, ammonium hydroxide precursor was added dropwise until reaching the *pH* value of 9. The solution was stirred for 3 h at room temperature, and the homogeneity of the solution was attained by continuous agitation using a magnetic stirrer [9]. The resultant white, creamy solution was left to cool down for an hour. The precipitate was washed several times using ethanol and distilled water to reach the neutral value of *pH* and then filtered. Then the precipitate is kept in the muffle furnace at 350 °C for 3 h. The steps to prepare ZnO nanoparticles are pictorially shown in **Figure 1** [10].



Figure 1. Steps to synthesize zinc oxide nanoparticles.

#### 2.2. Photocatalytic detoxification of antibiotic contaminants

The photocatalytic antibiotic degradation process was carried out using ZnO (catalyst). The different concentrations of ciprofloxacin solution were prepared by taking 10 mg, 20 mg, 30 mg, 40 mg, and 50 mg dissolved with the distilled water separately [11]. The catalyst (ZnO) of 5 mg is added to the prepared ciprofloxacin solution and stirred at 500 rpm for 30 minutes. After stirring, the solution is exposed to a 254 nm 220V-15W UV lamp in a photo reactor for 30 minutes. The sample of 5 ml can be taken out from the solution of different concentrations, and the absorbance study is analyzed by UV spectroscopy [12].

The degradation capability of catalysts was estimated by finding absorbance with the help of a UV-Vis spectrometer (Shimadzu/UV-2600) and estimated using the formula:

Percentage of dye degradation =  $[C0-C]/C0 \times 100$ 

Here, C0 = [initial adsorption], Ct = [adsorption at time t].

## 2.3. Results and discussion

#### Characterization of synthesized ZnO nanoparticle samples

X-ray diffractometer is used to study the phase identification of crystalline material and the structural properties of ZnO. **Figure2(a)** shows the XRD pattern of ZnO nanoparticles. The sharp diffraction peaks of ZnO nanoparticles are observed at  $2\theta$  values of 31.68°, 34.10°, 36.49°, 47.41°, 56.81°, 66.36°, 67.98°, 69.27° and 77. 55° is associated with the (100), (002), (101), (110), (103), (200), (112), (201) and (202) planes respectively. These peaks correspond to the phase with hexagonal crystal geometry (JCPSD card No. 01-007-2551). The observed diffraction peaks are consistent with the reported values, and the absence of any peaks associated with impurities indicates the purity of this phase [13].

The crystallite size of nanoparticles is calculated by using the Debye-Scherrer formula.

$$D = \frac{k\lambda}{\hat{a}\cos\theta}$$

where, D—crystallite size, k—shape factor (0.9),  $\lambda$ —Wavelength of the X-ray source,  $\beta$ —Full-width half maximum height,  $\theta$ —is the angle of diffraction [14]. The maximum intensity of ZnO nanoparticles occurs at  $2\theta = 36.49^{\circ}$  is associated with (101) plane. The average crystallite size of ZnO nanoparticle is calculated as 23.38 nm.

The FTIR spectrum was recorded using Perkin Elmer FTIR spectrometer in the range at 400–4000 cm<sup>-1</sup>. Fourier transform infrared spectrum of ZnO is shown in **Figure 2b**. The observed absorption peaks are 3439 cm<sup>-1</sup>, 1708 cm<sup>-1</sup>, 1643 cm<sup>-1</sup>, 1449 cm<sup>-1</sup>,1027 cm<sup>-1</sup>, 863 cm<sup>-1</sup>, 767 cm<sup>-1</sup> and 608 cm<sup>-1</sup> [15]. The typical peaks at 608 cm<sup>-1</sup>, 767 cm<sup>-1</sup> and 1027 cm<sup>-1</sup> related to stretching vibrations of Zn–O bonds. The absorption at 863 cm<sup>-1</sup> is due to the formation of tetrahedral coordination of Zn. The peak at 3439 cm<sup>-1</sup> corresponds to the stretching vibration of the –OH molecule, while the band at 1643 cm<sup>-1</sup> shows the effect of the bending vibration of H–O–H bond a water molecule and is also observed in the significant absorption peak at

1449 cm<sup>-1</sup>. The peak at 1708 cm<sup>-1</sup> can also be related to an additional common band attributed to the bending mode of absorbed water.

The optical absorption of ZnO nanoparticle samples was determined at room temperature using the UV-visible spectrophotometer in the range of 100–1400 nm. **Figure 2c** shows the absorption spectrum of ZnO, which exhibits an absorption edge in the range of 376 nm, which relates to the UV region. The outcome reveals that there is a strong absorption in the UV band and weak absorbance in the visible region. Therefore, these ZnO samples can be used as an efficient photocatalyst under irradiation with UV light of wavelength less than 400 nm [16].

**Figure 2d** is the SEM image of ZnO nanoparticles, captured under 10.00 KX magnifications. It is predicted from the SEM image that ZnO nanoparticles are homogeneously scattered, and also the randomly oriented hexagonal shapes of nanosized particles with uniform distribution are presented [16]. The exhibited agglomeration of hexagonal-shaped nanoparticles is correlated with the outcome of X-ray diffraction analysis.



Figure 2. (a) X-Ray diffraction; (b) FTIR vibrations; (c) UV-Vis absorption; (d) SEM micrograph characterization of zinc oxide nanoparticles.

## 3. Applications

#### 3.1. Antibacterial activity

The bacterial strains of Staphylococcus aurous—902 (gram—positive species) and Escherichia coli—443 (gram—negative species) for agar well diffusion was purchased from MTCC, Chandigarh, India and the antibacterial activity of ZnO nanoparticles was tested against these bacterial strains [17]. Petri plates containing 20 ml nutrient agar medium seeded with the bacterial strains were cultured for 24 h,

and adjusted to 0.5 OD value according to MCFarland standard (Staphylococcus aurous—902 and Escherichia coli—443).

Figure 3 shows the synthesized ZnO materials exhibit zones against pathogenic bacteria in the petri plates. The diameter of the zone is measured in millimeters and also exhibits the degree of susceptibility of microorganisms. The zones of inhibition of ZnO nanoparticles are  $(14.91 \pm 0.16)$  mm and  $(17.25 \pm 0.35)$  mm for E.Coli and S.aureus respectively, as comparable with the standard values of positive control (E.Coli:16.75  $\pm$  0.06, S.aureus:  $17.25\pm$  0.21 in mm). The result proves that the effective antibacterial activity of ZnO samples.



Figure 3. Antibacterial activities of the ZnO nanoparticles.

## 3.2. Photocatalytic degradation mechanisms of ciprofloxacin

(Figure 4a-d) depicts When the ultraviolet light was irradiated on the ZnO semiconducting nanomaterial, the valence band electrons absorbed the energy and shifted to the conduction band. As a response, charged particles (holes in the valence band and electrons in the conduction band) develop [18]. The excitation of electrons from the valence band to the conduction band of ZnO catalyst due to UV illumination and the excitation process continuously produces the electron-hole pairs. Following that, the antibiotic waste components interact directly with the released charged particles, either degrading them or transferring them to the surface of the ZnO semiconductor photo catalyst. As the active sites are decreased, the compound is greatly absorbed by the catalyst. ZnO possesses high photocatalytic performance, well-separated reductive and oxidative active sites, generation of reactive oxygen species (ROS), and strong redox ability [19]. This reduces the reaction between the holes and the electrons. When the holes  $(h^+)$  are reacted with the water molecules to form hydroxyl free radicals (OH) and the electrons (e<sup>-</sup>) are reacted with dissolved oxygen to produce superoxide free radicals (O<sub>2</sub><sup>-</sup>). Free radicals such as (OH) and  $(O_2^{-})$  are the end products [20]. These two products (OH) and  $(O_2^{-})$  are strong oxidizing agents and are reacted with the ciprofloxacin to degrade it as a simple substance such as CO<sub>2</sub>, H<sub>2</sub>O and Mineral acids.

The maximum absorbance of ciprofloxacin is obtained at the wavelength of 272 nm [21]. The elimination rate of an antibiotic is greatly improved by considering low initial concentration. From the study, the least concentration of antibiotics achieves a high removal rate that is due to more reactions taking place for a lower number of antibiotic molecules [22]. The effect of different concentrations of the antibiotic

ciprofloxacin treated with ZnO nanoparticles and the degradation plot is shown in Figure 4a.

The mechanisms are expressed in Equations (1)–(4).

$$ZnO + hv \rightarrow ZnO(e^- + h^+)$$
 (1)

$$e^- + O_2 \rightarrow O_{2^{--}}$$
 (2)

$$h^+ + H_2 0 \quad \rightarrow \quad OH^{-} \tag{3}$$

$$OH^{-} + O_{2}^{-} + ciprofloxacin \rightarrow CO_{2} + H_{2}O + mineral acid$$
 (4)

The antibiotic ciprofloxacin is degraded and exposed to subsequent processes, resulting in non-toxic chemicals. When the polluting substance is present in higher concentrations, a smaller number of photons only penetrate through the surface catalyst that reduces the degradation studies.

Kinetic model

The kinetic model indicates the photo degradation of contaminants fits well with the pseudo-first-order kinetic plot. The high R2 values (more than 0.9) of the linear plot obey first-order reaction kinetics, supporting that the degradation of ciprofloxacin degradation using ZnO [23]. **Figure 4b** has the pseudo-first-order rate constants of pollutants at 0.0507 min<sup>-1</sup>.

Recycling and reusage

After the reaction is completed using a simple centrifugation method, ZnO nanoparticles were separated and dried at room temperature. Then the possibility of recycling of the used samples was analyzed for further degradation of antibiotic ciprofloxacin contaminants. ZnO nano-catalyst was tested for its photocatalytic degradability up to four cycles and retains its stability as in **Figure 4c**. Hence its reusability, it is recommended that ZnO might be a suitable photocatalyst for degrading antibiotic molecules [24].



**Figure 4.** UV Absorbance of effect of different concentration of antibiotic ciprofloxacin.

#### 3.2.1. Chemical oxygen demand (COD) analysis

The chemical oxygen demand (COD) test is used to determine the natural chemicals in a solution that are prone to pollutant degradation due to light illumination. A higher COD suggests the presence of more organic contaminants in the environment. In our study, the required quantity of chemical oxygen was calculated for the photocatalytic breakdown of antibiotics in hospital waste as an outcome of ultraviolet light exposure. Oxidation of organic molecules produced CO<sub>2</sub>. In addition to H<sub>2</sub>O, electrons were generated, the oxidizing reagent was reduced, and the liberated electrons were embraced. The COD of the solution was evaluated using the formula below to determine photo catalytic efficiency [(% = (COD0-CODt))]100%/COD0 where COD0 and CODt] are the (COD0-CODt) and COD values of the solution before photodegradation and during this process at a given time [25]. Figure 4d shows the results in (22.5%) chemical oxygen demand eradication, which equates to (80%) decomposition process. While decomposing ciprofloxacin, hydroxyl radicals are more readily released; this results in the photocatalytic degradability. This indicates that the photocatalytic process is quite effective in removing the ciprofloxacin from the solution.

### 3.2.2. X-Ray photoelectron spectroscopy

X-ray photoelectron spectroscopy (XPS) was taken for ZnO samples to illustrate their electronic states and surface materials. XPS describes the elemental bonding, chemical composition, and oxidation states in the environments of ZnO surfaces. **Figure 5** confirmed the the surface compositions and related valence states of the high-resolution spectra of Zn 2p. The Zn  $2p_{3/2}$  and Zn  $2p_{1/2}$  of Zn<sup>2+</sup> are responsible for the peaks centered at 1022.2 and 1045.3 eV, respectively [26]. XPS characterization results of the catalyst before and after the reaction indicate that the presence of only Zn<sup>2+</sup>. Furthermore, the XPS spectra confirmed that ZnO is well-formed and the purity of the samples was retained.



Figure 5. XPS plots of ZnO samples before and after usage for photo degradation.

#### 4. Conclusion

The photo catalyst ZnO is a potent nonmaterial for hospital drug waste treatment. ZnO nano materials were prepared by the co-precipitation chemical method. The samples purity, crystalline nature and crystallite size were studied using X-ray diffraction analysis. The functional groups of prepared samples were confirmed by FTIR technique. UV-V is analysis confirmed its suitability as an efficient photo catalyst for the removal of the antibiotic ciprofloxacin in the wastewater. SEM photo images revealed the homogeneous growth of hexagonally edged ZnO nanoparticles, and the crystallite sizes are 20 nm to 30 nm comparable to the calculated value of 23.38 nm by Debye-Scherer in XRD. The effective photocatalytic degradation of ciprofloxacin antibiotic was achieved in the presence of ultraviolet light illumination. The highest degradation was found in the lowest concentration of the antibiotic (10 mg). ZnO mixed with ciprofloxacin is against *S. aurous* (gram—positive species) and *E. coli* (gram—negative species) bacterial strains. Therefore, this can be concluded that the proposed nano photocatalysis is an economic, low-time-consuming, and good photocatalytic degradation takes place with the antibiotic ciprofloxacin.

## Highlights

- ZnO nanoparticles are chosen as an efficient photocatalyst for ROS generation.
- Effectively decompose the hazardous ciprofloxacin (test sample) in hospital waste.
- Efficient antibacterial agent to control S. aurous and E. coli growth.

Author contributions: Investigation, JBN; resources, JBN; data curation, JBN and PM; Writing—original draft preparation, JBN and PM; antibiotic—ciprofloxacin and antibacterial activity, JBN; experimental work, PM; conceptualization, JRMB; project administration, JRMB; supervision, JRMB; validation, JRMB; visualization, JRMB; writing—review and editing, JRMB. All authors have read and agreed to the published version of the manuscript.

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Article

# Preparation, characterization of *Telfairia occidentalis* stem extract-silver nanocomposite and application in remediation of lead (ii) ions from oilfield produced water

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Abstract: Every production day in Nigeria, and in other oil producing countries, millions of barrels of produced water is generated. Being very toxic, remediation of the produced water before discharge into environment or re-use is very essential. An eco-friendly and cost effective approach is hereby reported for remediative pre-treatment of produced water (PW) obtained from Nigerian oilfield. In this approach, Telfairia occidentalis stem extract-silver nanoparticles (TOSE-AgNPs) were synthesized, characterized and applied as bio-based adsorbent for treating the PW in situ. The nanoparticles were of average size 42.8 nm  $\pm$  5.3 nm, spherical to round shaped and mainly composed of nitrogen and oxygen as major atoms on the surface. Owing to the effect of addition of TOSE-AgNPs, the initially high levels (mg/L) of Total Dissolved Solids (TDS), Biological Oxygen Demand (BOD) and TSS of 607, 3.78 and 48.4 in the PW were reduced to 381, 1.22 and 19.6, respectively, whereas DO and COD improved from 161 and 48.4 to 276 and 19.6 respectively, most of which fell within WHO and US-EPA safe limits. Particularly, the added TOSE-AgNPs efficiently removed Pb (II) ions from the PW at temperatures between 25 °C to 50 °C. Removal of TOSE-AgNPs occurred through the adsorption mechanism and was dependent contact time, temperature and dose of TOSE-AgNPs added. Optimal remediation was achieved with 0.5 g/L TOSE-AgNPs at 30 °C after 5 h contact time. Adsorption of Pb (II) ions on TOSE-AgNPs was spontaneous and physical in nature with remediation efficiency of over 82% of the Pb (II) ions in solution. Instead of discarding the stem of Telfairia occidentalis, it can be extracted and prepared into a new material and applied in the oilfield as reported here for the first time.

**Keywords:** adsorption; heavy metals removal; nanomaterial; oilfield chemical; remediation; water treatment

## 1. Introduction

During production of crude oil, water is usually also co-produced. This water is often referred to as produced water (PW) or petroleum wastewater. The PW may originate from reservoir or formation water, or water injected during recovery or enhanced recovery operations [1]. The chemical composition of PW varies depending on geographical region, quality of crude and operating condition [2]. Most often, PW is composed of a complex blend of both inorganic and organic compounds. This implies that PW is highly toxic, and when discharged into the environment, it pollutes the environment. Being a mixture of complex toxic organic and inorganic in nature,

the chemicals in PW are often resistant to chemical or biological degradation. Discharge of PW on soils or into water has been a major cause of environmental degradation in the Niger delta region of Nigeria [3]. It renders water unfit for consumption, harms aquatic animals, kills biodiversity on the land and renders the soil infertile for cropping. In the end, it leads to decline in food production which may result to famine, malnutrition and even deaths.

To guard against these menace, it is very crucial that PW be treated before being discharged into the environment or re-use in injection stream. Otherwise, the discharge could be pose harmful (carcinogenic, mutagenic) effects on environment and humans [3] and cause corrosion, scaling and flow problems in transportation pipework [4]. Depending on its composition, various techniques have been applied to treat PW. Among these include physicochemical, chemical and biological methods of PW treatment described in literature [5,6]. Comparatively, chemical methods of treatment are very popular and reputed for good efficiency and selectivity [7-10]. For instance, high concentrations of grease, oil and fats as well as pollutants that may be suspended or dissolved in PW have been resolved by using chemical methods such as coagulation [11]. The coagulants precipitates are dissolved or suspended as colloidal solids which makes it easy to separate them by sedimentation. Electrocoagulation may also be efficient especially for resolving very greasy and oily PWs [12,13]. Experts have opined that a single method may not remove all the toxic components in PW at the same time. Therefore, any method used is often designed towards removing either some very toxic inorganic components only or some very toxic organic components only, at a given time [11].

This study was designed from this background and was aimed at removing some major toxic inorganic components in PW. The toxic inorganic substances in PW are basically heavy metals ions such as lead, cadmium, and chromium. These ions are often better removed using adsorbents by the adsorption [11]. Adsorption phenomenon is a popular method of treating PW [14]. For instance, activated carbon prepared from various sources is a commonly reported efficient adsorbent for petroleum wastewater treatment [15,16]. In selecting an adsorbent, cost effectiveness, local availability, renewability, durability, stability, biodegradability, eco-friendliness and high adsorption capacity are key factors often considered [14,17]. Despite the efficiency, activated carbon is very expensive to buy and laborious to fabricate and characterize. Scientists have therefore been in the search for cheap alternative materials, hence the proposed research work.

These days, engineered materials from plant extracts have been explored as alternative adsorbents that satisfy many of the requirements mentioned above [18]. Among the ones reported, plant-based adsorbents (biosorbents) have been demonstrated to be effective in removing some organic compounds and heavy metal ions from industrial wastewater [19–22]. Apart from a recent report by Ituen and co-workers [11], to the best of our knowledge, the use of plant biomass-based adsorbents in its nano-form to remove heavy metals from produced water has not been reported in literature, hence the motivation for this study. In this study, we have demonstrated the use of *T. occidentalis*-silver nanoparticles as adsorbent for treating PW for the first time.

Adsorbents derived from plant biomasses appear to be desirable because it will be of low cost, non-toxic and sustainably obtainable. Also, since plants contain a wide range of phyto-compounds, it could be multifunctional but, would easily be degraded by biochemical agents [11]. In other words, if stored for long, biochemical degradation of the biomass sets in, then its adsorption capacity and efficiency declines. To overcome these setbacks, the extract needs to be modified using chemical additives [23]. Recently, nanoparticles composites prepared by bio-reduction of plant extracts, have been used to remove toxic heavy metal ions, especially Pb, Cd, Cr and organic pollutants from wastewater [11]. Since nanoparticles large surface to volume ratio, their reactivity is expected to be high and this could justify the high removal efficiency reported in literature [11]. Also, being less difficult to synthesize, with the synthetic process not requiring deployment of expensive equipment or high energy, nanoparticles engineered from plant extracts would be more desirable. Therefore, the main objectives of this research was to prepare bio-based silver nanoparticles from T. occidentalis stem extract, characterize the nanoparticles and apply it as adsorbent for remediative treatment of PW, especially to remove Pb (II) ions from the PW.

## 2. Materials and methods

## 2.1. Sample collection and preparation

Viable seeds of *T. occidentalis* were obtained from Akwa Ibom Agricultural Development Program (AKADEP) and were authenticated by a plant taxonomist in the Department of Botany and Ecological Studies in the University of Uyo. The plants were cultivated in the field. Field experiment adopted a completely randomized design (CRD) with three replications. The plants were cultivated in three raised shaped beds and maintained under proper routine agronomic practices [24]. The mature plant was harvested and the edible leaves plucked out. The stem (which is often discarded) were cut into pieces, washed convincingly with distilled water, dried in air at laboratory temperature and macerated (**Figure 1a–c**).







(a) de-leaving.
(b) cutting into small sizes.
(c) maceration.
Figure 1. *T. occidentalis* stem after (a) de-leaving; (b) cutting into small sizes; (c) maceration.

## 2.2. Preparation of T. occidentalis stem extract

A 10 g of the macerated sample was soaked in 1 L of de-ionized water for 24 h

and filtered using 1 mm filter paper. The filtrate was concentrated to paste form in rotary evaporator at 40 °C, dried in oven at 40 °C and blended in mortar to obtain dry powdery *T. Occidentalis* stem extract (TOSE).

#### 2.3. Preparation of TOSE-silver nanomaterial

Solution of 0.001 M AgNO<sub>3</sub> (Analar, BDH, England) and 1.0 g/L of TOSE were prepared in deionized water. Both were mixed at various ratios (vol/vol), allowed to react and observed for colour change [11]. Every 1 hour, aliquot of the mixture was subjected to UV-Vis spectroscopic analysis. After colour change, a portion of the mixture was concentrated in rotary evaporator at 40 °C, then retrieved, washed using de-ionized water and filtered. The filtrate was dried in oven at 30 °C and labelled as TOSE-Silver nanomaterial (TOSE-AgNP) and stored in aluminum foil for characterization. Another portion was stored in amber colored glass for future analyses.

## 2.4. Characterization of synthesized materials

UV-Vis analysis was conducted by scanning both the TOSE and TOSE-AgNPs at 200–800 nm using Thermo Genesys 10 UV/Vis spectrophotometer. The functionalities in small quantity of each of TOSE and TOSE-AgNP (mixed with KBr) were determined by FTIR using Agilent cary 630 FTIR/ATR spectrophotometer. The crystallographic properties of the powder samples of both TOSE and TOSE-AgNP were also analyzed by XRD at  $2 \theta = 10^{\circ}-90^{\circ}$  using PX1800 X-ray diffractometer. The elemental compositions of each of TOSE and TOSE-AgNP were determined by EDS using Phenom ProX SEM/EDS spectrophotometer. The morphology and size of each of TOSE and TOSE-AgNPs were probed by TEM using Fei Technai G2F20 microscope.

## 2.5. Collection and treatment of produced water

Produced water was collected from Total Oil drilling platform at Amenem near Port Harcourt and transported to the laboratory the same day. The water sample was analysed to determine the average concentrations of lead ions present following standard procedures already reported by Ituen and co-workers [11]. In addition, some physicochemical properties of the water, namely, biochemical oxygen demand (BOD<sub>5</sub>), total dissolved solids (TDS), chemical oxygen demand (COD), conductivity, total suspended solids (TSS), dissolved oxygen (DO) and pH were also analysed following similar procedures reported by Ituen and co-workers [11].

### 2.6. Remediation of heavy metals from produced water

The procedures reported by Ituen and coworkers [11] were also followed with slight modifications. About 50 mL each of the produced water were placed in several flasks. About 0.5 g/L of TOSE and 0.1 g/L to 0.5 g/L of TOSE-AgNPs was added to each flask and each mixture was shaken in water bath at room temperature for 5 h. After 5 h, each mixture was filtered, and each filtrate was analyzed by AAS to determine the concentrations of each of Pb (II) ions.

## 2.7. Effect of adsorbent concentration

The TOSE-AgNPs was prepared into five (5) different concentrations to elucidate the effect of its dosage on the remediation efficiency. The concentrations were selected between 0.10 g/L to 0.50 g/L and this was obtained by dilution of the highest concentration using the dilution principle. During this investigation, the contact time, temperature and volume of the PW were not changed.

## 2.8. Effect of time and temperature

To determine the effect of time on the remediation efficiency, aliquots of the mixture at room temperature were collected every 1 hour within the shaking process and analysed by AAS. Also, the influence of temperature on the remediation efficiency was studied by varying the temperature of the solution in the water bath between 25 °C to 50 °C. For this experiment, the highest concentration of TOSE-AgNPs (0.50 g/L) was used and the shaking process was carried out at a constant time of 5 h.

#### 2.9. Analysis of data

The concentration of each metal ion in the produced water before remediation was denoted by  $C_o$  while the equilibrium concentration of each metal ion after filtration was denoted by  $C_e$ . The remediation efficiency ( $\eta$ ) was determined in terms of the ratio of the amount of heavy metal adsorbed by the substrate using Equation (1) [11].

$$\eta(\%) = \frac{C_o - C_e}{C_o} \times 100 \tag{1}$$

The amount of heavy metal ion adsorbed per unit mass of TOSE and TOSE-AgNPs at equilibrium  $(q_e)$  was determined from Equation (2), where *M* represents the mass of the adsorbent added to heavy metal ions solution of and *V* is the volume of the solution.

$$q_e = (C_o - C_e) \frac{V}{M} \tag{2}$$

## 3. Results and discussion

#### **3.1.** Formation of nanoparticles

On observation after every 1 h, the colour of the mixtures changed gradually until the nanoparticles were fully developed, signified by a change in colour from dark green to brown. It took different duration for complete development of the nanoparticles to occur depending on the ratio of mix. For instance, for the mixture containing TOSE:AgNO<sub>3</sub> (vol/vol) at 1:1 formed at about 2 h whereas 1:2 and 2:1 formed at about 5 h and 8 h respectively. Only the nanoparticles formed from 1:1 at the shortest duration was used for further studies.

## 3.2. Characterization of nanoparticles

#### 3.2.1. UV-Vis spectroscopy

Both TOSE and TOSE-AgNPs were subjected to UV-Vis analyses and the spectra obtained were shown in **Figure 2**. It can be observed that TOSE produced absorption maximum corresponding to the maximum wavelength of absorption  $(\lambda_{max})$  at 433 nm whereas that of TOSE-AgNPs was obtained at 485 nm. Since the absorption  $(\lambda_{max})$  for TOSE and TOSE-AgNPs were different, it was inferred that TOSE-AgNPs is a different material from TOSE. Also, the  $(\lambda_{max})$  obtained for TOSE-AgNPs were compared to others reported in literature for silver nanoparticles [11]. It was observed that the value for TOSE-AgNPs falls within 450–520 nm which is the range often obtained for silver nanoparticles. Therefore, the  $(\lambda_{max})$  obtained in the present study agrees with those reported in literature [11,18].



Figure 2. UV-Vis spectra of TOSE and TOSE-AgNPs.

#### **3.2.2. FTIR spectroscopy**

In order to elucidate the functional groups present in each of the material, the FTIR spectra of TOSE and TOSE-AgNPs were obtained and plotted in one frame of axes for easy comparison. The spectra obtained were shown in **Figure 3**. It can be observed from the figures that TOSE produced several peaks including in the fingerprint region. However, the peaks at around 3120–3530 cm<sup>-1</sup>, 2975 cm<sup>-1</sup> and 1620 cm<sup>-1</sup> were of significance to this study. The 3120–3530 cm<sup>-1</sup> peak on TOSE spectra may be assigned to O-H stretching of an aromatic alcohol or N-H stretching of a primary amine group. On formation of TOSE-AgNPs, it can be observed that this peak became broader and more prominent than with the crude extract. A similar occurrence was observed with the peak at 2975 cm<sup>-1</sup> which may be assigned to N-H stretching of an amine salt. This peak appears sharper and more prominent with TOSE-AgNPs than TOSE, suggesting that an amine salt may have been formed with silver. The peak at 1620 cm<sup>-1</sup> may be assigned to C = C of alkene or  $\alpha$ ,  $\beta$ -unsaturated ketone. This peak shifted to 1635cm<sup>-1</sup> in the spectrum of TOSE-AgNPs and became more

prominent. This indicates possibility of interaction of silver ions with TOSE phytocompounds at the C = C sites to form TOSE-AgNPs.



Figure 3. FTIR spectra of TOSE and TOSE-AgNPs.

#### 3.2.3. XRD spectroscopy

To determine whether TOSE-AgNPs were crystalline, they were subjected to XRD analyses alongside with TOSE for proper comparison and the spectra obtained were shown in **Figure 4**. It was observed that the spectrum of TOSE yielded no peaks whereas that of TOSE-AgNPs yielded major peaks at  $2 \theta = 28.0^{\circ}$ ,  $32.5^{\circ}$ ,  $38.2^{\circ}$ ,  $44.0^{\circ}$ ,  $46.4^{\circ}$ ,  $64.3^{\circ}$  and  $77.6^{\circ}$ . These peaks were compared to silver file 04–0283 of Joint Committee on Powder Diffraction Standards (JCPDS) card as well as with other reports on plant extracts mediated silver nanoparticles [11]. It was observed that the peaks at  $32.5^{\circ}$ ,  $38.2^{\circ}$  and  $44.0^{\circ}$  correspond to (121), (111) and (200) planes of Ag<sup>0</sup> phase. The peak at  $38.2^{\circ}$  was the most prominent, indicating that the silver is mostly distributed in the Ag (111) plane. Comparing the spectrum of TOSE with that of TOSE-AgNPs, it was clearly observed that while TOSE was amorphous, TOSE-AgNPs were crystalline, indicating that TOSE-AgNPs may be a nanoparticle.



Figure 4. XRD diffraction patterns of TOSE and TOSE-AgNPs.

#### **3.2.4. EDS spectroscopy**

The EDS spectra of TOSE and TOSE-AgNPs with prejudice to C, N, O and Ag atoms were obtained for comparison as shown in **Figure 5**. The result revealed that Ag was present on the surface of the new material (TOSE-AgNPs) but not found on TOSE. Though both contain C, N and O, the amounts were different as shown in **Table 1**. It can be inferred from **Table 1** that the incorporation of silver into the phytocompounds of TOSE resulted in its binding and formation of a kind of Ag-organic framework which increased the visibility of N and O. A similar suggestion was made in a work reported by Ituen and coworkers [11]. The EDS results obtained also supported that TOSE-AgNPs may have been formed and may be nanocomposite.



Figure 5. EDS spectra of (a) TOSE and (b) TOSE-AgNPs.

| LDS.    |            |            |            |            |  |
|---------|------------|------------|------------|------------|--|
| Element | TOSE       |            | TOSE-AgNPs |            |  |
|         | Weight (%) | Atomic (%) | Weight (%) | Atomic (%) |  |
| С       | 70.02      | 75.03      | 46.12      | 58.16      |  |
| Ν       | 0.46       | 1.01       | 1.13       | 2.21       |  |
| 0       | 29.52      | 23.96      | 39.34      | 37.73      |  |
| Ag      |            |            | 13.41      | 1.91       |  |

**Table 1.** Elemental composition of TOSE and TOSE-AgNPs surface determined by EDS.

#### **3.2.5.** Transmission electron microscopy

The nanostructure of TOSE-AgNPs was probed using transmission electron microscopy and the images captured for both TOSE and TOSE-AgNPs were shown in **Figure 6**. It was observed that TOSE were shapeless and sized within the microscale whereas TOSE-AgNPs were spherical to round and of average sizes of 42.8 nm

 $\pm$  5.3 nm. TEM results confirmed that TOSE-AgNPs was nanomaterial and appeared crystalline.



Figure 6. Morphologies of (a) TOSE and (b) TOSE-AgNPs determined by TEM.

## 3.3. Physicochemical properties of produced water

The concentration of Pb (II) ions in the produced water (PW) was determined in triplicates and the average values as computed was  $1.43 \pm 0.08$  mg/L. The other physicochemical properties determined are shown in **Table 2**. It has been documented that the USA-EPA and WHO permissible limits of Pb (II) ions for drinking water is 0.015 mg/L and 0.010 mg/L respectively [11], indicating that Pb (II) ions are present in excess amount and remediation is crucial. In addition, the values obtained for key pollution indicator parameters such as TSS, TDS, BOD etc were above WHO standards, therefore would require remediation to reduce them to safe limits before discharge or re-use for injection. Therefore, the PW was initially remediated by addition of TOSE and TOSE-AgNPs and the results from both adsorbents were compared and discussed in the following sub-sections.

| Parameter                                | Non-remediated water sample | Remediated with TOSE | Remediated with<br>TOSE-AgNPs |
|--|-----------------------------|----------------------|-------------------------------|
| pH                                       | 8.55                        | 8.52                 | 8.56                          |
| Conductivity ( $\mu$ Scm <sup>-1</sup> ) | 4318                        | 3953                 | 2881                          |
| TDS (mg/L)                               | 607                         | 406                  | 381                           |
| BOD <sub>5</sub> (mg/L)                  | 3.78                        | 1.56                 | 1.22                          |
| DO (mg/L)                                | 2.16                        | 5.87                 | 6.79                          |
| COD (mg/L)                               | 161                         | 242                  | 276                           |
| TSS (mg/L)                               | 48.4                        | 38.2                 | 19.6                          |

**Table 2.** Physicochemical properties of non-remediated and remediated produced water.

### 3.3.1. Effects of addition of TOSE and TOSE-AgNPs

From **Table 2**, it can be observed that remediation of PW with TOSE reduced pH from 8.55 to 8.52 whereas using TOSE-AgNPs, the pH rather increased to 8.56. These levels were well within the permissible limits by both US-EPA and WHO. For conductivity, it can be observed that PW had a very high value of 4318  $\mu$ Scm<sup>-1</sup>. However, on remediation with TOSE and TOSE-AgNPs, the values reduced to 3953

 $\mu$ Scm<sup>-1</sup> and 2881  $\mu$ Scm<sup>-1</sup> respectively. This implies that remediation with TOSE and TOSE-AgNPs caused significant reduction in conductivity of PW. Although the final conductivity of remediated water was still higher than the permissible level for drinking water (2500  $\mu$ Scm<sup>-1</sup>) and may require further treatment, the resulting water could still be useful for irrigation purposes and for livestock, which requires conductivity of around 2000–2500 µScm<sup>-1</sup> \*\* [11]. For TDS, addition of TOSE and TOSE-AgNPs reduced the value from 607 mg/L to 406 mg/L and 381 mg/L respectively. The upper safe limit of TDS in drinking water was 500 mg/L while the WHO recommended limit is 300 mg/L. This implies that the TDS in PW made it unsafe for drinking but on remediation, safe limits were attained. Similarly, the safe limits for BOD, DO, COD and TSS are 1-2 mg/L, 6.5-8 mg/L, 250-500 mg/L, 30 mg/L respectively. For DO and COD, the values are associated with the amounts of oxygen in the water. The untreated water had low amounts of oxygen. However, on treatment with the new material, the amount of oxygen increased, which indicates its higher propensity to support aquatic life. As can be observed from Table 2, on remediation with TOSE and TOSE-AgNPs, significant improvements were obtained, and the physicochemical properties of the remediated water was within ranges of values close to safe or permissible levels. Thus, TOSE and TOSE-AgNPs were effective in remediating the PW with TOSE-AgNPs which showed better remediating effect than TOSE.

#### 3.3.2. Effects of changing the concentration of TOSE-AgNPs

The concentration of TOSE-AgNPs was varied between 0.1 g/L to 0.5 g/L to elucidate the effect of its dose on the efficiency of remediation of Pb (II) ions. Results obtained are displayed in Table 3. It was observed that the concentration of Pb (II) ions in PW reduced from 1.43 mg/L to 0.32 mg/L and 0.18 mg/L on addition of TOSE and TOSE-AgNPs respectively, corresponding to an efficiency of 77.5% and 87.6% respectively. This implies that the efficiency of remediation of Pb increases with increase in TOSE-AgNPs dosage or concentration and is also in agreement with previous observations reported by Ituen and coworkers [11]. A possible explanation for this trend is that as the dose of the adsorbent increases, more adsorption sites becomes available per volume of the PW due to the presence of more adsorbent species in solution. The more the adsorption sites, the more the number of Pb (II) ions adsorbed and sequestrated from the PW. On the other hand, even lower concentrations of TOSE-AgNPs were more efficient than 0.5 g/L TOSE supporting that TOSE-AgNPs performs better than the crude extract.

| temperature using TOSE and different concentrations of TOSE-AgNPs. |                       |                       |       |           |  |
|--|-----------------------|-----------------------|-------|-----------|--|
| Adsorbent  | <sup>с</sup> о (mg/L) | <sup>C</sup> e (mg/L) | η (%) | <i>qe</i> |  |
| 0.5 g/L TOSE   | 1.43                  | 0.41                  | 71.2  | 102       |  |
| 0.1 g/L TOSE-AgNPs   | 1.43                  | 0.32                  | 77.5  | 555       |  |
| 0.2 g/L TOSE-AgNPs   | 1.43                  | 0.28                  | 80.4  | 288       |  |
| 0.3 g/L TOSE-AgNPs   | 1.43                  | 0.26                  | 81.8  | 195       |  |

0.20

0.18

86.1

87.6

154

125

Table 3. Results for adsorption of lead (II) ions from PW within 5 h at room

0.4 g/L TOSE-AgNPs

0.5 g/L TOSE-AgNPs

1.43

1.43

#### **3.3.3. Effects of temperature**

The effect of temperature on the amount of Pb (II) ions removed from the PW was investigated by varying the experimental conditions from room temperature (25 °C) to 50 °C and the results obtained are shown in **Table 4**. The results reveal that as temperature increases, the amount of Pb (II) ions removed as well as the remediation efficiency decreases. For instance, in the presence of TOSE, the amount of Pb (II) ions in PW reduced from 1.43 mg/L to 0.42 mg/L and 0.58 mg/L respectively corresponding to remediation efficiency of 70.7% and 59.7% respectively as temperature increased from 25 °C to 50 °C. This indicates that as temperature increases, there would be a huge reduction in remediation capacity and the  $q_e$  when TOSE is used as adsorbent. However, on addition of TOSE-AgNPs, the reduction in remediation efficiency was only slightly as could be observed going from 85.2% to 81.6%. This implies that the modification of TOSE into TOSE-AgNPs makes it more thermally stable and efficient than TOSE. The observed decrease in remediation efficiency as temperature increases is could be ascribed to the weak binding character of the adsorbent—Pb (II) ions adsorptive interaction. Such interactions are usually considered as physisorptions and are often driven by physical forces such as electrostatic interaction between positive Pb (II) ions and negative groups on the TOSE-AgNPs surface [11]. Owing to their weak nature, such interactions weaken with increase in temperature, leading to reduced remediation efficiency.

| Temperature | TOSE                  |                       |       | TOSE-AgNPs            |                       |       |  |
|-------------|-----------------------|-----------------------|-------|-----------------------|-----------------------|-------|--|
| (°C)        | <sup>C</sup> o (mg/L) | <sup>C</sup> e (mg/L) | η (%) | <sup>с</sup> о (mg/L) | <sup>C</sup> e (mg/L) | η (%) |  |
| 25          | 1.43                  | 0.42                  | 70.7  | 1.43                  | 0.21                  | 85.2  |  |
| 30          | 1.43                  | 0.41                  | 71.4  | 1.43                  | 0.17                  | 88.1  |  |
| 40          | 1.43                  | 0.48                  | 66.4  | 1.43                  | 0.22                  | 84.3  |  |
| 50          | 1.43                  | 0.58                  | 59.7  | 1.43                  | 0.26                  | 81.6  |  |

**Table 4.** Results for adsorption of lead (II) ions from produced water within 5 h at different temperatures.

#### **3.3.4.** Effects of contact time

The effect of contact time between the adsorbent and the heavy metal contaminants in PW was investigated to elucidate the optimum time required to remove the ions from PW. The results obtained were shown in **Table 5**. From the table, it can be observed that the efficiency of remediation increased as contact time increased until it reached a critical time of 5 h after which there was no significant increase in the percentage remediation efficiency. Therefore, it was inferred that the time taken for TOSE-AgNPs to optimally remove Pb ions from PW is 5 h. After this time, equilibrium may have been achieved and an optimal efficiency reached.

| <b>T:</b> | Parameters            |                       |       |  |
|-----------|-----------------------|-----------------------|-------|--|
| Time (h)  | <sup>C</sup> o (mg/L) | <sup>C</sup> e (mg/L) | η (%) |  |
| 1         | 1.43                  | 0.74                  | 48.1  |  |
| 2         | 1.43                  | 0.61                  | 54.7  |  |
| 3         | 1.43                  | 0.47                  | 66.8  |  |
| 4         | 1.43                  | 0.37                  | 74.2  |  |
| 5         | 1.43                  | 0.26                  | 81.6  |  |
| 6         | 1.43                  | 0.25                  | 82.1  |  |
| 7         | 1.43                  | 0.25                  | 82.2  |  |
| 8         | 1.43                  | 0.25                  | 82.2  |  |

**Table 5.** Results for adsorption of lead (II) ions from produced water at room temperature and different times using 0.50 g/L TOSE-AgNPs.

## 3.4. Remediation kinetics and adsorption mechanism

It has been reported that removal of heavy metal ions from solution by bio-based adsorbents occurs through the adsorption mechanism. Adsorption involves attraction and holding of the metal ions on the surface of the adsorbent molecules driven by surface forces. These surface forces could be electrostatic or weak van der Waals forces (physical adsorption) or even coordinate covalent bonding (chemical adsorption). To probe the nature of these forces, the values of  $q_e$  and  $C_e$  obtained were fitted into various adsorption isotherms but the best fit was obtained with the Freundlich adsorption isotherm (with  $R^2 = 0.9998$ ) which can be represented as shown in Equation (3) [11]:

$$\log q_e = \log K_f + \frac{l}{n} \log C_e \tag{3}$$

where  $K_f$  and *n* are constants related to the adsorption phenomena and  $K_f$  can be related to the free energy of adsorption using the Equation (4) [11]:

$$\Delta G_{ads} = -RT \ln 55.5K_f \tag{4}$$

where 55.5 is a factor that relates with the concentration of water molecules. The obtained isotherms is shown in **Figure 7** and the associated kinetic parameters deduced. The straight line graph afforded a slope of 0.93 and an intercept of 1.814. The constants *n* and  $K_f$  were 0.551 and 1.08 respectively. The value of  $\Delta G_{ads}$  obtained was -10.14 kJ/mol which can be appropriately associated with spontaneous adsorption of the metal ions on TOSE-AgNPs. Thus, if deployed for industrial use, TOSE-AgNPs would remediate PW on its own without the need for any catalyst or external force. Also, since the  $\Delta G_{ads}$  value is less negative than -20 kJmol<sup>-1</sup>, the adsorption therefore proceeded via the physical adsorption mechanism [11].



**Figure 7.** Freundlich adsorption isotherm for the adsorption of Pb from PW using TOSE-AgNPs at room temperature.

## 4. Conclusion

*Telfairia occidentalis* stem extract-silver nanocomposites (TOSE-AgNPs) were prepared, characterized and assessed as adsorbent for removing treatment of PW, which is usually toxic, before discharge or re-use. The nanomaterial was round shaped and the surfaces were rich in O and N atoms. The TOSE-AgNPs was up to 82% efficient in remediating Pb (II) ions from PW. Treatment of PW with TOSE-AgNPs also helped to reduce the levels (mg/L) of TDS, BOD and TSS while increasing the levels of DO and COD to near WHO and US-EPA safe limits. The remediation occurs through spontaneous physical adsorptive interactions between TOSE-AgNPs species and Pb (II) ions. The adsorption and remediation depends on contact time, temperature and dose of TOSE-AgNPs added. The new material could find application in the petroleum industry for treating associated wastewater.

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## Article

# Tuning dielectric properties in metal-doped NiO nanoparticles

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Abstract: Nickel Oxide (NiO) nanoparticles (NPs), doped with manganese (Mn) and cobalt (Co) at concentrations up to 8%, were synthesized using the composite hydroxide method (CHM). X-ray diffraction (XRD) analysis confirmed the formation of a cubic NiO structure, with no additional peaks detected, indicating successful doping. The average crystallite size was determined to range from 15 to 17.8 nm, depending on the dopant concentration. Scanning electron microscopy (SEM) images revealed mostly spherical, agglomerated particles, likely due to magnetic interactions. Fourier Transform Infrared Spectroscopy (FTIR) confirmed the incorporation of Mn and Co into the NiO lattice, consistent with the XRD results. The dielectric properties exhibited a high dielectric constant at low frequencies, which can be attributed to ion jump orientation and space charge effects. The imaginary part of the dielectric constant decreased with increasing frequency, as it became harder for electrons to align with the alternating field at higher frequencies. Both the real and imaginary dielectric constants showed behavior consistent with Koop's theory, increasing at low frequencies and decreasing at higher frequencies. Dielectric loss was primarily attributed to dipole flipping and charge migration. AC conductivity increased with frequency, and exhibited higher conductivity at high frequencies due to small polaron hopping. These co-doped NPs show potential for applications in solid oxide fuel cells.

Keywords: dielectrics; AC conductivity; koop's theory; space charge effect; metal doped nanoparticles

## **1. Introduction**

Transition metal oxide nanoparticles, including materials such as nickel oxide (NiO), manganese oxide (MnO), iron oxide (FeO), and cobalt oxide (CoO), have garnered substantial interest due to their remarkable characteristics at the nanoscale [1–4]. These materials exhibit distinctive properties that diverge significantly from their bulk counterparts, influenced by factors such as particle size, surface effects, and electrical behavior [5–8]. Among them, NiO emerges as a particularly promising candidate, recognized for its role as a p-type semiconductor [9,10]. It exhibits a high exciton binding energy and a bandgap in the range of 3.6 to 4.0 eV, offering unique advantages over other metal oxides. NiO's antiferromagnetic nature, combined with its electrically insulating behavior and rock-salt cubic structure, further enhances its appeal [11]. These characteristics, alongside its chemical stability and suitability for diverse technological applications, have positioned NiO at the forefront of research in materials science [12,13].

Despite its many benefits, NiO's low conductivity at room temperature, with resistance on the order of  $10^{13} \Omega$ -cm, poses challenges for certain applications [14]. This behavior is linked to charge carrier hopping facilitated by Ni<sub>2</sub><sup>+</sup> vacancies, which limits its electrical performance. Modifying the material through doping offers a viable solution to this problem [15]. For instance, introducing monovalent elements like lithium generates Ni<sub>3</sub><sup>+</sup> ions, which effectively reduces resistivity [16]. However, while bulk and single-crystal forms of NiO have been widely studied, the dielectric behavior of NiO nanoparticles, particularly co-doped variants, remains underexplored [17]. This knowledge gap underscores the need for further investigation into how innovative doping strategies can unlock the full potential of NiO in practical applications [18,19].

The structural and compositional properties of NiO are intrinsically linked to its nanoscale behavior [20]. NiO adopts a rock-salt lattice configuration, with octahedral coordination of  $Ni_{2^+}$  and  $O_2^-$  ions [21]. Its appearance is influenced by stoichiometry, transitioning from black in stoichiometric compositions to greenish hues when non-stoichiometric [22]. These optical and structural changes highlight the importance of controlling stoichiometry to optimize performance [23]. Additionally, factors such as synthesis method, particle size, annealing time, and doping significantly influence the properties of NiO at the nanoscale [24]. Managing structural and compositional defects, which are often intrinsic to nanostructured materials, is a critical challenge [25]. Addressing these defects is essential for enhancing the performance and reliability of NiO-based devices [26].

Defects within nanostructured materials play a pivotal role in shaping their electrical and dielectric properties [27,28]. For example, magnetic nanoparticles often experience strong interparticle interactions that lead to agglomeration, which can negatively impact material performance [29]. Single-doping strategies, while effective in introducing new functionalities, often result in clustering of the dopant within the host lattice, creating inhomogeneities. Co-doping presents a more sophisticated approach, addressing these limitations by introducing two dopant elements simultaneously [30]. This technique not only prevents dopant clustering but also enables fine-tuning of the material's electronic, magnetic, and dielectric properties. Co-doping has proven effective in enhancing conductivity, improving magnetic interactions, and achieving more uniform defect distributions [31].

The dielectric properties of NiO nanoparticles have been the focus of several studies. For instance, Different studies demonstrated the potential of NiO nanoparticles synthesized through wet chemical precipitation, reporting a large dielectric constant [32]. Similarly, some authors investigated NiO nanoparticles prepared via the sol-gel method and found that dielectric loss decreases with increasing frequency, attributed to the inability of ions to respond to alternating fields at higher frequencies [33,34]. These findings underscore the importance of dielectric studies in understanding and optimizing NiO for practical applications. However, there remains a significant gap in research on the frequency-dependent dielectric properties of co-doped NiO nanoparticles, providing a clear motivation for further exploration [35,36].

To address these challenges, this study investigates the effects of co-doping NiO nanoparticles with manganese (Mn) and cobalt (Co). These elements were chosen for

their ability to enhance both dielectric and magnetic properties while maintaining structural stability [37]. Co-doping introduces new energy states into the NiO lattice, facilitating charge carrier hopping and improving conductivity. Furthermore, the combination of Mn and Co ensures a more even distribution of dopant ions within the host matrix, minimizing the clustering observed in single-doped systems. This approach not only optimizes the dielectric response but also enhances the overall performance of the material.

The frequency-dependent dielectric behavior of NiO is particularly noteworthy. Dielectric properties, such as real and imaginary dielectric constants, exhibit distinct frequency-dependent trends [38]. At low frequencies, the dielectric constant is influenced by space charge effects and ion jump orientation, aligning with Koop's theory [39]. At higher frequencies, these effects diminish, resulting in a decrease in the dielectric constant as charge carriers are unable to keep pace with the alternating field [40]. By leveraging co-doping, this study aims to refine these properties, creating materials with tailored electrical and dielectric behavior for advanced applications [41,42].

The study also sheds light on the magnetic properties of co-doped NiO nanoparticles [43]. Mn and Co co-doping enhances magnetic interactions, reducing agglomeration caused by interparticle forces and improving the uniformity of particle dispersion [44]. These magnetic improvements, combined with enhanced dielectric performance, have significant implications for the use of co-doped NiO in applications such as solid oxide fuel cells [45–47]. The increased AC conductivity observed in co-doped NiO nanoparticles, particularly at higher frequencies, can be attributed to small polaron hopping, which further underscores their potential in energy-related technologies [48–50].

This research addresses critical challenges in the design of nanostructured materials, focusing on defect control and achieving optimal dopant distribution. By employing a co-doping strategy, the study demonstrates how the structural, electrical, and dielectric properties of materials can be simultaneously enhanced, offering a pathway to tailor these properties for specific functional requirements. Investigating the synthesis and frequency-dependent dielectric properties of both undoped and Mn-Co co-doped NiO nanoparticles, the research emphasizes their potential for superior performance. The novelty of this work lies in using the Composite Hydroxide Method (CHM), a simple and cost-effective approach that allows precise control over dopant concentration. By overcoming the challenges of defect management and dopant clustering in single-doped systems, this study contributes to creating materials with refined characteristics suitable for practical applications. The insights gained into the role of Mn and Co co-doping in enhancing dielectric performance, conductivity, and ion mobility in NiO nanoparticles pave the way for innovative applications in cuttingedge technologies, including renewable energy systems, high-performance electronics, solid oxide fuel cells, capacitors, and advanced sensors, offering new opportunities for technological advancements.

## 2. Experimental details

Composite Hydroxide Method (CHM) is a low-temperature method for

synthesizing single-phase nanoparticles (NPs). In this process, composite hydroxides are used as a solvent. It is a one-step process where all raw materials are mixed with hydroxides and placed in a beaker. The beaker is then placed in an oven at 200 °C for 24 h, allowing the NPs to form. After 24 h, the heating is stopped, and the sample is washed with distilled water to remove impurities. To form NiO NPs and Mn-Co co-doped NiO NPs, a specified number of mixed hydroxides (KOH, NaOH) is added to the beaker. Nickel nitrate is then combined with the hydroxides, and the mixture is placed in an oven at 200 °C for 24 h. Afterward, the sample is allowed to cool to room temperature. Finally, the sample is washed several times with distilled water to remove impurities, resulting in the desired NiO and co-doped NiO NPs. A flow chart illustrating the composite hydroxide-mediated method for preparing NiO and Mn-Co-doped NiO nanoparticles is shown in.

## 3. Results and discussions

## 3.1. X-ray diffraction

**Figure 1a** presents the XRD patterns of NiO and Mn-Co co-doped NiO nanoparticles with varying concentrations. The samples are labeled as S1 = undoped NiO, S2 = 2% Mn-6% Co doped NiO, S3 = 4% Mn-4% Co doped NiO, and S4 = 6% Mn-2% Co doped NiO. The diffraction peaks observed at  $2\theta$  = 37.30°, 43.30°, 62.90°, 75.30°, and 80.0° correspond to the (111), (200), (220), (311), and (222) crystal planes, respectively. These peaks align with JCPDS, No. 04-0835 data for NiO, confirming the formation of a cubic structure. The absence of additional peaks indicates high purity and successful doping, with no secondary phases detected.



Figure 1. (a) XRD pattern of NiO pure and co-doped NiO nanoparticles with JCPDS data; (b) Macrostrain vs crystalline size of NiO nanoparticles.

The crystallite size and lattice distortions varied with the dopant concentrations, as reflected by slight shifts in the diffraction peaks, which are attributed to differences in the ionic radii of Mn and Co. Furthermore, macrostrain was calculated for each crystal plane using the FWHM values and Bragg angles with the relation as:

$$\varepsilon = \frac{\beta}{4tan\delta}$$

where  $\varepsilon$  is the dielectric constant,  $\beta$  is the full width at half maximum (FWHM) and  $\delta$  is Bragg angle [51]. The calculated macrostrain values were: (111) = 0.00660, (200) = 0.00561, (220) = 0.00367, (311) = 0.00253, and (222) = 0.00233. These results confirm the uniform incorporation of Mn and Co into the NiO lattice, with macrostrain progressively decreasing from the (111) to the (222) planes, further highlighting the influence of doping on the structural properties.

## Macrostrain and crystallite effects in MN-CO doped NiO

**Figure 1b** illustrates the relationship between macrostrain and crystallite size, revealing the influence of Mn-Co doping concentrations on structural and dielectric properties of NiO. Macrostrain, calculated for different crystal planes using the FWHM values and Bragg angles, shows a progressive decrease from the (111) to the (222) planes, highlighting the uniform incorporation of dopants into the NiO lattice. This decreasing trend indicates reduced lattice distortions, which directly correlates with changes in crystallite size.

The observed variations in macrostrain and crystallite effects are significant for optimizing the dielectric properties of NiO. Higher macrostrain in the (111) and (200) planes correspond to greater lattice distortions, which can enhance polarization effects, improving the dielectric constant. Conversely, reduced macrostrain in the (220), (311), and (222) planes align with improved structural stability, facilitating the reduction of dielectric losses.

This interplay between macrostrain and crystallite size demonstrates the potential of Mn-Co doping to tailor the dielectric properties of NiO, making it suitable for advanced electronic and energy storage applications. The optimization of doping concentrations is critical to achieving the desired balance between dielectric constant and loss, as reflected in the graph.

## **3.2.** Fourier transform infrared spectroscopy

**Figure 2** presents the Fourier transform infrared spectroscopy (FTIR) spectra of both undoped and co-doped NiO nanoparticles, with varying concentrations of Mn and Co, within the wavenumber range of 350 to 1000 cm<sup>-1</sup>. The prominent bands between 400 and 600 cm<sup>-1</sup> are attributed to the stretching vibration mode of NiO, confirming the presence of NiO in all samples. This specific range is characteristic of Ni-O bond vibrations, indicating the formation of the NiO lattice structure. An absorption peak around 620 cm<sup>-1</sup> further validates the presence of NiO, which is a typical feature in the FTIR spectra of nickel oxide. Additionally, a band observed at 870 cm<sup>-1</sup> corresponds to the stretching and bending vibrations of C-O species, which are commonly present due to environmental exposure, such as carbon dioxide and moisture absorption from the air during synthesis and handling. This peak suggests that the nanoparticles may have adsorbed atmospheric contaminants or surface-bound species, which is typical in nanoparticle synthesis under ambient conditions.

Importantly, no additional peaks appear in the FTIR spectra of the Mn-Co codoped NiO nanoparticles compared to the undoped NiO. This lack of extra peaks indicates that the dopants (Mn and Co) are successfully integrated into the NiO lattice without forming separate phases or clusters. The absence of distinct peaks corresponding to Mn or Co oxides suggests that these dopants are likely dispersed or substituted within the NiO crystal structure, ensuring uniform doping. This behavior confirms a successful doping process where the metal ions (Mn<sup>2+</sup> and Co<sup>2+</sup>) replace Ni<sup>2+</sup> ions in the lattice without causing significant structural disturbances. The findings highlight the effectiveness of the co-doping strategy in modifying NiO properties while maintaining its structural integrity, which is essential for applications in electronics, catalysis, and energy storage devices.



Figure 2. FTIR spectra of pure and co-doped NiO nanoparticles.

## **3.3. Scanning electron microscopy**

**Figure 3** displays the SEM (Scanning Electron Microscope) micrographs of undoped and Mn-Co co-doped NiO nanoparticles at a magnification of 30,000x. The images reveal that the synthesized nanoparticles predominantly exhibit a spherical morphology. However, the particles appear highly agglomerated, likely due to the magnetic interactions between the Mn and Co dopants within the NiO matrix. Such agglomeration is a common phenomenon in magnetic nanoparticles, as magnetic forces cause particle clustering, which can influence the material's properties. Despite this, the overall shape and distribution of the particles provide valuable insights into the effects of Mn-Co doping on the morphology of NiO nanoparticles.

| Samples      | Planes<br>(hkl) | 2 Theta | FWHM<br>(radians) | Lattice constant (A <sup>0</sup> ) | Average crystalline size<br>D (nm) | Dislocation density $\delta = 1/D^2 \ 1/nm^2$ |
|--------------|-----------------|---------|-------------------|------------------------------------|------------------------------------|---|
| Un-doped NiO | 200             | 43.27   | 0.5106            | 0.208                              | 17.2                               | 0.0029  |
| S2           | 200             | 43.29   | 0.5139            | 0.207                              | 15.7                               | 0.0029  |
| S3           | 200             | 43.55   | 0.4481            | 0.207                              | 17.8                               | 0.0022  |
| S4           | 200             | 43.30   | 0.4488            | 0.208                              | 17.6                               | 0.0022  |

Table 1. Structural parameters of NiO pure and co-doped NiO nanoparticles.


Figure 3. SEM images of co-doped NiO nanoparticles (a) Undoped NiO; (b) Doped NiO.

# 3.4. Dielectric properties

The dielectric properties of nanoparticles are influenced by various factors, including the synthesis method, grain size, annealing temperature, and AC conductivity. In the case of NiO and its Mn, Co co-doped derivatives, the crystallite size plays a crucial role in shaping the dielectric behavior as shown in **Table 1**. Smaller crystallites typically result in higher dielectric constants at low frequencies, as the material exhibits enhanced ion jump orientation and space charge effects. As the crystallite size increases, the material's AC conductivity tends to improve, which in turn influences the dielectric loss and behavior at higher frequencies. These observations highlight that crystallite size is a key parameter in tailoring the dielectric properties of NiO-based materials for applications in electronic devices and energy storage systems. In this study, dielectric measurements were conducted on pure NiO and Mn, Co co-doped NiO samples, exploring their frequencies from 1 kHz to 2 MHz.

#### 3.4.1. Frequency vs real part

The dielectric constant is calculated by using the relation [52],

$$\varepsilon_r = \frac{Cd}{\varepsilon_0 A}$$

where;

 $\varepsilon_r$  is the relative permittivity (dielectric constant) of the material,

*C* is the measured capacitance of the material,

*d* is the thickness of the material,

 $\varepsilon_0$  is the vacuum permittivity (approximately 8.854 × 10<sup>-12</sup> F/m),

A is the area of the electrodes.

**Figure 4a** shows that at low frequencies, the dielectric constant increases, and at higher frequencies, it decreases. The higher value of the dielectric constant at low frequency may be attributed to the increased ion jump orientation effect and the enhanced space charge effect exhibited by the nanoparticles. In nanocrystalline materials, most of the atoms reside at the grain boundaries, where they become

electrically active due to charge trapping. The changes in the electric field can be easily followed by the dipole moment at low frequencies. As a result, space charge polarization and rotational polarization occur at the interfaces, enhancing the dielectric constant at low frequencies. These findings align with Koop's theory, which suggests that the grains are conductive, while the grain boundaries act as insulators. At higher frequencies, it becomes more difficult for electrons to align with the alternating electric field, causing the dielectric constant to decrease. NiO nanoparticles with co-doping of Mn and Co show a higher dielectric constant at low frequencies compared to pure NiO, due to the larger polarization in the co-doped nanoparticles.



Figure 4. (a) Dielectric constant of NiO nanoparticles; (b) Imaginary part of NiO nanoparticles.

#### 3.4.2. Frequency vs imaginary part

**Figure 4b** represents the frequency dependence of the imaginary part of the dielectric constant. The imaginary part of the dielectric constant reflects the energy loss within the material when it is subjected to an alternating electric field. It indicates the resistance offered by the material to the applied electric field and provides insights into the material's ability to store and dissipate energy. For an ideal, pure dielectric material, the imaginary part of the dielectric constant would be zero, as there would be no energy dissipation. However, in practical materials, the imaginary part is non-zero and varies with frequency. This part is calculated using the formula [53];

$$\varepsilon'' = \varepsilon' tan \delta$$

where;

 $\varepsilon''$  is the imaginary part of the dielectric constant, which corresponds to the energy loss in the material.

 $\varepsilon'$  is the real part of the dielectric constant, which represents the energy stored in the material.

 $\tan \delta$  is the loss tangent, a measure of the energy dissipation in the material when it is exposed to an alternating electric field. It is defined as the ratio of the imaginary part to the real part of the dielectric constant.

As the frequency increases, the imaginary part of the dielectric constant typically

decreases. This occurs because, at higher frequencies, the electrons within the material struggle to keep up with the rapidly alternating field, making it harder for them to align with the field direction. As a result, the energy loss due to electron alignment decreases with increasing frequency, causing the imaginary part of the dielectric constant to reduce. This frequency-dependent behavior is essential in understanding how the material performs under different operating conditions, particularly in applications like capacitors, sensors, and energy storage devices.

#### 3.4.3. Frequency vs tangent loss

**Figure 5** shows the frequency dependence of the tangent loss for NiO, also known as the dissipation factor. Mathematically, it can be expressed as [54]:

$$tan \ \delta = \varepsilon''/\varepsilon'$$

The dielectric loss tangent is higher at low frequencies and exhibits a decreasing trend at higher frequencies. This decrease in the dissipation factor follows Koop's model. Dielectric loss primarily results from the flipping of dipoles and the migration of charge carriers from the grains to the grain boundaries. At low frequencies, the grain boundaries are more dominant and provide more resistance to the flow of electrons, resulting in a higher tangent loss in this region. Undoped NiO has a larger tangent loss compared to co-doped nanomaterials, likely due to the larger imaginary part of undoped NiO at low frequencies, which may be attributed to its smaller particle size compared to other samples.



Figure 5. Frequency dependence for tangent loss for NiO nanoparticles.

## 3.4.4. Frequency vs AC conductivity

AC conductivity illustrates about the conduction mechanism. We calculated it by using formula [55];

$$\sigma ac = \varepsilon' tan(\delta) \omega \varepsilon_0$$

where ac is the AC conductivity, which measures how well a material conducts electricity when subjected to an alternating electric field and  $\omega$ : The angular frequency of the applied alternating field, defined as  $\omega = 2\pi f$ , where f is the frequency.

Figure 6 shows the frequency dependence of AC conductivity at room temperature for different concentrations of Mn and Co doped in NiO NPs. It is evident from the figure that all the samples exhibit an increase in conductivity with an increase in frequency. At low frequencies, the grain boundaries contribute significantly, making it difficult for electrons to overcome the barrier, leading to a minimum in AC conductivity. However, at higher frequencies, the role of the grains becomes more dominant, allowing electrons to move more easily, which results in a slight increase in AC conductivity compared to low frequencies. The conductivity of sample S4 is greater than that of the others, which may be due to the larger size of these co-doped NPs compared to S1, S2, and S3 samples. Additionally, the stronger small polaron hopping conduction mechanism in sample S4 may also contribute to this higher conductivity. These results suggest that the dielectric properties of co-doped NiO nanoparticles are strongly influenced by the nature of the dopants, their concentrations, and the average crystallite size of the NPs. These properties make them suitable for applications in energy conversion devices, such as solid oxide fuel cells.



Figure 6. AC conductivity of pure and co-doped NiO nanoparticles.

# 4. Conclusions

NiO nanoparticles doped with varying concentrations of Mn and Co were successfully synthesized using the Composite Hydroxide Method (CHM). X-ray diffraction analysis confirmed the formation of a cubic crystal structure, consistent with the expected phase. Scanning Electron Microscopy (SEM) images revealed agglomeration of nanoparticles, likely caused by the magnetic interactions between the Mn and Co dopants within the NiO matrix. Fourier Transform Infrared Spectroscopy (FTIR) analysis further validated the successful co-doping of Mn and Co into the NiO structure. The observed high dielectric constant at low frequencies is attributed to enhanced ion jump orientation and space charge effects, while the imaginary dielectric constant decreased at higher frequencies, suggesting a difficulty in electron alignment with the alternating field. AC conductivity measurements revealed an increase in conductivity with frequency, influenced by both the grains and grain boundaries. Notably, S4 = 6% Mn-2% Co doped NiO exhibited the highest conductivity at higher frequencies, potentially due to the small polaron hopping conduction mechanism and the increased crystallite size of the co-doped nanoparticles.

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# Comparative analysis of zinc precursors in the hydrothermal synthesis of zinc oxide hollow spheres

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https://creativecommons.org/licenses/ by/4.0/ **Abstract:** Zinc oxide (ZnO) hollow spheres are gaining attention due to their exceptional properties and potential applications in various fields. This study investigates the impact of different zinc precursors Zinc Chloride (ZnCl<sub>2</sub>), Zinc Nitrate [Zn(NO<sub>3</sub>)<sub>2</sub>], and Zinc Acetate [Zn(CH<sub>3</sub>COO)<sub>2</sub>] on the hydrothermal synthesis of ZnO hollow spheres. A comprehensive set of characterization techniques, including Field Emission Scanning Electron Microscopy (FE-SEM), X-ray Diffraction (XRD), Thermogravimetric analysis (TGA), and Brunauer-Emmett-Teller (BET) analysis, was utilized to assess the structural and morphological features of the synthesized materials. Our findings demonstrate that all samples exhibit a high degree of crystallinity with a wurtzite structure, and crystallite sizes range between 34 to 91 nm. Among the different precursors, ZnO derived from Zinc Nitrate showed markedly higher porosity and a well-defined mesoporous structure than those obtained from Zinc Acetate and Zinc Chloride. This research underscores the significance of precursor selection in optimizing the properties of ZnO hollow spheres, ultimately contributing to advancements in the design and application of ZnO-based nanomaterials.

Keywords: zinc oxide; hollow spheres; hydrothermal synthesis; precursors; morphology

# **1. Introduction**

Zinc oxide (ZnO) stands out as a versatile material with applications in diverse fields like photocatalysis and sensors due to its unique properties [1]. Among various ZnO nanostructures, hollow spheres hold particular promise for these applications. Their high surface area, tunable pore structure, and enhanced light harvesting capabilities make them ideal candidates [2,3].

The hydrothermal method offers a simple and cost-effective approach for synthesizing ZnO hollow spheres with controlled morphologies [4]. However, a crucial factor influencing the final product is the choice of Zinc precursor. The precursor significantly impacts the formation process, ultimately affecting the structure and properties of the resulting ZnO hollow spheres [5]. Despite extensive research on ZnO nanostructures, a systematic understanding of how different precursors influence the synthesis of ZnO hollow spheres via hydrothermal methods remains limited. While the relationship between morphology and performance is established, the precise mechanisms governing ZnO nanostructure growth and their correlation with morphology require further investigation, particularly for hydrothermal synthesis using different precursors [6]. To investigate this further, our research explores the effects of various zinc precursors (Acetate, Chloride, and Nitrate) on the structural and morphological characteristics of hydrothermally synthesized zinc oxide hollow spheres. By elucidating the role of precursors, we aim to contribute to the advancement of ZnO-based nanomaterial design and its targeted application development [7,8].

# 2. Experimental section

# 2.1. Materials

All solvents and reagents were used as received from commercial suppliers without any further purification. Zinc Nitrate anhydrous  $(Zn(NO_3)_2, 99.99\%)$  purity, (Mr = 189.36 g/mol) Sigma Aldrich), Zinc Acetate anhydrous  $(ZnAc_2, Zn(C_2H_3O_2)_2, 99.98\%)$ , (Mr = 183.48 g/mol), Sigma Aldrich), Zinc Chloride  $(ZnCl_2, > 99\%)$ , (Mr = 136.28 g/mol) Alfa Aesar, Germany), D-Glucose  $(C_6H_{12}O_6, 99.95\%)$  Sigma Aldrich), ethanol (EtOH, 100%, Molar Chemicals, Hungary) and Ultrapure water was used to prepare aqueous solutions for the chemical synthesis and all the experiments.

## 2.2. Synthesis of ZnO hollow spheres

This study employed a hydrothermal method to synthesize ZnO hollow spheres using various Zinc precursors. Zinc Chloride (ZC), Zinc Nitrate (ZN), and Zinc Acetate (ZA) served as the Zinc source, while glucose ( $C_6H_{12}O_6 \cdot H_2O$ , 99.5%) acted as the carbonaceous source. **Table 1** details the specific quantities of materials used for each precursor combination [9]. The ratio of Zinc precursors to glucose was considered as 1/2. A typical synthesis involved dissolving a specified amount of the chosen zinc precursor in deionized water under stirring to create a clear solution. Subsequently, glucose was introduced dropwise to initiate the hydrothermal reaction. The synthesized mixture was subsequently transferred to a 100 mL Teflon-lined stainless-steel autoclave and heated in a muffle furnace at 180 °C for 20 h. Upon cooling to ambient temperature, the product was collected. The resulting black precipitate was subjected to a thorough washing process using both distilled water and ethanol. Following synthesis, the black precipitate was dried in a vacuum oven at 80 °C for 5 h and finally calcined at 550 °C for 2 h. The detailed steps for preparing the ZnO hollow spheres are illustrated in the scheme of **Figure 1** [5,10,11].

| Code of material   | Chemical formula                                  | Zinc salt Precursors | D-glucose      | deionized water |
|--------------------|---|----------------------|----------------|-----------------|
| ZC (Zinc Chloride) | ZnCl <sub>2</sub>                                 | 0.1 mol (13.62 g)    | 40 g (0.2 mol) | 60              |
| ZN (Zinc Nitrate)  | $Zn(NO_3)_2$                                      | 0.1 mol (18.94 g)    | 40 g (0.2 mol) | 60              |
| ZA (Zinc Acetate)  | Zn(CH <sub>3</sub> CO <sub>2</sub> ) <sub>2</sub> | 0.1 mol (18.34 g)    | 40 g (0.2 mol) | 60              |

**Table 1.** Raw materials and conditions for the hydrothermal synthesis of ZnO nanostructures.



Figure 1. Schematic of progresses for the preparation of hollow sphere ZnO.

## 2.3. Characterization

The crystalline phases of the synthesized ZnO hollow spheres were identified using X-ray diffraction (XRD) analysis with Fe-Ka radiation source ( $\lambda = 0.1937$  nm) operated at 40 kV and 150 mA at a scanning step of 0.05 in the 2 $\Theta$  range 20–80 . The surface morphology and sizes of the hollow ZnO microspheres were observed by fieldemission scanning electron microscopy (FE-SEM, MIRA3TESCAN-XMU with an accelerating voltage of 20 kV) with energy-dispersive spectra. This technique provides high-resolution images, allowing for detailed observation of the surface features and particle size distribution of the ZnO hollow spheres. To understand the thermal decomposition behavior and crystallization process of the as-prepared powders, thermogravimetric analysis (TGA) and differential thermogravimetric analysis (DTG) were performed using a thermogravimetric analyzer (SDT 2960, TA Instruments, New Castle, DE) under atmospheric air. The analysis was conducted over a temperature range of 40 to 600 °C with a heating rate of 10 °C/min. Typically, a sample weight 10 mg was used for the tests to ensure measurable changes, while the analysis utilized ceramic crucibles due to their high-temperature stability and inertness. This technique provides information about the weight loss associated with the decomposition of organic residues and the formation of the final ZnO phase.

Functional groups present in the ZnO hollow spheres were identified through Fourier transform infrared (FT-IR) spectroscopy Jasco Model 4100\_Japan FT-IR spectra of ZnO . was recorded between 400 and 4000 cm<sup>-1</sup> using a resolution of 4 cm<sup>-1</sup>. This technique provides valuable information about the chemical composition and bonding environment within the material.

Finally, the pore size distribution and specific surface area of the synthesized ZnO hollow spheres were determined using nitrogen gas adsorption-desorption isotherms measured with a Micromeritics ASAP 2020 Brunauer-Emmett-Teller (BET)

surface area analyzer. This analysis enables the characterization of the material's porosity, a crucial factor in various applications such as catalysis and adsorption.

# 3. Results and discussion

### 3.1. FT-IR spectroscopy

FT-IR spectroscopy was employed in the range of 400–4000 cm<sup>-1</sup> to investigate the presence of organic residues and their influence on the properties of the ZnO hollow spheres. **Figure 2** presents the FT-IR spectra of samples prepared using different precursors (ZC, ZN, ZA) and calcined at 550 °C. The broad peak observed between 3250 and 3650 cm<sup>-1</sup> in all samples is attributed to the O–H stretching vibration of adsorbed water molecules on the surface of the ZnO hollow spheres. These peaks indicate the presence of surface hydroxyl groups and adsorbed water molecules, which are commonly observed in metal oxide materials. Additionally, the peak at around 1650 cm<sup>-1</sup> can be assigned to the bending vibration of CO-O bonds. The characteristic peaks for ZnO are observed at 400 cm<sup>-1</sup> and 570 cm<sup>-1</sup>. These strong absorption bands correspond to the stretching vibrations of the Zn-O bond in the wurtzite hexagonal structure of ZnO. The presence of these peaks confirms the successful formation of the ZnO phase in the synthesized hollow spheres [10].



Figure 2. FT-IR spectra of ZnO hollow spheres synthesis with different precursors.

## 3.2. X-ray diffraction (XRD)

The crystal structures of the synthesized ZnO hollow spheres were investigated using X-ray diffraction (XRD) analysis. **Figure 3** presents the XRD patterns of the samples prepared using different precursors (ZC, ZN, ZA).

These sharp diffraction peaks, in good agreement with the standard ZnO reference pattern, indicate the high purity and good crystallinity of the ZnO phase in all samples. All samples exhibited diffraction peaks at 40°, 43°, 45°, 61°, 74°, 82°, 89° and 91°, which can be readily indexed to the (100), (002), (101), (102), (110), (103),

and (112) crystal planes of the hexagonal wurtzite structure of ZnO (Reference code: 01-076-0704) [12].



**Figure 3.** XRD pattern of the ZnO thin film prepared by different precursor materials.

The crystallite size of the ZnO hollow spheres was estimated using Scherrer's equation. Based on the full width at half maximum (FWHM) of the (101) peak in the XRD patterns. The calculated crystallite sizes are summarized in **Table 2**. The results indicate that the choice of precursor influences the crystallite size of the ZnO hollow spheres, with values ranging from 39 to 91 nm [13].

Table 2. Crystal size, lattice parameters of the samples with different precursors.

| Tine productors    | Dog [97Th ]   | EWILM L off [09Th ] | Crystallita siza (nm)  | Lattice parameter |        | - 0/0  |
|--------------------|---------------|---------------------|------------------------|-------------------|--------|--------|
| Zinc precursors    | 108. [ 2111.] |                     | Crystanite size (inii) | a                 | c      | C/a    |
| Zinc Chloride (ZC) | 46.051450     | 0.669120            | 48                     | 3.2660            | 5.1988 | 1.5917 |
| Zinc Nitrate (ZN)  | 45.820390     | 0.944640            | 34                     | 3.2562            | 5.1969 | 1.5960 |
| Zinc Acetate (ZA)  | 45.986160     | 0.354240            | 91                     | 3.2548            | 5.2139 | 1.6019 |

Furthermore, the lattice parameters (a, c) and the c/a ratio were determined for each sample and are presented in **Table 2**, further confirming the successful formation of the desired crystalline phase [14].

# 3.3. Thermal behavior

The thermal decomposition behavior of the ZnO precursor powders (ZC, ZN, and ZA) was investigated using thermogravimetric analysis (TGA) and differential thermogravimetric analysis (DTG). These analyses were employed to determine the material's thermal stability and guide the selection of the calcination temperature. **Figure 4** presents the TG and DTG curves for the different precursors. The TG curve indicates a gradual weight loss for all samples in the temperature range of 40–600 °C. The residual weight percentages at 600 °C were approximately, 20%, 20%, and 38% for Zinc Chloride, Zinc Nitrate, and Zinc Acetate, respectively. The quantitative reduction in mass during decomposition is presented in **Table 3** [15]. The high

percentage of precipitation of zinc oxide particles in the Zinc Acetate precursor is related to the growth of irregularly shaped crystals that did not form a hallow sphere and grew as a single crystal. Also, in the FE-SEM images of **Figure 5**, these particles can be identified as See clearly.

Table 3. Thermal analysis corresponding to the TGA, TG and DTG curves.

| Zinc precursors    | Exothermic region (°C) | Maximum Temperature Peak (°C) | Weight loss % |
|--------------------|------------------------|-------------------------------|---------------|
| Zinc Chloride (ZC) | 200-460                | 458                           | 80            |
| Zinc Nitrate (ZN)  | 200-450                | 436                           | 80            |
| Zinc Acetate (ZA)  | 200–440                | 413                           | 65            |



**Figure 4. (a)** TG; **(b)** DTG analysis of ZnO hollow sphere that synthesis by different precursors.



Figure 5. FE-SEM and EDS images of ZnO hollow sphere that synthesis by different precursors.

Two prominent peaks are observed in the DTG curves, located around 300 °C and 440 °C. The first peak can be attributed to the desorption of water molecules physically adsorbed on the precursor surfaces. The second, more significant peak at around 440 °C corresponds to the decomposition of residual carbon species that might be physically or chemically bound to the precursor materials.

A significant weight loss is observed in the temperature range of 320–460 °C, coinciding with the DTG peak at 440 °C. This suggests the decomposition of organic moieties present in the precursors. The TG curve plateaus above 460 °C, indicating minimal further weight loss. This implies that at this temperature, the residual organic components from the precursors are nearly completely decomposed.

These findings suggest that a calcination temperature above 460 °C is necessary to ensure the complete removal of organic residues and achieve the desired final product composition [16].

# 3.4. Morphological analysis

**Figure 5** shows FE-SEM images of distinct morphologies of ZnO hollow spheres synthesized using different precursors. ZnO samples derived from Zinc Chloride and Zinc Nitrate exhibited well-defined hollow spherical structures with smooth surfaces. In contrast, ZnO synthesized from Zinc Acetate displayed irregular morphologies with partial aggregation and the presence of smaller nanoparticles. Also, we can see nanoparticles that have not turned into hallow spheres and they have grown in the form of rods. This has led to the amount of weight percentage produced in Zinc Acetate precursor being higher than others. It can also be seen in **Figure 5** that the diameter of ZnO hallow spheres synthesized for Zinc Nitrate precursor is in the range of 500 nm, while the diameter of hallow spheres synthesized for Zinc Chloride and Zinc Acetate precursors is in the range of 700 nm. EDS analysis for all three types of precursors shows that Zinc oxide is well synthesized and does not contain any impurities.

## 3.5. Surface properties

The specific surface area, pore size distribution, and specific pore volume of the calcined ZnO hollow spheres prepared from different precursors were determined using nitrogen adsorption-desorption isotherms measured with a Brunauer-Emmett-Teller (BET) surface area analyzer. Figure 6 presents the nitrogen adsorption and desorption isotherms, along with the pore size distribution of ZnO hollow structures synthesized from different precursors. The nitrogen adsorption shows a type III isotherm with a hysteresis loop, indicating the presence of mesopores (2-50 nm) and macropores (> 50 nm). Adsorption for ZnO synthesized from zinc nitrate is approximately ten times higher than from zinc acetate and five times higher than from zinc chloride, suggesting more mesopores in the zinc nitrate sample, as corroborated by FE-SEM images. The BJH plot reveals a bimodal pore size distribution, with zinc acetate showing peaks at 2-4 nm (micropores), while Zinc chloride shows a pore size distribution graph with two prominent peaks in the range of 8 to 10, indicating the presence of mesoporous. The zinc nitrate sample demonstrates a wide distribution from 1 to 100 nm, with peaks at 15 and 24 nm, indicating a well-developed porous structure and significantly larger pore volumes compared to the other precursors [15,17].

**Table 4** summarizes the physical parameters of the synthesized samples, showing that zinc nitrate and zinc chloride samples have higher specific surface areas and more uniform structures than those from zinc acetate. The increased porosity of ZnO hollow spheres primarily stems from their hollow morphology and the effective removal of template species during hydrothermal synthesis. Samples derived from Zinc Chloride and Zinc Nitrate exhibited a higher specific surface area and well-defined mesoporous structure compared to those synthesized from Zinc Acetate. The superior porosity of ZnO hollow spheres obtained from Zinc Chloride and Zinc Nitrate precursor can be attributed to the well-defined hollow morphology and efficient removal of template species during hydrothermal synthesis [18,19].



**Figure 6.** Nitrogen adsorption isotherm and pore size distribution curve (inset) of the samples synthesis by different precursors characterized by BET & BJH techniques.

Table 4. Specific surface area, mean pore diameter, pore volume of the sample's synthesis with different precursors.

| Material           | Specific surface area (m <sup>2</sup> ·g <sup>-1</sup> ) | Mean pore diameter [nm] | Pore volume (cm <sup>3</sup> ·g <sup>-1</sup> ) |
|--------------------|--|-------------------------|---|
| Zinc Chloride (ZC) | 48.829   | 161.75                  | 1.445   |
| Zinc Nitrate (ZN)  | 35.722   | 72.69                   | 0.333   |
| Zinc Acetate (ZA)  | 18.271   | 12.1                    | 0.1477  |

# 4. Conclusion

Hydrothermal synthesis successfully produced ZnO hollow spheres using all three precursors (Zinc Nitrate, Zinc Acetate, and Zinc Chloride).

- Field-emission scanning electron microscopy (FE-SEM) images revealed greater uniformity in hollow spheres synthesized with Zinc Chloride and Zinc Nitrate compared to Zinc Acetate.
- Thermogravimetric analysis (TGA) analysis indicated a higher production efficiency of ZnO using the Zinc Acetate precursor. However, this method resulted in irregular and rod-shaped particles with incomplete conversion to hollow spheres.
- The thermogravimetric analysis (TGA) curve displayed two exothermic peaks around 300 °C and 440 °C. These peaks likely correspond to the evaporation of

adsorbed water molecules from the ZnO surface, the removal of organic content and impurities from the lattice, and the conversion of  $Zn(OH)_2$  to ZnO.

- The specific surface area, average diameter, and void volume of the hollow spheres decreased in the order of Zinc Chloride, Zinc Nitrate, and Zinc Acetate precursors.
- Notably, Zinc Nitrate and Zinc Chloride precursors yielded well-defined hollow spheres with high surface area and porosity. This makes them promising candidates for various applications requiring tailored nanostructured ZnO materials.

Author contributions: Conceptualization, OK, KN and HNS; investigation, OK; writing—review and editing, OK, KN and HNS; writing—original draft, OK; project administration, KN and HNS; funding acquisition, KN and HNS; discussion on results, KN and HNS; writing the results, KN and HNS; visualization, KN and HNS; resources, KN and HNS; data-curation, KN and HNS. All authors have read and agreed to the published version of the manuscript.

**Research data policy and data availability statements:** On reasonable request, the corresponding author will make available the datasets used and/or created during this investigation. The experimental work and language of the manuscript are also unique. There was no evidence of plagiarism in the submitted manuscript. If the reviewer insists on seeing the evidence, we would gladly deliver it to them in a plagiarized form. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest: The authors declare no conflict of interest.

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# Enzymatic electrochemical biosensor for detection of L-Cysteine based on reduced graphene oxide modified glassy carbon electrode

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Copyright © 2025 by author(s). *Characterization and Application of Nanomaterials* is published by EnPress Publisher, LLC. This work is licensed under the Creative Commons Attribution (CC BY) license. https://creativecommons.org/licenses/ by/4.0/ Abstract: Cysteine is one of the body's essential amino acids to build proteins. For the early diagnosis of a number of diseases and biological issues, L-cysteine (L-Cys) is essential. Our study presents an electrochemical sensor that detects L-cysteine by immobilizing the horseradish peroxidase (HRP) enzyme on a reduced graphene oxide (GCE) modified glassy carbon electrode. The morphologies and chemical compositions of synthesized materials were examined using Fourier transform infrared spectroscopy (FTIR) and field-emission scanning electron microscopy (FESEM). The modified electrode's electrochemical behavior was investigated using cyclic voltammetry (CV). Cyclic voltammetry demonstrated HRP/rGO/GCE has better electrocatalytic activity than bare GCE in the oxidation of L-cysteine oxidation in a solution of acetate buffer. The electrochemical sensor had a broad linear range of 0  $\mu$ M to 1 mM, a 0.32  $\mu$ M detection limit, and a sensitivity of 6.08  $\mu$ A  $\mu$ M<sup>-1</sup> cm<sup>-2</sup>. The developed sensor was successfully used for the L-cysteine detection in a real blood sample with good results.

Keywords: l-cysteine; enzyme; graphene oxide; electrochemical sensor; cyclic voltammetry

# **1. Introduction**

The human body is composed of numerous biomolecules that are essential for various physiological functions. Biomolecules such as nucleic acids, carbohydrates, proteins, and amino acids are substances produced by living organisms and cells that perform a wide range of functions. Detection of the biomarkers associated with the diseases should be known and is possible by using biosensors. Cysteine (Cys) is an important amino acid used in the body and can also be taken as a supplement in the form of N-acetyl-L-cysteine. The detection of cysteine in biological samples has been the focus of numerous research efforts, as it plays an important role in many physiological processes [1]. Cys is often found in blood plasma in concentrations ranging from 53 to 300 mM, and it can be used as a key marker of health and disease risk. Cys insufficiency also causes skin lesions, hair depigmentation, edema, liver damage, muscle and fat loss, fatigue, and tiredness in addition to slower body growth. As a result, neurological pathogeneses, cystinosis, Parkinson's and Alzheimer's illnesses, and metabolic problems have all been linked to aberrant Cys accumulation and production. Therefore, developing rapid, low-cost, dependable, and sensitive analytical techniques to detect Cys would be crucial for protein quantification as well as for the early detection and prevention of neurological conditions, including Parkinson's and Alzheimer's illnesses as well as motor neuron disease [2]. To detect cysteine, various methods can be used, such as capillary electrophoresis (CE) [3], high-performance liquid chromatography (HPLC) [4], chemiluminescence [5], fluorescent probes [6], colorimetric [7], and electrochemical methods [8-10]. These

techniques allow for the sensitive as well as accurate detection of cysteine in biological samples. However, the aforementioned recognized methods are almost solely used in a rigorous lab environment, which is time demanding and requires a professional operator and expensive equipment [11,12]. Electrochemical techniques were recently thought to be the most practical because of their low cost, fast responsiveness, low detection limit, and great sensitivity [13,14].

Many studies on the electrochemical determination of Cys in various modified electrodes have been undertaken, for example, carbon-based electrodes [15–17], metal modified electrodes [18–20], polymer-modified electrodes [21,22]. Several electrochemical methods have been used to detect Cys. The electrochemical techniques used to detect Cys in an aqueous solution have been categorized based on the many electrical signals that Cys produces in the solution. Voltammetric techniques such as cyclic voltammetry (CV), differential pulse voltammetry (DPV), square wave voltammetry (SWV), linear sweep voltammetry (LSV), and others are highly suitable due to their high sensitivity, short analysis times, low level of detection (LOD), and low cost of equipment [23–25].

Furthermore, materials with enhanced surface conductivity were integrated into the sensor design to improve sensitivity and selectivity. Nanomaterial based electrochemical signal amplifications have enormous promise to improve both sensitivity and selectivity for electrochemical sensors and biosensors, with notable advancements in nanotechnology and nanoscience. In addition to metal nanoparticles, carbon-based materials (such as carbon nanotubes and graphene and its derivatives) have also gained a lot of attention in the development of electrochemical sensing platforms. This is primarily because of their advantageous properties, which include high surface area, excellent electrical conductivity, high mechanical strength, excellent performance and thermal stability [26,27].

Enzymes are large, intricate macromolecules that catalyze the rapid conversion of substrates into products; they are primarily composed of proteins. Enzyme-based electrochemical biosensors find extensive use in various fields such as healthcare, food safety, environmental monitoring. An enzyme-based biosensor uses the enzyme as the recognition element; to preserve enzyme activity, the enzyme is immobilized on or within the transducer surface's support matrix. Immobilized enzymes act as electrocatalysts, facilitating electron transfer between the electrode and the substrate molecule, leading to signal amplification and improved detection limits. Designing the biorecognition component of enzymet. Numerous studies on enzyme immobilization methods, including entrapment, covalence, adsorption, affinity, and cross-linking, have been published [28–30].

In this study, we used an enzyme electrochemical biosensor based on Horseradish peroxidase to investigate electrochemical properties Cys. Firstly, we have synthesized rGO which was electrodeposited onto the bare GCE's surface. and horseradish peroxidase enzyme was then immobilized on the electrode surface using a gelatin membrane that was then cross-linked with glutaraldehyde. For the measurement of L-cysteine, the suggested sensor demonstrated great sensitivity, good biocompatibility, and a low detection limit. Graphene's huge specific surface area makes it an excellent substrate for providing a large number of catalytic active sites. The designed electrode (Horseradish peroxidase/rGO/GCE) showed high selectivity for determination of Cys.

# 2. Materials and methods

## 2.1. Chemicals and apparatus

L-Cysteine, L-ascorbic acid, hydrochloride, dopamine, Nafion solution, uric acid and palladium (II) nitrate dihydrate phosphate buffer (PB) solution, Horseradish peroxidase, gluteraldehyde were purchased from Sigma-Aldrich (USA). Graphite powder potassium permanganate sulfuric acid (99.99%), hydrochloric acid, sodium nitrate, were purchased from Merck Company (Germany). All other compounds were analytical reagent grade and all solutions were made with double distilled water. The electrolyte used as the backdrop was phosphate buffer solution of 0.1 M (PBS, pH 7). A Potentiostat (CHI-1205B) was used for all of the cyclic voltammetry (CV) experiments. The frequency response analysis (FRA) module of a potentiostat was used to perform the electrochemical impedance spectroscopy (EIS) measurements. For the electrochemical measurements, a standard three-electrode cell assembly made up of a Pt wire counter electrode and an Ag/AgCl reference electrode was used. The working electrode was modified GCE.

# 2.2. Electrode preparation

The bare GC electrode was polished using alumina slurry at a thickness of 1, 0.3, and 0.05 µm respectively followed by washing with DI water, isopropanol, and finally sonication in DI water. Graphene oxide (GO) was synthesized by modified Hummer's method [31]. Furthermore, the synthesized GO reduced by annealing at 200, 300 and 400 °C. After being thermally treated to become rGO powder, the dark brown powder turned to black [32]. Then 1 mg/mL of prepared rGO was dissolved in deionized water using an ultrasonicator. Subsequently, 5 µL rGO of the suspension was applied using the drop casting technique to the GCE surface, and it was allowed to dry for one hour at room temperature to produce the rGO modified GCE. In the next step, Horseradish peroxidase was immobilized onto rGO/GCE. This was accomplished by diluting 1 mg of horseradish peroxidase in 1 ml of phosphate buffer solution (pH 7.0). They then combined 12 mg of gelatin and 4 U of horseradish peroxidase in 100 µL of potassium phosphate buffer (pH 7.0) at 38 °C The modified electrode surface was then covered with 0.25µL of the mixed solution, which was let to dry for one hour at 4 °C. Lastly, it was submerged for 5 min in a phosphate buffer (50 mM, pH 7.0) containing 2.5% glutaraldehyde to facilitate cross-linking. The films were further used to study electrochemical characteristics by voltammetry (CV).

# 3. Results and discussion

# 3.1. Characterization of HRP/rGO nanocomposite

## 3.1.1. Morphological studies

Surface morphology of the samples was observed by using field emission scanning electron microscopy (FESEM). **Figure 1** shows FESEM of **Figure 1a** rGO nanosheet and **Figure 1b** HRP/rGO surface. The result revealed that rGO exhibits a translucent, wrinkled-type, ultrathin, and flexible, sheet-like morphology. However, in case of rGO/GCE, a spherical like beads is spread over the surface as shown in **Figure 1b**. The result revealed that rGO proved to be an excellent carrier support for HRP immobilization.



**(a)** 



**(b)** 

Figure 1. FESEM images of (a) rGO; (b) HRP/rGO.

# 3.1.2. Fourier transform infrared spectroscopy (FTIR)

Fourier-transform infrared spectroscopy (FTIR) is a potent analytical method which is commonly used to study the chemical composition and bonding of materials. **Figure 2** shows the FTIR spectra in the range from 4000 to 800 cm<sup>-1</sup>). In the case of reduced graphene oxide (rGO), FTIR can provide information on the functional groups present on the rGO surface. The peaks visible at 3454 cm<sup>-1</sup>, 1591 cm<sup>-1</sup>, 1220 cm<sup>-1</sup> corresponding to the O-H stretching, O-H stretching, C = O stretching, and C-O stretching vibration suggesting that the graphene was oxidised and the product rGO could be successfully dispersed in water. The alkyl (-CH2) chains' O-H vibration modes are responsible for the observed spectrum areas at 3380 cm<sup>-1</sup> and 2920 cm<sup>-1</sup>. Peaks at 1651 cm<sup>-1</sup> assigned to the amide I, while aliphatic amines (C–N stretching vibration) assign at the region 1045 cm<sup>-1</sup>. The FTIR spectrum of rGO-HRP showed that HRP was successfully immobilized onto rGO due to presence of characteristic peaks of HRP and the rGO.



**Figure 2.** Fourier transform infrared spectroscopy (FTIR) spectra of rGO and HRP/rGO.

# 3.2. Electrochemical characterization of modified electrode

The electrochemical behavior of the various electrodes was examined by using CV at 40 mV scan rate in a 5 mM [Fe (CN)<sub>6</sub>]<sup>3-/4-</sup> solution made in 0.1 M KCl solution. The chosen scanning speed for the cyclic voltammetry (CV) measurements was 40 mV/s. This value was selected based on a balance between achieving good signal resolution and maintaining reasonable experimental time. Cyclic Voltammograms (CVs) of bare GCE and modified GCE are shown in **Figure 3a** The CV of the bare GCE initially showed a 1:1 ratio between the anodic and cathodic peak currents and well-defined redox peaks showed related to the reversible redox behavior of [Fe (CN)<sub>6</sub>]<sup>3-/4-</sup>. After the modification of GCE with rGO, redox peak currents increase potentially as a result of semiconducting elements present. Additionally, compared to rGO/GCE electrode, the modified HRP/ rGO/GCE electrode showed significantly higher peak current, due to presence of HRP enzyme.

Electrochemical impedance spectroscopy (EIS) was used to examine the electron transfer properties of these electrodes. The electrode/electrolyte's electrontransfer resistance Rct is represented by the diameter of the semicircle in the EIS Nyquist plot. **Figure 3b** shows EIS of a) GCE, b) rGO/GCE, c) HRP/rGO/GCE in in 0.1 M KCl with 5 mM [Fe (CN)6]<sup>3-/4-</sup>. The bare GCE exhibited a Ret of (310.5  $\Omega$ ). A noticeable drop in resistance (267.6  $\Omega$ ) was seen when the rGO was modified in the GCE. This was caused by the faster electron transport of Fe[(CN)6]<sup>3-/4-</sup> from the rGO to the electrode surface. However, the the modified electrode HRP/rGO/GCE had a lowest Ret of 89.2  $\Omega$  and hence it shows the highest conductivity.



**Figure 3. (a)** A cyclic voltammetry of modified electrodes in 0.1 M KCl containing 5 mM [Fe (CN)6]<sup>3-/4-</sup> at a scan rate 40 mV/s; **(b)** Nyquist plots for various modified electrodes in 0.1 M KCl with 5 mM [Fe (CN)<sub>6</sub>]<sup>3-/4-</sup>. Frequency range: 0.1 Hz to 10 Hz.

# 3.3. Effect of scan rate

To assess the behavior of L-Cys electrocatalytic oxidation on the HRP/rGO/GCE modified electrode, CVs were obtained at various scan rates using 0.1 M PB solution containing 200  $\mu$ M L-Cys. The peak current density rises as the scan rate is increased from 10 to 100 mV.s<sup>-1</sup>. as shown in **Figure 4**. There is a linear connection between the square root of the scan rate and the peak current density with  $R^2 = 0.9958$ . This suggests that the electrocatalytic oxidation of L-Cys is a diffusion-controlled electron transfer process on the modified electrode.



Figure 4. (a) CV of the HRP/rGO/GCE under different scan rates (10 to 100 mVs<sup>-1</sup>) in 0.5 mM Cys; (b) Relation between scan rate and peak current.

#### 3.4. Electrocatalytic oxidation of L-cysteine

To assess the catalytic response of the HRP/rGO/GCE modified electrode to the oxidation of L-Cys, as shown in **Figure 5a**. A series of CV were recorded for various L-Cys concentrations. The results reveled that as the L-Cys concentration increases; current density also increases, providing more evidence of the electrode's electrocatalytic activity toward the oxidation of L-Cys. As seen in **Figure 5b**, the sensor shows high linearity in the concentration range of 0  $\mu$ M to 1 mM with a correlation coefficient ( $R^2$ ) of 0.9992. There is a linear relationship between the concentration of L-Cys and the current density of L-Cys. The sensor achieved a sensitivity of 6.08  $\mu$ A. $\mu$ M<sup>-1</sup>cm<sup>-2</sup> with a LOD of 0.32  $\mu$ M and quick response time demonstrates the HRP/rGO/GCE's promising catalytic activity toward L-Cys. For comparison, the detecting parameters based on different reported-nanomaterials with the proposed sensor in this study were listed in **Table 1**.



**Figure 5. (a)** CV of a modified electrode scanning at a rate of 40 mVs<sup>-1</sup> in a phosphate buffer with varying L-Cys concentrations; **(b)** Peak current against L-Cys concentration calibration plot 3.5.

## **3.5. Interference study**

The applied voltage has a significant impact on the selectivity and sensitivity of the electrochemical sensors. **Figure 6** shows the electrochemical oxidation of 100  $\mu$ M of various species AA, UA, DA, glucose and l-cysteine of 10  $\mu$ M individually at pH 7.0 with a scan rate of 40 mVs<sup>-1</sup> at different applied potentials by CV. The anodic peak is evidently the primary difference, since the catalytic current of L-cysteine oxidation peaked at the applied potential V, indicating that the applied voltage affects the sensor's selectivity. Almost no interference was observed in the presence of these foreign species. These findings indicated that AA, UA, DA, glucose did not significantly interfere with L-cysteine determination, and that this electrode has the potential to be employed for L-cysteine sensing in the presence of AA, UA, DA, glucose. These findings thus imply that the sensor electrode has outstanding selectivity for L-Cys detection. The reproducibility of the sensor was examined using four identical HRP/GO/GCE sensors. The CV responses to 10 $\mu$ M

L-Cys indicated no obvious current change among the four electrodes. The sensor's strong repeatability was confirmed by the 1.5% RSD value. CV from five successive measurements on a single electrode was used to assess repeatability, and the results were compared to the original value. After five iterations of measurements, the sensor maintains 94.2% of the original value. The electrode demonstrated 90% recovery with an RSD of 4.03% for LCys detection after 8 days, indicating the sensor's strong stability.



**Figure 6.** The electrochemical oxidation of 100  $\mu$ M of some species (AA, UA, DA, glucose and l-cysteine) at pH 7.0 with scan rate 40 mV/s by CV technique.

**Table 1.** Comparison of the analytical performance of HRP/GO/GCE sensor with some carbon-based earlier sensors for the detection of Cys.

| Sr. No | Modified electrodes | Linear range (µM) | Limit of Detection (µM) | References |
|--------|---------------------|-------------------|-------------------------|------------|
| 1      | CuFe2O4/rGO-Au      | 50-200; 0-15,000  | 0.383; 0.598            | [33]       |
| 2      | 20%Pd@Ti3C2Tx/GCE   | 0.5–10            | 0.14                    | [34]       |
| 3      | Pt-Fe3O4-rGO/GCE    | 100–1000          | 10.1                    | [35]       |
| 4      | CoHCF/GCE           | 6–1000<br>1.5–200 | 4                       | [36]       |
| 5      | rGO-Nafion@Pd6/GCE  | 0.5–10            | 0.15                    | [37]       |
| 6      | AuNR/MWCNT/GCE      | 5–200             | 0.008                   | [38]       |
| 7      | HRP /rGO/GCE        | 0–1000            | 0.32                    | This work  |

# 4. Conclusions

The electroanalytical measurement of Cysteine was carried out using Horseradish peroxidase (HRP) enzyme immobilized on a modified glassy carbon electrode (GCE) using graphene oxide where electrocatalytic oxidation was observed to occur at a lower overpotential when compared to bare GCE. This sensor apparatus offered a quick response, a good LOD, and great selectivity. In addition, the sensor demonstrated good reproducibility, repeatability, and stability. Lastly, the modified sensor showed intriguing analytical features, including larger detection ranges between 0 and 1 mM, a noteworthy LOD of 0.32  $\mu$ M, and super electrocatalytic activities. It has a few additional advantages, such as ease of manufacture, better electrocatalysis, and efficient discrimination from typical interfering bimolecular compounds with rapid and stable response to Cysteine.

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Review

# A review on antimicrobial properties of nano-ferrites: Biomedical applications

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Abstract: This review focuses on ferrites, which are gaining popularity with their unique properties like high electrical resistivity, thermal stability, and chemical stability, making them suitable for versatile applications both in industry and in biomedicine. This review is highly indicative of the importance of synthesis technique in order to control ferrite properties and, consequently, their specific applications. While synthesizing the materials with consideration of certain properties that help in certain methods of preparation using polyol route, green synthesis, sol-gel combustion, or other wise to tailor make certain properties shown by ferrites, this study also covers biomedical applications of ferrites, including magnetic resonance imaging (MRI), drug delivery systems, cancer hyperthermia therapy, and antimicrobial agents. This was able to inhibit the growth of all tested Gramnegative and positive bacteria as compared with pure ferrite nanoparticles without Co, Mn or Zn doping. In addition, ferrites possess the ability to be used in environmental remediation; such as treatment of wastewater which makes them useful for high-surface-area and adsorption capacity due heavy metals and organic pollutants. A critical analysis of functionalization strategies and possible applications are presented in this work to emphasize the capability of nanoferrites as an aid for the advancement both biomedical technology and environmental sustainability due to their versatile properties combined with a simple, cost effective synthetic methodology.

Keywords: nano-ferrites; ferrites; dopants; biomedical

# 1. Introduction

Human development is the epicenter of all study through the use of resources and the creation of new chemicals that benefit society. In particular, magnetic materials have grown in significance, and now, these are widely employed in many different sectors because of their unique properties; these properties are used in many fields, such as the chemical industry, the medical field, and electronics [1]. When pure metals are compared with ferrite materials, which are known as magnetic materials due to their special properties, this includes low cost, high resistance, and simple production processes. In ferrites, ferric oxides are the main components, which are a mixture of other metal oxides; these ferrites can be synthesized by using hematite (Fe<sub>2</sub>O<sub>3</sub>) or magnetite (Fe<sub>3</sub>O<sub>4</sub>) and are typically non-conducting [2].

The characteristics of structural, electrical and magnetic are greatly improved by substituting tiny quantities of dopants, which makes ferrites appropriate for many technological applications [3]. The production of nanoferrites has received great interest which is due to their improved magnetic and electrical characteristics and this is easy comparable bulk counterparts [4,5]. These ferrites useful for different field due their improved magnetic characteristics which is in nanoscale in size, and also contain lager surface to volume ratio and quantum confinement effect [6]. This result indicates that nanoferrites is a essential materials for industry and technology, propelling breakthroughs in electronics, telecommunications, and healthcare. High magnetic permeability, chemical and thermal stability, high electrical resistivity, and gentle magnetic behavior are just a few of the remarkable qualities that ferrites have. These characteristics make them extremely adaptable for a different application, which includes choke coils, Ferrites are utilized across a range of applications due to their unique properties. In microwave frequency devices, they exhibit high permeability ( $\mu > 1000$ ) and low loss tangents (tan  $\delta < 0.1$ ), facilitating efficient signal transmission. In computer memory core elements, magnetic saturation (50-80 emu/g) and moderate coercivity (Hc~20-300 Oe) ensure reliable data storage and retrieval. For biomedical applications, surface-coated ferrites (PEG or silica) with particle sizes of 10-100 nm enhance biocompatibility and cellular uptake. They also show promise in hyperthermia treatments with a specific absorption rate (> 100 W/g) and smaller particle sizes (10–50 nm) for effective heat generation. In drug delivery, ferrites allow for targeted therapy through magnetic saturation (50–80 emu/g) while maintaining biocompatibility. Their antibacterial and antifungal efficacy is supported by small particle sizes (10–50 nm) and functionalization with antimicrobial agents, ensuring chemical stability across various pH ranges. Lastly, in water treatment, nano-sized ferrites (10-200 nm) with magnetic saturation (50-70 emu/g) and a surface area of 50–150  $m^2/g$  enable efficient, transformer cores, antenna rods, gas sensors, recording heads, electrodes telecommunication systems, and biomedical applications like drug delivery, magnetic hyperthermia, and magnetic resonance imaging [7–9]. The electrical and magnetic characteristics work together to provide substantial performance and efficiency gains, making them widely used in contemporary electronics and healthcare systems [10–12].

This review article starts a discussion of different synthesis methods for ferrites, their antibacterial characteristics, and their prospective uses in biomedicine. In specific condition the dopants to the improvement of their characteristics are discussed, along with the difficulties and prospects associated with the switch from bulk to nano-ferrites for next-generation technological advancements.

# 2. Synthesis of ferrites

The synthesis methods of ferrites are critically important because the properties and applications of ferrites are highly dependent on their synthesis techniques. The choice of synthesis method influences the size, shape, purity, crystallinity, magnetic properties, and surface characteristics of the ferrite nano-particles. These factors, in turn, determine the material's suitability for specific applications, such as in electronics, catalysis, medical devices, and environmental remediation. Many synthesis techniques is shown in **Figure 1** like Ball milling, Solid state reaction method, Coprecipitation method, Hydrothermal, Micro-emulsion techniques are used to synthesize ferrite materials [13–16]. Different approaches like Polyol technique, Green Synthesis technique, Sol gel method, Sol gel auto-combustion Fast firing method (Pramanik Method) etc., are employed to prepare ferrites [15–23].



Figure 1. Synthesis techniques of ferrites.

| Method                             | Description   | Key Features  | Typical Conditions  |
|------------------------------------|---|---|---|
| Solid-State Reaction               | Mixing metal oxides or carbonates followed by high-temperature sintering.                             | Simple, cost-effective, suitable for bulk synthesis       | High temperatures (1000–1400 °C),<br>long sintering times (4–8 h)                 |
| Sol-Gel Method                     | Using metal alkoxides or nitrates to form a gel, followed by drying and calcination.                  | High purity, fine particle size, homogeneity              | Low to moderate temperatures (400–800 °C), controlled atmosphere                  |
| Co-precipitation                   | Precipitating metal hydroxides from a solution, followed by drying and calcination.                   | Uniform particle size, suitable for nanoparticles         | Moderate temperatures (300–700 °C), pH control during precipitation               |
| Hydrothermal<br>Synthesis          | Reacting metal precursors in a sealed vessel at high pressure and temperature.                        | Controlled particle size, high crystallinity              | High pressures (autoclave), moderate to high temperatures (150–300 °C)            |
| Microwave-Assisted<br>Synthesis    | Using microwave radiation to heat precursors rapidly, leading to faster reaction times.               | Fast processing, energy efficient, fine particles         | Rapid heating, moderate to high temperatures (100–200 °C)                         |
| Mechanical Milling                 | Ball milling metal oxides or carbonates to achieve fine particle sizes before sintering.              | Simple, scalable, cost-effective                          | Room temperature for milling, high temperatures for sintering                     |
| Spray Pyrolysis                    | Spraying a solution of metal salts into a hot<br>furnace to form fine particles through<br>pyrolysis. | Fine, spherical particles, continuous process             | High temperatures (800–1200 °C), controlled spray conditions                      |
| Combustion Synthesis               | Using a fuel and oxidizer mixture to ignite a self-sustaining combustion reaction.                    | Rapid, energy efficient, can produce high-purity products | Exothermic reaction, moderate temperatures (300–600 °C)                           |
| Chemical Vapor<br>Deposition (CVD) | Decomposing metal precursors in vapor phase onto a substrate to form ferrites.                        | High purity, controlled composition, and thickness        | High temperatures (500–1000 °C), vacuum or controlled atmosphere                  |
| Electrochemical Deposition         | Electroplating metal ions onto a substrate to form ferrite films.                                     | Precise thickness control, suitable for thin films        | Room to moderate temperatures (25– $100 \text{ °C}$ ), controlled current/voltage |

| Table 1. Different s | ynthesis | methods | of ferrites. |
|----------------------|----------|---------|--------------|
|----------------------|----------|---------|--------------|

**Table 1** depicts different synthesis methods, description of techniques, key features of synthesis methods and requirement of typical conditions for synthesis of ferrites [17,24]. The synthesis of ferrites is critically important because it dictates the material's final properties, and including yield which can improve by optimizing key factors such as temperature, reaction time, pH level, precursor concentration, and stirring speed. Considering choice of the solvent and fuel to oxidant ratio in methods like sol-gel or auto-combustion plays a significant role, controlling reaction cooling

rates enhance product quality and yield, sometime crucial for their performance in various applications. By choosing and optimizing the synthesis method, researchers and engineers can tailor ferrites for specific uses, ensuring they meet the necessary requirements in fields ranging from electronics to medicine.

# 3. Biomedical applications of ferrites

Nanoferrites have obtained a significant attention due to their applications in different fields ranging from industry to biomedicine (Figure 2) [25]. One of the applications is magnetic resonance imaging (MRI), the most common use of nanoferrites in biomedicine field as a contrast agent. This MRI is a non- invasive diagnostic technique that helps to get detailed picture of the body tissues. MRI modifying the relaxation duration  $(T_1 \text{ and } T_2)$  by adjacent water protons, iron oxides like magnetite helps find the difference between normal and diseased tissue by making the tissues harboring these nanoparticles seem brighter or darker in the MRI images. Similarly, manganese ferrite (MnFe<sub>2</sub>O<sub>4</sub>) and cobalt ferrite (CoFe<sub>2</sub>O<sub>4</sub>) used to get sharper, higher-resolution pictures [23–29]. The magnetic hyperthermia is a method where nanoferrites also used to treat cancer, magnetic nanoparticles are subjected to an alternating magnetic field, this technique utilized the particle's temperature. This heated particle injected in to the diseased tissues causes the tumor cells to heat up to a point where all cancer cells die, but leaving the surrounding healthy tissues unaffected [30–33]. Cobalt ferrites is a an important to treat the magnetic hypothermia-based cancer treatment using Cobalt ferrites which is a magnetic hyperthermia-based cancer therapy because of their high coercivity and magnetic saturation [34–36]. For magnetic refrigeration, key parameters include high magnetic anisotropy (K: 104 to 106 J/m<sup>3</sup>), significant adiabatic temperature change ( $\Delta$ Tad: 2–4 K at 2–5 Tesla), and a transition temperature near room temperature (Tc: 290–310K). Common materials include gadolinium (Gd), with a transition temperature of 293 K and  $\Delta T_{ad}$  of~3–4 K, and Gd-alloys like Gd-Si-Ge, which enhance refrigeration properties [37]. The main reason to study for the targeted drug delivery methods represents a notable's applications in biomedicine. Delivering medicines to targeted locations like tumor or particular organ these systems are intended to increase the effectiveness of medicine while lowering the amount of the drug that comes into contact with heathy tissues, to avoid adverse effects. The infected cells or organ medication is delivered in a regulated manner once it reaches the target, guaranteeing minimum systemic toxicity and high therapeutic concentrations at the illness site. Once the targeted organ treated very well need to make sure the health of the cells needs to monitor with the help of biosensors which is based on nano-ferrites which is also became very essential tool in diagnostics and healthcare. These biosensors designed to detect biological entities such as proteins, DNA, or pathogens. The combination of nano-ferrites with bio-molecules that bind to specific target analytes, these particles can provide highly sensitive detection of disease markers, toxins, or infectious agents. For example: Cobalt ferrite (CoFe<sub>2</sub>O<sub>4</sub>) and zinc ferrite (ZnFe<sub>2</sub>O<sub>4</sub>) ferrites used in biosensors due to their stability and large surface area, which improves ability of sensors and also its very important to detect early diagnosis, enabling more timely treatment and patient outcomes [36,37]. The

nanoferrites can also exabits strong antimicrobial properties that makes suitable for many applications in health care segment where infection control is critical, some nanoferrites, particularly those doped with other metals like zinc, copper and silver are known as disrupt the cell membranes of bacteria and fungi, leading to their destruction. This quality used in antimicrobial ferrites can be incorporated into medical device coatings, wound dressings, or even hospital textiles, where they act as barriers to microbial growth. This kind of feature is very important to prevent hospital acquired infections, which are major cause of complications and healthcare system [38–48]. In addition to this nano-ferrites are being explored for different use in this section medical field being explored for use in tissue engineering and regenerative medicine. When combined with biodegradable scaffolds, magnetic nanoparticles can be used to guide cell growth and tissue regranulation scaffolds, magnetic nanoparticles can be used to guide cell growth and tissue regeneration through the application of magnetic fields. This approach has been particularly promising in regeneration of bones and nerves, where magnetic fields can help to align bio cells in a way that mimics tissue natural growth, accelerating the healing process. Ferrites, NdFeB magnets, and Samarium Cobalt (SmCo) magnets exhibit distinct magnetic properties, making them suitable for various applications. Ferrites typically have a coercivity (H<sub>c</sub>) ranging from 400 to 450 kA/m, a Curie temperature (Tc) between 300 and 450 °C, and an energy product (B<sub>Hmax</sub>) of 1 to 5 MGOe (8 to 40 kJ/m<sup>3</sup>). In contrast, NdFeB magnets possess higher coercivity values, ranging from 800 to 2000 kA/m, with a Curie temperature of 310 to 400°C (which can be elevated with doping), and an impressive energy product of 30 to 55 MGOe (240 to 440 kJ/m<sup>3</sup>). Samarium Cobalt magnets also demonstrate significant coercivity, ranging from 600 to 2000 kA/m, with a higher Curie temperature of 720 to 820 °C and an energy product between 16 to 30 MGOe (128 to 240 kJ/m<sup>3</sup>) [23,49–54].



Figure 2. Schematic diagram of biological applications of ferrites.

### 3.1. Diagnosis and MRI imaging

Medical imaging being used an important tool by using ferrite nanoparticles which is very actively and effective in diagnosing cancer. Actually, these nanoparticles are very useful and have protentional to high to provide high quality interior picture of human body. Magnetic Resonance Imaging (MRI) is the most widely used therapeutic instruments [55,57]. diagnosing cancer or ill cell is not only that much important but finding exact locations, dimensions and distinction from healthy tissues. Nano ferrites such as  $CoFe_2O_4$  and  $FeGa_2O_4$  also one of the best examples for diagnostic applications because of their advantageous qualities, such as magnetic features that make them appropriate for improving contrast in MRI scans. Fe<sub>3</sub>O<sub>4</sub>and  $\gamma$ -Fe<sub>2</sub>O<sub>3</sub>Iron oxides nano-particles is studied for long time and being used as contrasting agents, beyond these improved imaging capabilities, manganese and Zinc doped zinc ferrite nano-particles, as well as Mn–ZnFe<sub>2</sub>O<sub>4</sub> are also emerging as viable possibilities [41,50].

 $MnFe_2O_4$  ferrites are the nano particles are new MRI contrast agents that provide better performance than conventional ferrites like  $Fe_3O_4$ ,  $\gamma$ - $Fe_2O_3$ ,  $CoFe_2O_4$ , and  $NiFe_2O_4$  best for magnetic characteristics including their reduced toxicity and biocompatibility. Using  $MnFe_2O_4$  nano-particles in MRI and developing new ferrites nanoparticles to open new possibilities for better early diagnosis and management of a range of illnesses [35,41].

# 3.2. Hyperthermia

Magnetic hyperthermia is important and cutting-edge technical tool to cure cancer, in this method heat applies to tumor location in order to kill cancerous cells. The process of heating at exact location is possible by only using ferrite-based nanoparticles have a special capacity to absorb energy when exposed to an external alternating magnetic field [32,34,35]. The successful elimination of malignant cells while protecting healthy ones, a condition known as hyperthermia [54,55]. This treatment technique is very sensitive technique to eliminate malignancy at exact location resulting in classifications of localized, regional, whole-body hyperthermia [54]. Timer cells are intrinsically more heat-sensitive than normal cells because of their atypical blood arteries, these arteries works differently so this is very week and more sensitive towards heat. The  $Fe_3O_4$  applied for tumor treatment are proficiently studied, these nanoparticles uses Néel and Brownian relaxation to collect energy from the magnetic field and transform it into heat [55]. CoFe<sub>2</sub>O<sub>4</sub>nanoferrite has immense capacity of self-heating and therefore is the most encouraging nanoferrite for application of hyperthermia [57]. These nanoparticles magnetic nature, size and shape of a particle, including intensity and frequency of the applied magnetic field, all these depends on how much heat they produce. The Fe<sub>2</sub>O<sub>4</sub> nanoferrite or Co Fe<sub>3</sub>O<sub>4</sub>are able to absorbing magnetic energy and releasing it as heat (42-45 °C) due to this is used in hyperthermia treatments. This type of treatment helps to kill directly or make very week towards the treatment like radiation and chemotherapy. This technological development provides focused, non-invasive approach to cancer treatment which has great protentional to improve the efficacy of currently available medicines and lessons the adverse effects of old traditional approaches.

## 3.3. Drug delivery and release

Ferrite nanoparticles show significant advantages such as treating cancer, delivery of drug and its release and safe excretion from the human body. For instance,
the test carried on synthesized  $CoFe_2O_4$  nanoparticles disclosed all the abovementioned benefits [58]. In comparison with conventional drug use, the utilization of nanoferrites has helped to minimize the requirement of drug needed and related side effects [59,60]. In treating cancer by this system, the nanoferrites act as core whereas various biocompatible organic moieties act as shell. Ferrite nanoparticles are capable of carrying drugs and circulating them without dripping. They also effortlessly travelto the site of target tumor with the help of an external magnetic field. They support in lending effective treatment by bypassing normal cells [61]. After delivering the drugs, either they get removed from the human body or get biodegradable [62]. The method of targeted drug delivery is having variousbenefit's like depletion of wastage of drug, minimizing the drug administration frequency, lowering side-effects, increasing efficacy of treatment, being safe and reliable [32] etc. manganese (II) complexes is a high catalytic activity which has a potential benefit in medical applications, for drug synthesis or therapeutic applications which is helpful medication manufacturing and treatment procedures [63]. Zirconium oxide  $(ZrO_2)$  synthesized material which has high optical characteristics and cubic structure with size of the grain  $ZrO_2$  is 10–30 nm due to this which suitable to get improved by surfactants like polyethylene glycol (PEG) have great potential which is used for drug delivery [64]. Copper (II) hexaaza macrocyclic complexes is new content which is synthesized by using situ one-pot template synthesis (IOPTS) ultimately a good for drug delivery [65]. Ferrites are valuable in various applications, including drug delivery, antibacterial/antifungal treatments, and water treatment, due to their unique properties. For drug delivery, key parameters such as particle size (10-100 nm), magnetic saturation (50-80 emu/g), biocompatibility (surface-coated with PEG, silica, dextran), and zeta potential (-30 to +30 mV) enhance cellular uptake and ensure effective targeting and stability. In antibacterial and antifungal applications, small particle size (10–50 nm), appropriate magnetic saturation (40–70 emu/g), surface functionalization with antimicrobial agents, and chemical stability in various environments are crucial for maximizing antimicrobial efficacy. For water treatment, ferrites should exhibit a particle size of 10–200 nm, magnetic saturation of 50–70 emu/g, high chemical stability across pH ranges, and a large surface area (50–  $150 \text{ m}^2/\text{g}$ ) to optimize pollutant removal and ensure durability in treatment processes [54,66–68].

#### 3.4. Antibacterial and antifungal studies

Nano ferrites exhibit antibacterial and antifungal properties due to several key factors related to their unique chemical composition, surface characteristics, and magnetic properties. Nano ferrites possess a high surface-to-volume ratio, which increases the interaction between the nanoparticles and microbial cells. This enhanced contact can lead to more efficient microbial killing. The surface of nano ferrites can generate reactive oxygen species (ROS) when exposed to environmental conditions. ROS, such as hydroxyl radicals, superoxide anions, and hydrogen peroxide, can damage microbial cell membranes, proteins, and DNA, leading to cell death. Magnetic nanoparticles are significantly used as antibacterial and antifungals. The preparation and verification are done for nanoferrites for their extensive usage in

medicinal field [69,70]. As antifungals are toxic, less efficient and resistant, there is a need for developing novel antifungal drugs that are safe and efficient. Therefore, taking into account these aspects, new antifungal substances have evolved [71]. Cobalt ferrite nanoparticles have been shown to exhibit significant antibacterial activity. The mechanism involves the generation of ROS and the release of cobalt ions, which can penetrate bacterial cells and cause oxidative damage. Zinc ferrite nanoparticles are known for their antifungal activity. Zinc ions can interfere with fungal cell wall synthesis and membrane integrity, while the ferrite structure helps in the generation of ROS, leading to fungal cell death. Thus Nano ferrites show antibacterial and antifungal properties due to their high surface area, magnetic properties, metal ion release, and ability to generate reactive oxygen species. These properties make them effective in disrupting microbial cells and killing bacteria and fungi.

The Kirby–Bauer also called agar diffusion test is an antibiotic susceptibility test that makes use of discs of antibiotics to examine the extent of bacteria and fungi [72]. Zinc Copper ferrites were studied for antibacterial activity where it was noticed that activity was dependent of zinc concentration [53]. The Zinc substituted Cobalt ferrite and Manganese substituted Cobalt ferrite were utilized for antibacterial and antibiofilm activities towards bacteria that commonly diffused on the surfaces of medical operating room walls [73]. The Mg substituted Mn-Zn ferrites act as outstanding antimicrobial potentials [42].

Also, the cobalt doped manganese ferrites are proposed as a candidate material for industries manufacturing antifungal products [74]. Ag doped Ni Co nanoferrites show an exceptional antifungal action [75]. Figure 3 is a schematic representation of biological applications of ferrites whereas Table 2 provides information about different biological applications of ferrites along with the description. Thenanoferrite sample Ni<sub>0.45</sub>Zu<sub>0.45</sub>Cu<sub>0.1</sub>Fe<sub>2</sub>O<sub>4</sub> exhibited the highest antibacterial activity against Bacillus cereus, with inhibition zones measuring 21, 23, 23, and 23 mm for concentrations of 25, 50, 100, and 250  $\mu$ g/ml, respectively (Table 3). Figure 4 and Figure 5 illustrate the antibacterial studies of nickel zinc ferrites and copper-doped nickel zinc ferrites. In contrast, the other nanoferrite samples demonstrated negligible antibacterial activity. The antifungal activity was evaluated for cobaltdoped nickel zinc ferrites, with  $Ni_{0.45}Zn_{0.35}Co_{0.2}Fe_2O_4$  showing the highest inhibition zones of 25, 27, 30, and 30 mm for 25, 50, 100, and 250 µg/ml concentrations against Aspergillus niger (Table 4) [56]. Figures 6 and 7 present the antifungal studies of nickel zinc ferrites and cobalt-doped nickel zinc ferrites. The results highlight the importance of compositional variations in enhancing the antimicrobial properties of nanoferrites, paving the way for their potential use in biomedical applications.

| <b>Biological application</b> | Description  | Reference |
|-------------------------------|--|-----------|
| MRI Contrast Agents           | Ferrite nanoparticles enhance MRI contrast by affecting the relaxation times of hydrogen nuclei in tissues.  | 71        |
| Drug Delivery                 | Magnetic ferrite nanoparticles can be directed to specific locations in the body using an external magnetic field, allowing for controlled drug release. | 72        |
| Hyperthermia Treatment        | Magnetic ferrite nanoparticles generate heat when exposed to an alternating magnetic field, which can be used to kill cancer cells selectively.          | 73        |
| Biosensors                    | Ferrite nanoparticles enhance the sensitivity and specificity of biosensors used to detect various biological molecules.                                 | 38        |
| Cell Separation               | Cells can be tagged with magnetic ferrite nanoparticles and separated from a mixture using a magnetic field.   | 74        |
| Antifungal Applications       | Ferrite nanoparticles exhibit antifungal properties, inhibiting the growth of various fungal species.  | 42        |
| Antimicrobial Applications    | Ferrite nanoparticles have antimicrobial properties effective against a wide range of bacterial strains.   | 43        |
| Antibacterial Coatings        | Ferrite nanoparticles can be used in coatings to prevent bacterial colonization on medical devices.  | 44        |
| Antimicrobial Textiles        | Ferrite nanoparticles are incorporated into textiles to provide long-lasting antimicrobial properties.   | 45        |
| Water Purification            | Ferrite nanoparticles can be used to remove microbial contaminants from water, providing an effective purification method.                               | 46        |

| Table 2. | Biological | applications | of ferrites | with    | description |
|----------|------------|--------------|-------------|---------|-------------|
| 14010 20 | Diological | apprications | of ferrices | ** 1011 | desemption  |



# Figure 3. Schematic diagram of biological applications of ferrites.

**Table 3.** Antibacterial activity of copper doped nickel zinc nano ferrites against bacillus cerus.

| Sample                              | Zone of inhibition(mm) |         |           |           |
|-------------------------------------|------------------------|---------|-----------|-----------|
|                                     | 25µg/mL                | 50µg/mL | 100 µg/mL | 250 μg/mL |
| Ni0.45 Zn0.55Fe2O4                  | 1                      | 1       | 2         | 1         |
| Ni0.45 Zn0.45 Cu0.1 Fe2O4           | 21                     | 23      | 23        | 23        |
| $Ni_{0.45}Zn_{0.35}Cu_{0.2}Fe_2O_4$ | 1                      | 1       | 2         | 1         |
| Ni0.45 Zn0.25Cu0.3Fe2O4             | 1                      | 1       | 2         | 1         |



Figure 4. Antibacterial activity of nickel zinc nanoferrites ( $Ni_{0.45}Zn_{0.55}Fe_2O_4$ ) against bacilluscerus.



Figure 5. Antibacterial activity of copper doped nickel zinc nanoferrites ( $Ni_{0.45}$  Zn<sub>0.45</sub>Cu<sub>0.1</sub>Fe<sub>2</sub>O<sub>4</sub>)againstbacillus cerus.

**Table 4.** Antifungal activity of cobalt doped nickel zinc nanoferrites againstAspergillus niger.

| Sample   | Zone of inhibition(mm) |         |           |           |
|--|------------------------|---------|-----------|-----------|
|  | 25µg/mL                | 50µg/mL | 100 μg/mL | 250 μg/mL |
| Ni0.45 Zn0.55Fe2O4   | 1                      | 2       | 2         | 1         |
| Ni0.45 Zn0.45Co0.1Fe2O4  | 1                      | 2       | 2         | 1         |
| Ni <sub>0.45</sub> Zn <sub>0.35</sub> Co <sub>0.2</sub> Fe <sub>2</sub> O <sub>4</sub> | 25                     | 27      | 30        | 30        |
| Ni0.45 Zn0.25Co0.3Fe2O4  | 1                      | 2       | 2         | 2         |



**Figure 6.** Antifungal activity of nickel zinc nanoferrites (Ni<sub>0.45</sub> Zn<sub>0.55</sub>Fe<sub>2</sub>O<sub>4</sub>) against Aspergillus niger.



**Figure 7.** Antifungal activity of cobalt doped nickel zinc nanoferrites ( $Ni_{0.45}$  Zn<sub>0.35</sub>Co<sub>0.2</sub>Fe<sub>2</sub>O<sub>4</sub>) against Aspergillus niger.

Thus unique magnetic properties and biocompatibility of ferrites (Table 5) make them invaluable in various biological and medical applications, shown in Figure 8. Research continues to expand their potential uses, offering promising advancements in diagnostics, treatment, and research methodologies in the life sciences. Ferrites exhibit notable antibacterial and antifungal properties, with particle sizes typically ranging from 10-50 nm for Fe<sub>3</sub>O<sub>4</sub> (magnetite), effective against E. coli and S. aureus, and 20-60 nm for CoFe2O4 (cobalt ferrite), demonstrating antibacterial activity against E. coli. Their magnetic saturation (Ms) values are 40-60 emu/g for magnetite, enhancing drug targeting, and 25-35 emu/g for ZnFe<sub>2</sub>O<sub>4</sub> (zinc ferrite), which still shows moderate antibacterial activity. Zeta potential for magnetite ranges from -10 to -20 mV, ensuring stability in colloidal suspension. Minimum inhibitory concentrations (MIC) for Fe<sub>3</sub>O<sub>4</sub> nanoparticles are 50-100 µg/mL for E. coli and S. aureus. CoFe<sub>2</sub>O<sub>4</sub> achieves 80%–90% antibacterial efficiency against E. coli, while NiFe<sub>2</sub>O<sub>4</sub> (nickel ferrite) shows 70%-85% antifungal efficiency against C. albicans. Functionalizing ferrites, such as with silver, further enhances antibacterial activity. Ferrites are biocompatible, with cytotoxicity showing  $\geq 80\%$ cell viability at  $\leq 100 \ \mu g/mL$  [68,76–80].

| Application                | Important Parameters  | Reasons for Importance   |  |
|----------------------------|---|--|--|
| Microwave Frequency        | Permeability, Loss Tangent (High ( $\mu$ > 1000, Low (tan $\delta < 0.1$ ))                   | High permeability ensures efficient signal transmission, while low loss tangents minimize energy loss.               |  |
| Devices                    | Frequency Response  | Affects device performance at various microwave frequencies.   |  |
| Computer Memory            | Magnetic Saturation (50–80 emu/g), Coercivity(Hc~20–<br>300 Oe) (Hc~20–300 Oe) (Hc~20–300 Oe) | High saturation magnetization allows for reliable data storage and retrieval; moderate coercivity ensures stability. |  |
| Core Elements              | Thermal Stability   | Essential for maintaining performance under operating conditions.  |  |
|                            | Biocompatibility, Particle Size   | Biocompatibility is crucial for safety; smaller particles<br>enhance cellular uptake and interaction with tissues.   |  |
| Biomedical<br>Applications | Particle Size10–100 nm  | Enhances cellular uptake and improves interactions with biological systems.  |  |
|                            | Surface Functionalization   | Modifications improve interactions with biological systems, reducing toxicity.                                       |  |
|                            | Magnetic Susceptibility,  | High susceptibility enhances imaging quality; biocompatible  |  |
| Diagnosis                  | Surface Coating   | coatings improve safety in medical applications.   |  |
|                            | Sensitivity and Resolution  | Crucial for improving diagnostic accuracy in imaging techniques.   |  |
| I Izza outh outro          | Specific Absorption Rate  | High SAR values indicate efficient heat generation, while  |  |
| Trypertnerma               | Particle Size (10–50nm)   | smaller sizes improve localization in tumors.  |  |
|                            | Magnetic Properties   | Essential for effective induction heating in targeted cancer therapy.  |  |
|                            | Magnetic Saturation (Ms),   | Enables targeted delivery through external magnetic fields;  |  |
| Drug Delivery              | Biocompatibility  | biocompatibility ensures safety.   |  |
|                            | Release Profile   | Important for controlling drug release rates in therapeutic applications.  |  |
|                            | Particle Size (10–50 nm)  |  |  |
| Antibacterial and          | Surface Functionalization,  | Smaller sizes enhance interaction with microbes;<br>functionalization improves antimicrobial efficacy.               |  |
| Antifungal                 | Chemical Stability  | 1  |  |
| C C                        | Efficacy in Biological Environments   | Chemical stability ensures prolonged activity in diverse conditions.   |  |
|                            | Particle Size (10–200 nm)   |  |  |
|                            | Magnetic Saturation (Ms), (50-70 emu/g)   | Nano-sized particles provide high surface area for<br>adsorption: magnetic properties enable easy recovery.          |  |
| Water Treatment            | Surface Area (50–150 m <sup>2</sup> /g)   |  |  |
|                            | Chemical Stability  | Ensures durability and effectiveness during treatment processes across various pH levels.                            |  |

# Table 5. Applications, key parameters, and their importance.



Figure 8. Various biological applications of nano ferrites.

#### 3.5. Waste water treatment

Water sources are at high risk of pollution. They get polluted because of discharging wastes into the water bodies such as plastic, glass, chemicals, etc. The common pollutants in waste water are metal ions, aromatic compounds, anions, phenols, dyes, pesticides, detergents, etc. Because of the presence of such contaminants in waste water, it makes the water unfit for drinking and also becomes poisonous to aquatic life. Ferrites, especially those with high surface areas, are effective adsorbents for removing heavy metals like lead ( $Pb^{2+}$ ), cadmium ( $Cd^{2+}$ ), chromium ( $Cr^{6+}$ ), and arsenic (As<sup>3+</sup>) from wastewater due to unique properties of ferrites (Figure 9). The metal ions are adsorbed onto the surface of the ferrite particles through electrostatic interactions and chemical bonding. Ferrites can adsorb organic pollutants, such as dyes, from wastewater due to their surface properties and ability to be modified with functional groups that enhance adsorption. All over the world, there is demand for clean and safe water. Hence, the purification of water is of utmost priority. New methods of purification of water are to be developed that are cost effective. Magnetic nanoparticles because of their adsorption and high surface area to volume ratio have become significant candidates for treating waste water. Therefore, nanoferrites are checked for removing contaminants and purifying water. They have proved to be promising candidates in this aspect. The process of adsorption or degradation is responsible for the removal of contaminants in water [47,81–84]. The waste water of the industries is treated to remove dyes and phenols, toxic metals by using nanoferrites [75-82]. Magnetite (Fe<sub>3</sub>O<sub>4</sub>), Cobalt Ferrite (CoFe<sub>2</sub>O<sub>4</sub>), Nickel Ferrite (NiFe<sub>2</sub>O<sub>4</sub>), Zinc Ferrite (ZnFe<sub>2</sub>O<sub>4</sub>), Copper Ferrite (CuFe<sub>2</sub>O<sub>4</sub>), Manganese Ferrite (MnFe<sub>2</sub>O<sub>4</sub>), and Barium Ferrite (BaFe<sub>12</sub>O<sub>19</sub>)—is used in wastewater treatment for specific applications based on their magnetic properties, ability to adsorb contaminants, and catalytic capabilities. Nanoferrites are good adsorbents that are of low cost, efficient, can be recovered with ease and reused. By literature review, it is clear that trend of using nanoferrites in waste water treatment has increased. The Fe<sub>3</sub>O<sub>4</sub> is a popular candidate for this. This might be because of non-toxicity, ease of availability of precursors required in its synthesis [32,85]. Dy<sub>2</sub>O<sub>3</sub>-SiO<sub>2</sub> nanocomposite is best and effective in photocatalysis which break down the pollutants like erythrosine so it's best for sanitation and environmental cleanup similarly reduced graphene oxide (RGO) from graphite oxide using urea also used as non-toxic reducing agent [70,86]. CsPbI<sub>3</sub> perovskite nanostructures is capable

enough fight against the Pseudomonas aeruginosa, Escherichia coli, and Streptococcus pyogenes which is good to addressing pollution [86]. Ferrites with a large surface area (50–150 m<sup>2</sup>/g) demonstrate high adsorption capacities, making them effective for removing heavy metals and dyes in water treatment applications. Their high magnetic saturation (Ms) values, particularly in magnetite (50–60 emu/g), facilitate easy magnetic separation, which is beneficial for magnetic filtration systems. The adsorption capacity of ferrites is quantified in mg of pollutant per gram of ferrite, with magnetite nanoparticles exhibiting significant adsorption capabilities for heavy metals like Pb<sup>2+</sup>, Cr<sup>6+</sup>, and As<sup>3+</sup>. Ferrites also show remarkable removal efficiencies, achieving 90%–95% removal rates for pollutants such as Pb<sup>2+</sup>, As<sup>3+</sup>, and Cr<sup>6+</sup>. Additionally, ferrites like Fe<sub>3</sub>O<sub>4</sub> maintain good stability across a wide pH range (4–9), enhancing their versatility for various wastewater treatment scenarios. Some ferrites, such as NiFe<sub>2</sub>O<sub>4</sub>, possess antimicrobial properties, allowing them to function as disinfectants in water treatment systems. [36,66,87–90]



**Figure 9.** Advantages of nano ferrites in using them for waste and waste water treatment as compared to conventional techniques.

#### 4. Conclusions

In conclusion, ferrite synthesis techniques are essential for determining their magnetic, chemical, and physical characteristics; all synthesis techniques are widely and effectively synthesized and utilized. Sol-gel, co-precipitation, hydrothermal, and green synthesis methods are used to get the desired particle size, shape, and magnetic properties, depending on the application synthesis method utilized. Using the best synthesis method, prepared ferrites provide flexibility in health care, demonstrated by their biomedical applications, mainly in medication administration, magnetic hyperthermia, biosensing, and magnetic resonance imaging (MRI). CoFe<sub>3</sub>O<sub>4</sub>and MnFe<sub>3</sub>O<sub>4</sub> are essential for MRI to get strong magnetic characteristics and biocompatibility, which helps MRI to contrast agents and cancer therapies. Various methods of synthesis of ferrites are discussed to get information related to antimicrobial properties and biological applications of ferrites, such as the biomedical field comprising cancer diagnosis, MRI, hyperthermia, drug delivery and release, antimicrobial properties, and wastewater treatment.

Compared with conventional drug use, the utilization of nano-ferrites has helped minimize the amount of drug needed and avoid side effects. In wastewater treatment, nano-ferrites are cost-effective and efficient compared to conventional methods. Also, nano-ferrites are promising candidates for antimicrobial and biomedical applications. The optimization of feature synthesis techniques is necessary to improve the biocompatibility, stability, and magnetic properties of ferrites for specific biomedical applications by considering green synthesis methods to avoid or minimize environmental impact while maintaining the exact cost-effectiveness and efficacy in applications such as wastewater treatment, drug delivery, and hyperthermia. Multifunctional ferrites are most important and have a high potential for new avenues in fields like theragnostic, fusing their medicinal and diagnostic properties and increasing their application in environmental sustainability and antimicrobial treatments.

Conflict of interest: The authors declare no conflict of interest.

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# Nanoparticles' classification, synthesis, characterization and applications— A review

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https://creativecommons.org/licenses/ by/4.0/ **Abstract:** This review provides an overview of the importance of nanoparticles in various fields of science, their classification, synthesis, reinforcements, and applications in numerous areas of interest. Normally nanoparticles are particles having a size of 100 nm or less that would be included in the larger category of nanoparticles. Generally, these materials are either 0-D, 1-D, 2-D, or 3-D. They are classified into groups based on their composition like being organic and inorganic, shapes, and sizes. These nanomaterials are synthesized with the help of top-down bottom and bottom-up methods. In case of plant-based synthesis i.e., the synthesis using plant extracts is non-toxic, making plants the best choice for producing nanoparticles. Several physicochemical characterization techniques are available such as ultraviolet spectrophotometry, Fourier transform infrared spectroscopy, the atomic force microscopy, the scanning electron microscopy, the vibrating specimen magnetometer, the superconducting complex optical device, the energy dispersive X-ray spectrometry, and X-ray photoelectron spectroscopy to investigate the nanomaterials. In the meanwhile, there are some challenges associated with the use of nanoparticles, which need to be addressed for the sustainable environment.

Keywords: nanomaterials; nanoparticles; characterization; top-down synthesis; bottom-up synthesis

# **1. Introduction**

Over the last few decades, nanotechnology has expanded at an incredible rate. Nanotechnology specializes in creating materials and devices at the nanoscale, allowing for precise manipulation of size, shape, and functionality. Nano has become a ubiquitous buzzword in advertising efforts. The Greek term "nano" means "dwarf," while the Latin "nanos" means "nanus.". Nanotechnology has broad potential uses across all of the technological and scientific domains. Nanoscience facilitates the investigation at atoms and molecules level that affect their fundamental properties, whereas, nanotechnology seems to be the act of manipulating substances on the atomic scale to develop unique nanomaterials with exceptional features. Richard P. Feynman first used word "nanotechnology" in his 1959 lecture, "In 1959 Capacity that at Bottom", since then, the field has made great progress. Several new types of nanoscale materials have been created, thanks to the advancements in nanotechnology. As it was found that a substance's size can affect its physiochemical properties, including its optical qualities, therefore, the importance of these materials became clear. Nanoparticles (NPs) of gold (Au), platinum (Pt), silver (Ag), and palladium (Pd) with varying size were synthesized. For instance, gold NPs of varying sizes and shapes, each with its own distinct hue and set of properties that could be put to use in biomedical, were introduced. Changes in the solution's defining properties are reflected in the color of the solution (viewing angle, nano shell width, and gold concentration). Changes from any of these variables affect the NPs' ability to absorb light and, by extension, their color [1].



Figure 1. Significance of nanoscience and nanotechnology in fields of engineering and science.

The public is unaware of the myriad ways nanotechnology is being employed in areas such as medical, building, nature conservation, electronics, national security, and even personal safety [2–6], despite the fact that it is getting increasing attention from scientists and engineers as depicted in Figure 1. Even if a lot of work already has been done with this technology, there is still opportunity for generating the new unique nanomaterials in a variety of fields for the development of humanity. Scientists spend their time, effort, and resources to advancing human understanding because they are passionate about the subject. Miniaturizing equipment while keeping prices down is thus a priority in different sectors. At some point in the future, nanotechnology will be able to dictate every facet of human existence. People's curiosity in nanotechnology is piqued, and they begin discussing the field's underlying principles and innovative uses. Nanotechnology cannot exist without nanomaterials. Nanomaterials are those with lengths approximately 100 nm or less. Nanoparticles have physicochemical properties that are unique from that of bulk material because of their size and shape. Nanomaterials take on a surprise new persona with unique characteristics and abilities when their quantum structure and size are altered. Several types of nanomaterials, like nanostructures, nanoclusters, and nanosheets, can be distinguished entrenched on their extent of range. As particles interact with one another, their physical properties will evolve.

# 2. Classification of nanomaterials on the basis of size

- One kind of nanomaterials is called zero-dimensional (or 0-D) because its dimensions are under a nanometer.
- With a 2-D nanomaterial, both dimensions are larger than a nanometer, whereas, in a 1-D nanomaterial, only one dimension is. This category includes structures like nanorods, nanotubes, and nanowires.
- 2-D nanomaterials have just two dimensions that are tiny, whereas the remaining dimension is macroscopic. Nanofilms, nanolayers, and nanocoating's are all examples of such materials.
- Three-dimensional or large nanomaterials (3-D) have a size of >100 nm in three arbitrary dimensions. Nanowire and nanotube bundles, as well as core-shell structures, multi-nanolayers, and nanocomposites are all examples of 3-D nanomaterials [7]. **Table 1** provides classification of nanomaterials on the basis of dimensions.

Table 1. Dimension, types in different forms of occurrence, properties, and potential applications of nanomaterials [8].

| Dimensionality                    | Type of nanomaterial  | Properties  | Potential Applications   |
|-----------------------------------|---|---|--|
| Zero dimensional                  | Nanoparticles, carbon dots                                    | High surface rea, isotropy, and confined electronic movement                                    | Applications include bio imaging, electronics, drug delivery, and catalysis.                 |
| One dimensional                   | Nanowires, nanorods,<br>nanotubes                             | High aspect ratio, anisotropy, outstanding electrical conductivity.                             | Application areas comprise energy storage devices, nanoelectronics, and composite materials. |
| Two dimensional                   | Graphene, MXenes  | Excellent surface area, better in-plane electrical and thermal conductivity, layered structure. | Such materials have applications in catalysis, electronics, and energy storage.              |
| Three dimensional or higher order | a bunch of nanowires,<br>core shells,<br>nanocubes, nanocages | Porous structure, multifunctionality, enhanced mechanical strength.                             | Application areas include tissue engineering, filtration, supercapacitors, and catalysis.    |

Many kinds of NPs exist, each with its own unique size, shape, characteristics, and synthesis. Nanomaterials may range from those based on carbon to those based on metal, semiconductors, polymers, or lipids. Different nanomaterials along with their synthesis procedure and specific examples are provided in **Table 2**.

Table 2. Nanomaterials, synthesis procedures [9], and corresponding examples [10].

| Nanomaterials                | Methods of synthesis  | Examples   |
|------------------------------|---|--|
| Metal nanoparticles<br>(NPs) | Biochemical synthesis, photochemical, thermochemical process, electrochemical | ZnS, Pt, Pd, Ir, Ag, Au, Cu, Rh, Co, Fe, Ni, Cu<br>Au, Ni, CoNi, CdTe, CdSe.   |
| Carbon nano-materials        | Arc-discharge technique, chemical vapor deposition, laser ablation method     | Cylindrical carbon nanotube like single walled nanotubes (SWNT) and<br>multi walled nanotubes (MWNT)<br>Fullerenes   |
| Polymer nanomaterials        | Polymerization and electrochemical techniques                                 | Nanowire of polypyrene, polyaniline, poly<br>(3,4-ethylenedioxythiophane) dendrimers (PAMAM)   |
| Nanocomposite                | Innovative processes  | Nanocomposite of polyethylene oxide and polyethyleneimine; carbon<br>nanotubes (CNTs) epoxy composites include hydrocarbon polymer<br>composites, polyethylene glycol, polyester polyamides, conjugated<br>polymer composites, CNTs with polycarbonates, fluoropolymers, and so<br>forth |
| Bio nanoparticles            | Biological operations   | Protein NPs, plasmids and viruses [11],  |

# 3. Nanoparticles and related terminologies

Nanoparticles are defined as "particles having a nanometric size of 100 nm or less would be included in the larger category of NPs". The British Standards Institution [12] officially presented the following definitions for the terminologies being used:

- Nanometer-scale refers to distances between 1 and 1,000,000 of them.
- Nanoscience, refers an extremely small range, aims to explain how different materials behave depending on their atomic or molecular composition or bulk size.
- Nanotechnology is the application of scientific knowledge to the controlling and manipulating of matter at the nanoscale.
- Nanomaterials are defined as those that include or exhibit structures on the nanometer scale.
- Nano-objects are those made of materials with at least one peripheral element on the nanometer scale.
- An item with three exterior dimensions on the nanometer scale is called a nanoparticle. When the lengths of the nanotube are varied, the term nanoparticle is replaced with nanorod or nanoplate.
- A nanomaterial is said to be a nanofiber if it has three dimensions, two of which are on the nanoscale and one of which is much bigger.
- When at least one of a multiphase structure's phases are on the nanoscale, we call it a nanocomposite.
- To put it simply, a nanostructure is a collection of tiny components that are linked together.

A brief history and recent developments of NPs is presented in Figure 2.



Figure 2. History and recent developments of NPs.

# 4. Classification of NPs

# 4.1. Organic NPs

Nanoparticles with composition of carbon or the one which are synthesized by

organic molecules are called organic nanoparticles. Common examples of polymers or organic NPs include micelles, dendrimers, ferritin, liposomes, etc. Some of these NPs (liposomes, micelles, etc.) contain a hollow core (also called a nano capsule) and are sensitive to thermal and electromagnetic radiation (heat and light) [7]. Because of their productivity and ability to reach peculiar areas of the physical body, organic NPs are widely used in the biomedical field, for example in drug delivery systems.

#### 4.2. Inorganic NPs

Nanoparticles without composition of carbon are called inorganic NPs. Most of inorganic NPs are made up of metals or metal oxides.

#### 4.2.1. Metal NPs

Metal based NPs are mainly synthesized using constructive and destructive processes. These types of NPs are made from all kinds of commonly used metals. Ascribable to their effective surface to volume correlation and quantum effect, they have excellent thermal, antibacterial, catalytic, and ultraviolent sensitive properties. As there are many atoms on their surface and being small in size, they exhibit marvelous conductivity.

#### 4.2.2. Metal Oxide NPs

Nanoparticles of metal oxides exist for nearly all metals. Some commonly used metals are aluminum (Al), copper (Cu), cobalt (Co), lead (Pb), manganese (Mn), silver (Ag), and zinc (Zn). However, NPs can be made using chemical techniques like electrochemical or photochemical ones. Metal oxide nanoparticles can be created by reducing metal-ion antecedents in solution with reducing agents. They may absorb small molecules due to their high surface energy. There are several potential applications for these NPs, including biomolecule detection and surveillance, and analytical and environmental testing. Samples are occasionally coated with gold NPs before being seen using a scanning electron microscope (SEM). This typically increases the quality of its electrical current, which in turn produces higher-resolution SEM images. Because of their remarkable optical properties, metal oxide NPs have several potential applications.

#### 4.2.3. Ceramic NPs

Ceramic NPs are inorganic solids formed by heating and cooling a mixture of materials such as carbonates, oxides, carbides, carbonates, and phosphates. Forms ranging from polycrystalline to amorphous, dense to porous to hollow, are all accessible. Researchers are paying a lot of attention to these NPs due to their potential in various fields, in addition to catalysis, photocatalysis, and the photodegradation of dyes. These NPs may be employed into a drug delivery system by adjusting certain physical characteristics; this is particularly useful for treating cancers, eye diseases and some bacterial and viral infections.

#### 4.2.4. Semiconductor NPs

Nanoparticles made of semiconductors show characteristics similar of both metals and nonmetals. These may be located in groups II–VI, III–VI, or IV–VI of the periodic table. These particles have large bandgaps, the tuning of which reveals new

characteristics. Their applications range from water splitting and photocatalysis to electronics and photo-optics [13]. NPs of semiconductors include the elements such as silicon and germanium from group IV and gallium nitride (GaN), gallium phosphide (GaP), indium phosphide (InP), and indium arsenide (InAs).

#### 4.2.5. Polymeric NPs

In the scientific literature, these particles are commonly referred to as polymer nanoparticles (PNPs) since they are often made of organic materials. They can be in the form of nanospheres or nano-capsules, depending on the method of manufacturing. The former are adsorbate molecules along the surface's periphery. These are easy to operate. PNPs provide a wide range of benefits, including controlled release, drug molecule protection, combined treatment for imaging, targeted delivery, and many more. They may be used in the medical diagnostics and medication delivery industries. PNPs used for medication delivery have excellent biodegradability and biocompatibility.

#### 4.2.6. Lipid-based NPs

Nanoparticles made of lipids are typically round and have a diameter between 10 and 100 nm. Almost predominance of lipid-based NPs are spherical platforms, comprise minimum one lipid bilayer and encompass one internal organic and aqueous compartment. There is a lipid solid in its center and a matrix of soluble lipophilic molecules around it. Surface agents and emulsifiers stabilize the NPs' outer core. Lipid-based NPs consist of a wide range of component configurations. Lipid-based NPs have many benefits including easy formulation, conscious arrangement, renewability, high bioaccumulation, capacity for carrying massive cargo loads, and a variety of properties to modulate their characteristics. These are mainly used in the treatment of cancer including both medication delivery and RNA release.

#### 4.3 Carbon-based NPs

Carbon nanotubes and Buckminster fullerenes are the two most common forms of these NPs. Graphene is simply rolled up into CNTs. They are widely used for reinforcing existing structures. The two most common types of CNTs are singlewalled carbon nanotubes and multi-walled nanotubes. Carbon nanotubes are unique in a way that they conduct heat only in one direction, making them ideal for uses that necessitate fine-tuned regulation of temperature. Fullerenes are a type of carbon allotrope distinguished by their hollow cage structure made up of sixty or more carbon atoms. These frameworks have a polyhedral and hexagonal agreement in place of carbon units [14]. Due to their high strength, electronic configuration, and ionic properties, these have useful applications in industry. Sub (SWNTs), two-fold (DWNTs), and multi-walled carbon nanotubes are defined by the number of walls given in the rolled sheets. Deposition of starting material, notably the atomic carboxylic acids, evaporated from tungsten by laser or by electrical discharge, is a common method of polymerization for these substances. Chemical vapor deposition (CVD) is a new method for synthesizing them. Nano-composites made from some of these materials are employed as supplements, effective gas biosorbents, in pollution control, and as assist medium for multiple organic as well as inorganic catalysts [15].

Nonetheless, they are also utilized in their basic state for a wide range of commercial applications.

#### 4.3.1. Fullerenes

Fullerenes, which are carbon-based NPs with a spherical shape, are bound through sp<sup>2</sup> hybridization. Depending on the number of layers, fullerenes may range in size from 4–36 nm in diameter for poly-layered fullerenes and to 8.3 nm in size for mono-layered fullerenes [16].

#### 4.3.2. Graphene

Graphene is the name given to isomorphous type of carbon that have a hexagonal structure and two-dimensional flat surface. A single layer of graphene is just 1 nm thick [17].

#### 4.3.3. Carbon nanotubes

Carbon monolayer nanotubes have a diameter of less than 0.7 nm. However, there is some variation in length of multilayer carbon nanotubes i.e., it may vary in micrometers to several centimeters, and their ends can be closed or hollow [18]. Carbon nanotubes are manufactured by winding the carbon atoms of micro graphene into hollow pipes.

#### 4.3.4. Nanofibers of carbon

Most of nano-foils are coiled in cylindrical shapes of cup or cone shapes, rather than straight tubes, to create carbon nanofibers [19].

#### 4.3.5. Carbon black

Black nanocarbon have a diameter of 20–70 nm and are amorphous in structure. When agglomerates of around 500 nm are produced, the interactions between the particles become very strong and the particles mix to create larger aggregates [19]. **Figure 3** demonstrates the classification of nanoparticles.



Figure 3. Overview of the classification of nanoparticles.

#### 5. Synthesis of NPs

Nanoparticles are fabricated by different approaches i.e., bottom-up along with top-down one and biological synthesis, that have been developed on behalf of synthesizing NPs. These approaches are briefly explained in the following section.

#### 5.1. Bottom-up methods

One example of a bottom-up or constructive approach is the construction of materials from their atomic level to the cluster or bunch of their nanoparticle level. The most commonly used prevalent bottom-up techniques for producing nanoparticles include sol-gel, spinning, chemical CVD, and pyrolysis.

#### 5.1.1. Sol-gel

A used prevalent colloidal solution is a suspension of solids particles in a liquid. The sol-gel approach appears to be the best bottom-up method because most nanostructures can be made using it. Common precursors used in the sol-gel method include metal oxides and chlorides [20]. The precursor in host liquid can be broken up into a liquid and a solid phase by shaking or sonicating the mixture. Phase separation methods like sedimentation, filtration, and centrifugation is used to remove the nanoparticles, and then they are dried to remove any remaining moisture. **Figure 4** presents the mechanism for the synthesis of BaTiO<sub>3</sub> NPs.



**Figure 4.** Suggested route for the synthesis of of BaTiO3 NPs along with byproducts (Reused with permission from WILEY - VCH Verlag GmbH & Co. KGaA, Weinheim [21]).

#### 5.1.2. Electrodeposition

Electrodeposition is a method which involves the reduction of metal ions from a solid metal being coated on a substance or in a solution when electric current is applied. Its basic principle is use of an electrolytic cell containing a metal salt solution [22]. When current is supplied, it results in reduction of metal cations from cathode in solution and then gives a metal coated surface of the nanoparticle.

#### 5.1.3. Hydrothermal method

Hydrothermal synthesis of NPs is chemical based which involves extraction of nanomaterials from hydrolysis reaction at high or wide range of temperatures [23]. This process is performed using a specific solvent below critical point at both pressure and temperature over wide range under supercritical conditions. However, this is convertible method for synthesis of nonorganic NPs at both extreme hot temperatures and pressures.

#### 5.1.4. Spin-synthesized

Nanoparticles are spin-synthesized in a furnace using a spinning like disc (SDR). It uses a disc and spins inside a closed chamber/reactor to control physical parameters. Reactors are routinely purged of oxygen, to nitrogen or any other inert gases to prevent chemical reactions. The precursor or water are placed inside the disc and spun at different speeds to create the liquid. Atomic or molecular fusion can be precipitated, gathered, and dried with the use of spinning [24]. Variables in the SDR's operation, such as fluid, disc engine speed, liquid/precursor ratio, feeder position, etc., all influence the characteristics of the produced nanoparticles.

#### 5.1.5. Deposition of Chemicals from gases

Chemical vapor deposition is a method of coating a substrate with some thin layer of gaseous reactants. Reaction causes the deposition i.e.; the joining of gas molecules takes place in a reactor at room temperature. A reaction happens when the mixed gas contacts a heated substrate [25]. The reaction product is a thin coating that is deposited on the substrate and can be removed and recycled for further use. Substrate temperature plays an important impact in chemical vapor deposition. Nanoparticles made using CVD are superior because they are pure, consistent, rigid, and robust. There are certain downsides to CVD, such as the fact that it requires specialized equipment and results in very toxic gaseous by-products. **Figure 5** represents step by step procedure for the synthesis of carbon nanofibers.



**Figure 5.** Step-by-step representation of synthesis route for carbon nanofibers. (a) Creation of SiC through reduction of SiO2 with the help of carbothermal reaction; (b)

coalescence of SiC NPs; (c) the degradation of SiC and formation of carbon caps on its surface (Reused with permission from American Chemical Society [26]).

#### 5.1.6. Pyrolysis

As far as industrial production is concerned, pyrolysis is the standard method for making NPs. In a flame, a precursor is burned up. Precursors are introduced into the furnace through a small hole and burned under extreme heat and pressures [27]. Most of the other furnaces use lasers in place of flames to generate the extremely feverish temperatures required for spontaneous evaporation of material. Advantages of pyrolysis include its simple operation, high throughput, minimal material and labor costs, and scalability.

#### 5.2. Top-down methods

The top-down also known as destructive method is breaking down a substance into smaller pieces until it reaches nanometer size. Some of the most common ways to create NPs are by mechanical milling, nanolithography, laser ablation, sputtering, and thermal breakdown.

#### 5.2.1. Mechanical milling

The most common top-down method for creating NPs is milling. Mechanical milling is used for milling, following annealing of nanostructures during synthesis, with each component milled inside an inert environment [28]. Particle shape is affected by ductile materials during mechanical milling, while particle size is affected by fracture and cold-welding.

#### 5.2.2. Nanolithography

Nanolithography is the study of making things that are often on a scale from 1 to 100 nm. It encompasses a wide range of techniques, including but not limited to nanoimprint lithographic technique, scanning probe photoresistor, and electron-beam lithography. In lithography, a light-sensitive substance is combined with a printing procedure that selectively removes material to create the desired shape and structure. The main benefit of nanolithography is that it can scale up the production of nanoparticles of a specific shape and size. There is a prohibitive cost associated with the complicated machinery.

#### 5.2.3. Etching

Etching is a chemical process of layers separation from some substance like wafer. It is mainly used for micro or nanofabrication. However, to protect other parts of the wafers from etching, special masks are used which provides resistance from this process. These masks are made of photoresist material which is contrived from photolithography [29].

#### 5.2.4. Laser ablation

Laser ablation is a popular method for fabricating nanoparticles in a wide range of materials. Nanoparticles can be created by concentrating a plume from plasma created by irradiating a metal coated in a fluid medium with a laser. It is reliable topdown method that can be used instead of the conventional method of chemically degrading metals to produce metal-based NPs. In water emulsion solvents, LASIS (laser ablation in liquids) might be called a "green" approach for manufacturing nanoparticles because no chemical or bonding agent is required.

#### 5.2.5. Sputtering

This process includes the deposition of some nanostructures on surface as a consequence of wrenching with ions. A covering of NPs is first deposited through sputtering and then it is annealed to harden. Layer thickness, processing temperature and surface texture, etc. are important parameters to be considered while using this method.

#### 5.2.6. Thermal decomposition

When anything is broken down by heat, it undergoes an endothermic chemical reaction. When an element reaches its breakdown temperature, it completely disintegrates chemically [30]. The NPs are the product of a chemical reaction triggered by the metal's breakdown at specific temperatures.

#### 5.3. Biological synthesis of nanoparticles

The following procedures are used in the biological production of NPs:

#### 5.3.1. Plant-based synthesis

The synthesis using plant extract is non-toxic, making plants the best choice for producing NPs. Plant extracts such as geranium, sun-dried cinnamon menthol, Azadi Acta indica, etc., may be used to create gold and silver NPs [25]. In the meanwhile, plant-based synthesis poses some challenges as well, such as inconsistency in yield, size, and shape of the NPs due to the variation in the nature of plant extracts which is further related to the change in geographical locations, seasons, and species.

#### 5.3.2. Synthesis by bacteria

The vast potential for synthesis of zinc oxide nanoparticles in the past has led to a dramatic expansion of the field. The capacity of Bacillus species to produce extracellularly has made them popular in the synthesis of metal nanoparticles. The dimensions are between 10 and 20 nm. Furthermore, gold NPs may be synthesized [27].

#### 5.3.3. Synthesis by fungi

Aspergillus nagger, aspergillus orizae, and fusarium solan are just a few examples of the types of fungus that may be used to create the NPs. The effectiveness of silver NPs against scherichia coli, staphylococcus aureus, and pseudomonas aeruginosa has been evaluated [31].

#### 5.3.4. Synthesis by yeast

Here, cadmium NPs are synthesized using the yeasts Candida glabrata and Schizosaccharomyce pombe. Extremophilic yeast strain obtained from acid mine drainage is also used to study silver and gold NPs. Stable lead sulfur NPs have been synthesized using the marine fungi rode sporidium diazoate [32].

#### 5.3.5. Synthesis by biological compounds

Nanoparticles may be synthesized using biological compounds such as proteins, peptides, viruses, and enzymes [23]. The mineralization of sulfides is aided by the tobacco mosaic virus. Viruses cause cowpea chlorotic mottle which is also present

on the M13 like bacteriophage's outer membrane. **Figure 6** provides different routes for the synthesis of NPs.



Figure 6. Synthesis routes for nanoparticles.

The advantages, disadvantages, and practical applications of top-down and bottom-up synthesis of NPs are provided in the **Table 3**.

| Table 3. Pros and | cons of different | synthesis a | approaches for ] | NPs. |
|-------------------|-------------------|-------------|------------------|------|
|                   |                   | 2           |                  |      |

| Methods                | Advantages   | Disadvantages   | Practical Applications  |
|------------------------|--|---|---|
| Top-down<br>Synthesis  | These methods offer large scale<br>production e.g., milling.<br>The synthesis procedures are simpler<br>one realized through mechanical and<br>chemical processes.<br>There is precise control over the shape<br>and size of the NPs.<br>Usually, no complex chemicals are<br>employed | The surface defects may lead to<br>roughness thus affecting the<br>characteristics of the NPs.<br>There is requirement of higher<br>amounts of energy.<br>There may be a lot of waste<br>associated with these processes. | Different electronic components such as<br>microchips, thin films, and nanoscale circuits can<br>be produced using these methods.<br>Catalysts can be synthesized using these methods.<br>Optical devices can be manufactured using these<br>methods. |
| Bottom-up<br>Synthesis | There is a better control over the<br>structure.<br>There is less likelihood towards the<br>defects.<br>Uniform size distribution can be<br>achieved.<br>These methods are versatile and<br>energy efficient.  | Comparatively, these methods are<br>time consuming and complex.<br>They require costly chemicals.<br>The scalability is limited.<br>There is tendency towards the<br>incorporation of impurities.                         | These methods are employed to produce NPs for<br>fuel cells, drug delivery, catalysis, batteries, and<br>supercapacitors.<br>Environmental remediation is also key area of<br>application for these methods.  |

#### 6. Characterization of NPs

Several physicochemical characteristics are shown by the NPs. Changing even a single nanometer in size causes a noticeable shift in behavior. Nanoparticles need to be characterized using a variety of tools so that their characteristics may be studied. A few examples are the ultraviolet (UV), spectrophotometer, the Fourier transform infrared spectroscopy (FTIR), dispersive energy X-ray spectrometry (EDS), SEM, atomic force microscopy (AFM), vibrating sample magnetometry (VSM), and superconducting quantum interference device (SQUID).

# 6.1. Structural arrangement, morphology, surface area, size, and shape of NPs

The size and shape of NPs are key determinants of their unique physical and chemical properties. You may examine the surface morphology using an AFM, field emission scanning electron microscopy (FESEM) or transmission electron microscope (TEM). The results obtained from these methods will help to determine whether the NPs are spherical, rod-shaped, or porous. Nanoparticle diameter may also be calculated. When put next to SEM and TEM, ability to reveal NPs' composition, morphology, and crystallinity stands out. Signals are generated when an electron beam strikes atoms in a sample. These signals will reveal the structure and content of the sample's surface. Thus, the samples' exterior needs to have some degree of electrical conductivity. Surface coating with ultrathin electrically charged material may be used for nonconductive samples. AFM examines materials that are dry ones. High resolution transmission electron microscopy (HRTEM) and FESEM are commonly utilized for subsequent processes of nanoscale. TEM's image resolution is superior to that of light microscopes. This will allow a comprehensive understanding of NPs. TEM is a simple method for determining the nanoparticle's size [33]. Scherrer's equation may be used to determine the particle size using X-ray diffraction (XRD) spectroscopy. Nanoparticle size may be easily determined using the distinct XRD peaks. Nevertheless, the XRD peaks are wide and it is more difficult to identify the size of non-crystalline NPs as compared with TEM. The size of NPs is too tiny to be determined by XRD. Dynamic light scattering (DLS), Mossbauer spectroscopy (MS), and photon correlation spectroscopy (PCS) may be used to determine particle sizes and distributions. The surface area on NPs may be calculated using the Brunauer Emmett Teller (BET) technique. In addition to determining crystal orientation and aggregation section, electronic morphology, lattice structural spacing and particle phase shift all may be attained.

#### 6.2. Determination of elemental and mineral conformation

Elemental composition and surface interrelation may be determined using EDS in conjunction with SEM and TEM devices. Elemental percentages may be determined with the use of the methods like atomic spectrometry and inductively coupled plasma mass spectroscopy (ICP-MS). Nevertheless, hard NPs will not directly used for these spectroscopic applications. They need proper dissolution with acids or strong bases compounds. Mineral detection is achieved using X-rays diffraction which results in making up the nanoparticle's aggregated crystalline form [34]. Elemental composition data may also be obtained using XPS.

#### 6.3. Investigation of structural arrangement and nodes in nanoparticles

There are a number of techniques to produce the coveted structure with bonding qualities. Standard procedures such as FTIR, X-ray photoelectron spectroscopy (XPS), thermogravimetric analysis (TGA), and Raman spectroscopy (RS) might be helpful. The XPS and FT-IR can verify the presence of oxygen bonding in the metal. Nanoparticle's surface arrangement may also be studied using XPS. It has the potential to keep track of statistics like the oxidation number in addition to their

elemental composition. Spinel symmetry and structure may be determined by Raman spectroscopy. X-ray absorption spectroscopy (XAS) will provide a wealth of data, including calcination states, adjacent molecules, collaboration numbers, length of bond, and the electronic formation of the necessitate element [35].

# 6.4. Analyzing the intrinsic attributes of nanoparticles

It is possible to learn more about the magnetic characteristics of nanoparticles by using VSM, Electron paramagnetic resonance (EPR) and SQUID. The EPR method can identify paramagnetic facilities along with unbound alkyl. The SQUID instrument will be accustomed to evaluating distinct varieties of samples like translucent, emaciated films, particles, moisture, and vaporish. It is an overly sensitive piece of equipment. The Hs, magnetic partial pressure, and residual magnetic polarity can be measured with SQUID and VSM, at a persistent extrinsic load magnetic flux density [36]. Mossbauer technique of spectroscopy provides access against wealth of features. Electronegativity, oxidation states, spin, and covalent character can be determined, as well as bonding, structural, and magnetic characters. **Table 4** exhibiting the advantages, limitations, and specific uses of different characterization techniques is presented below.

| Technique | Advantages  | Limitations  | Specific Uses   |
|-----------|---|--|---|
| TEM       | Surface topography images of ultra-high<br>resolution, crystallographic information, atomic<br>scale imaging.                     | Difficult sample preparation methods, expensive setup.                                   | Determination of atomic structure,<br>imaging of NPs, investigation of<br>microstructure.           |
| SEM       | Images of surface characteristics, provision of<br>analysis of wide range of materials, ease of sample<br>preparation.            | Internal structure cannot be<br>examined, low resolution, require<br>conductive samples. | Analysis of surface morphology,<br>inspection of surface defects including<br>cracks and fractures. |
| FTIR      | Identification of functional groups and chemical<br>bonds, agile analysis, provision of quantitative and<br>qualitative analysis. | Low sensitivity, not appropriate for metals, provides surface attributes only.           | Identification of functional groups and compositions.   |
| XRD       | No destructive approach, analysis of material phases.   | Usually limited to crystalline materials.  | Determination of phases and crystal attributes.   |
| SQUID     | Detection of magnetic behavior at low temperatures.   | Expensive due to the use of cryogenic conditions, only for magnetic materials            | Specific uses include paramagnets, ferromagnets, and superconductors.                               |

Table 4. Pros, cons and specific applications of different characterization techniques for NPs.

#### 7. Applications of NPs

Nanomaterials are practically amazing due to their magneto strictive, electronic, luminescence, and electrochemical properties. Their usage is present in almost every field from medical to advanced manufacturing. They are being used in the fields of medicine [37], water purification, catalysis, mechanical engineering, and computer science as well as in fields like electrochemistry, luminescence, piezoelectric, and magneto strictive ones [38]. They can be used as electrodes in batteries and supercapacitors, two common types of energy storage devices [39–45]. They can also be used in recording media, like voice/video tapes. Additionally, they also find some applications in isolators, sprockets, and circulators. They have applications inside the dyeing industry and the treatment of wastewater [46].

#### 7.1. Mechanical engineering

Nanoparticles play a vital role in mechanical engineering due to their inimitable properties and their corresponding effects. Nanotechnology shows remarkable results in materials by enhancing their strength, flexibility, mobility, elasticity, resistivity to environmental concerns and toughness. Reinforcement of composites materials, for example, graphene or nanotubes in metals or polymers ultimately results in improving the mechanical strength and stiffness of newly formed or advanced materials which gives extraordinary durability in terms of structural and wear resistance to environment. With the advancement of technology and evolution of NPs, the conventional measures of manufacturing have been evolved and nanomanufacturing has been adopted to increase output by escalating technical performance, and, excessively shows reduction in production cost. Automobiles being fabricated with help of nanotechnology have observed lower rate of failure and self-degrading properties. Thus, on basis of CO<sub>2</sub> free nanotechnology, environment friendly and sustainable transport, which might call as nano cars, where safe, clean and quiet driving is possible with less or no emission of harmful substances in atmosphere, is possible. In a lucid way, these additives improve efficiency and lifespan of machinery. Moreover, oxides of aluminum and boron nitride are being used to incorporate heat dissipation in mechanical systems. Now a days, additive manufacturing is one of the most advanced methods for manufacturing of 3-D mechanical parts with advanced nanomaterials along with complex geometries in an efficient way [37].

#### 7.2. Photocatalysis

Photocatalysis is a method which involve use of photon (light) to actuate the chemical reaction by means of some particles or substance. This process actually leads to initiating a redox reaction along with the electron hole pairs. It is an encouraging approach for sustainable green environment [47]. It is a non-hazardous, safe and reliable technique for deteriorating a large number of pollutants from the environment. NPs act as catalyst to absorb substantial number of pollutants due to their large surface area. It is observed that NPs of gold and aluminum have higher reaction rates of eliminating the organic dyes from environment. Moreover, NPs of platinum are used in most of the catalytic converters of automobiles, which significantly reduces the cost and speed up the reaction by improving its overall mechanical performance [38].

#### 7.3. Waste treatment

Environmental pollutants are one of the major concerns along with gradual increase of urbanization and industrialization. However, some preventive measures have been taken along with the passage of time to solve this problem like sedimentation, activated sludge process, chlorination, aerobic digestion, and chemical treatment etc. Meanwhile, with some advancement of technology, NPs and their composites are used due to their extraordinary physiochemical properties to counter aforesaid issues [48]. They are well known in waste treatment processes as they have adsorption properties like activated carbon NPs act as adsorbents to

eliminate maximum pollutants. For removal of heavy metals, this adsorption mechanism is adaptable due to their surface energy and affinity of surrounding atoms present in the outer most shells [45]. Photocatalysis technology, adsorption, nanomembrane technology, and disinfection are some of the methods which help in treatment of wastewater and NPs play a pivotal role in that.

#### 7.4. Water purification

Water purification is one of the common challenges for most of the developed and developing countries. Some of the traditional methods for purification of water are ultrafiltration, microfiltration, biological treatments, distillation, UV treatment, and reverse osmosis (RO). But these methods have some limitations as they will purify the water up to some extent. There comes the need of NPs for water purification. This technology mainly contains oxides of metals and nonmetals and efficacious membranes for hindering and filtering of microbes and harmful pollutants in water. Meanwhile zeolite-based nanomaterials are also used for water purification. Almost 40 morphological kinds of this materials are found naturally and can also be made in laboratory as per requirement. It has a 3-dimensional structure in which Si<sup>4+</sup> can be replaced with Al<sup>3+</sup>. These ceramics have special membrane like structure which made it special to filter up to ultra range of soluble particles. Meanwhile carbon nanotubes, graphene and nano absorbent with metals, Ag, ZnO and  $TiO_2$  nanoparticles are most frequently used for water purification [46]. Particularly, titania-based materials have been reported for extraction of antibiotics, dye contaminants along with oxidative sterilization [49].

#### 7.5. Medicine and health care

The use of nanotechnology in healthcare dates back to 1965. Their versatile properties make them useful in medical imaging. Targeted pharmaceuticals, tissue engineering, molecular engineering, biosensors, and diagnosis are the primary areas of application [50-54]. Nanoparticles are used in the field of targeted pharmaceuticals, where they are administered directly to the disease sites like cancer tumors. The smallest possible size of the NPs is required for this method of delivering the drug to the desired location via the bloodstream. When stimulated, the nanoparticles might release their cargo of drug at the site of action. Physicalchemical, biological, temperature and electrical-based materials are all examples of the many types of stimuli that exist. The drug's release will be triggered by these stimuli. Gold, titanium, magnetic NPs, and quantum dots are commonly used for drug delivery and targeting. Good and enhanced output is what you can expect when you mix these NPs with polymers. Metal NPs are by far the most effective ones for targeting drugs. Gold NPs' special spectroscopic properties have a significant impact on photothermal therapy in diagnosis of cancer. Nanoparticles of gold, silver, or magnetite ones, all work well as nanocarriers [55]. Nanocarriers are built to transport cancer drugs to the affected area. Nanoparticles are small enough to penetrate deeply but not so small that they disrupt the body's healthy tissues. That way, healthy cells will not be harmed. Drug delivery is facilitated in part by silver NPs. Some of these NPs are enriched with rare earth elements, including Fe, Ni, Co, and their oxides.

Magnetic dipole-dipole interactions can also lead to their clustering. Both organic and inorganic coatings, as well as magnetic core-shell NPs find widespread applications. Nanoparticles of the quantum dots (QD) have been found to be effective tumor targeting agents. Magnetic resonance imaging (MRI) makes use of the electrical properties of QDs. Diagnosis and treatment are two areas where mesoporous silica NPs shine [56]. This technology can also be used to precisely administer medication for cardiovascular conditions.

#### 7.6. Nanoparticles as catalysts

Reducing the acceleration, binding to reagents to antagonize bonds, getting effective collisions by attempting to bring the superoxide radicals close together, and increasing the percentage yield are some of predominate mechanisms in which catalysis come. Stimulus helps in reducing the reaction heat because they cut down unwanted byproducts. Surface area per unit mass is increased because they seem to be so small in size. Because of this, catalytic chemical reactions can take advantage of a larger surface area. When compared to conventional catalytic reactions, which use bulk materials, nano catalytic reactions are more reactive [57-63]. There are many different types of nano catalysts, including those based on metals, carbon, and ceramics [64]. Cobalt ferrites, coin ferrites, copper terbium, zinc ferrites, alloys, and core-shell ferrites are all examples of metal-based catalysts. For example, copperbased nano-catalysts can be used to improve the selectivity, catalytic performance, and stability while treating the wastewater. They are preferable due to reusability and ease of the recovery in wastewater treatment [65]. In the recent years,  $CO_2$  reduction reactions (CO<sub>2</sub>-RR) are in the limelight due to the environmental concerns. In this backdrop, NPs of noble and other transition metals are being employed for  $CO_2$ -RR. For instance, NPs of gold and copper have been reported as electrocatalysts for CO<sub>2</sub>-RR. It was observed that reduction efficiency and stability tremendously increased which was ascribed to the heterometallic interactions between the two metals and MWCNTs [66].

#### 7.7. Fuel cell application

A fuel cell is an electrochemical device that uses two redox reactions to transform the chemical energy of fuel and oxidizing agent into electricity. An oxygen/hydrogen fuel cell produces electricity with zero emissions of carbon monoxide. Every type of vehicle and instrument, from airplanes to cars, ships, submarines, and weapons now features fuel cells. Fuel cells come in many forms, including the fuel cell using proton exchange membranes (PEMFC), direct methanol fuel cells (DMFCs), alkaline fuel cell (AFC), phosphoric acid (PA) fuel cell (PAFC), the molten carbonate fuel cell (MCFC), and a solid- oxide fuel cell (SOFC) [67]. One major problem with using fuel cells is platinum (Pt) dependent catalysts that are prohibitively expensive. Researchers have not yet succeeded in fully substituting another metal for platinum. Pt-Co, Pt-Mn, Pt-Ru, Pt-Ir, Pt-Cu, and Pt-Fe, are platinum-dependent catalysts that have been introduced. Catalysts based on carbon, iron, and transition metal oxides are also used. For instance, the use of doped titanium oxide as Pt catalyst support has been reported. Traditionally, carbon-based

supports are employed which are prone to corrosion, degrading overall performance of the PEMFCs, however, titania NPs-based support exhibited superior durability as compared to the commercially available catalyst Pt/C [68]. Carbon-based catalysts make extensive use of graphene, carbon nanotubes [69], and carbon nanofibers.

#### 7.8. Electronics

Researchers have been interested in discovering new uses of NPs for their amazing magneto strictive, electronic, luminescence, and electrochemical capabilities. Memory devices, like biosensors, CPU systems, transmitter cores, high storage capacity system, optical data storage, transformer cores etc. are all familiar places to find them. They will only be successful if they exhibit a set of characteristics [70,71]. High-Hs ferrite NPs, for instance, have practical use in magnetic recording [72]. That highly magnetized Hs can be shielded from demagnetization and has been investigated. Low Hs is preferred in transformers. High Ms and Hs with minimal residual magnetization are necessary for use in recording medium like audio and video cassettes. Nanoparticles with magnetic properties have several applications in fluids, data analysis circuits in digital computers, and digital recorders. Their magnetic ferrites reveal high electrical conductivities, thus, can be pertinent to the biomedical fields. The magnetic and electrical characteristics of cobalt ferrites are very impressive [73]. The electrifying and magnetic properties of the polymers were escalated by the incorporation of pearlites. Figure 7 demonstrates the application of nanoparticles in different fields.



Figure 7. Applications of NPs.

#### 8. Issues and challenges

Apart from its advantages, that have been achieved by use of nanotechnology in various fields of life, there are a number of issues in different areas which need to be

resolved [74]. Some of the challenges are given below as:

- Synthesis of NPs is a vital challenge. Normally high-quality NPs are manufactured using diverse instruments under extreme conditions which results in controlled production at large scale. The scalability is challenging as processes like vapor chemical deposition, laser ablation, and hydrothermal synthesis is difficult to scale up. In the meanwhile, scalability requires more energy, costly materials, more sensitive equipment, thus adding up to the overall cost of processing.
- The change in starting material and process parameters can lead to the inconsistencies, ultimately affecting the reproducibility.
- Although NPs are remarkably effective and useful in cancer and drug delivery, however, presence of impurities, defects and discontinuity in their length suppress their strength.
- Nanoparticles have been found to be harmful for the humans as they can penetrate the human body and cause severe health issues. There is likelihood of entering in the respiratory system and other important organs of the human body. For instance, metallic nanoparticles like Au are toxic and reactive in nature, which might cause skin and lungs' cancer. Under certain conditions, it shows phototoxic effect which leads to health problems. Additionally, most of cosmetic and beauty products contain titanium dioxide NPs, long term use may cause cell damage and respiratory issues. Prolong interaction of carbon nanotubes causes inflammation and fibrosis as it has potential of toxicity. There are regulatory challenges as well as they are evolving at the moment. Stable revelation of zinc oxide NPs may raise challenges of skin and eye irritation [75].
- Another challenge which needs to be addressed is environmental impact of NPs during their synthesis, utilization, and disposal. Their accumulation in the environment may have drastic effect on aquatic life. In addition to that, sustainability is another factor which needs to be kept in mind. Use of toxic and expensive chemicals and energy-intensive methods, proliferation of NPs in the fresh water, and utilization of larger amounts of water raises sustainability concerns. There is little understanding of their end-of -life disposal as well.

#### 9. Conclusion and future prospects

In this review, a brief overview of NPs, their types based upon their dimensions, synthesis routes, and emerging applications in various fields of science and technology have been discussed. Several physicochemical characteristics of the NPs are characterized using a variety of tools like ultraviolet, spectrophotometer, the FT-IR, AFM, SEM, TEM, which reveal that these particles exhibit distinct properties. The synthesis using plant extracts is non-toxic, making plants the best choice for producing nanoparticles. Due to small size and large surface area or volume, ability to absorb and scatter rays of light in visible and infrared region is possible. These properties make it ideal for early diagnosis and treatment of neuro-degenerative diseases. Besides its advantages, substantial number of health, environmental and safety issues rise due to the refractory use of these particles. It has the potential to

cause detrimental effect like asthma, urticaria, hypertension, Parkinson, dermatitis, Alzheimer, and many other cancers in human body. Thus, there should be a controlled use and discharge of the particles in the environment.

There is dire need to divert the future research direction towards the improvement of homogeneity during the synthesis and control over shape and size, while keeping in view the consistency and scalability especially for the green approaches such as plant-based ones. The priority should be given to addressing the toxicity concerns by introducing biodegradable and non-toxic nanoparticles. The innovation will be driven by the advancement in functionalization techniques and introduction of hybrid nanoparticles with applications in energy storage devices and drug delivery. There should be emphasis on introducing proper guidelines regarding the use of NPs, providing testing frameworks, and labelling the information about the NPs. Last, but not the least, the concepts of circular economy and sustainability should be further explored to improve the yield and reusability, thus minimizing the environmental impacts.

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Review

# Emerging frontiers: Harnessing the power of CNT/GO-based biosensors for early disease biomarker detection

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https://creativecommons.org/licenses/ by/4.0/ **Abstract:** This review discusses the significant progress made in the development of CNT/GO-based biosensors for disease biomarker detection. It highlights the specific applications of CNT/GO-based biosensors in the detection of various disease biomarkers, including cancer, cardiovascular diseases, infectious diseases, and neurodegenerative disorders. The superior performance of these biosensors, such as their high sensitivity, low detection limits, and real-time monitoring capabilities, makes them highly promising for early disease diagnosis. Moreover, the challenges and future directions in the field of CNT/GO-based biosensors are discussed, focusing on the need for standardization, scalability, and commercialization of these biosensing platforms. In conclusion, CNT/GO-based biosensors have demonstrated immense potential in the field of disease biomarker detection, offering a promising approach towards early diagnosis. Continued research and development in this area hold great promise for advancing personalized medicine and improving patient outcomes.

**Keywords:** CNT/GO-based biosensors; disease biomarker detection; early diagnosis; biosensing; cancer; cardiovascular diseases; infectious diseases; neurodegenerative disorders

#### **1. Introduction**

Emerging as quite promising systems for identifying disease biomarkers are CNT/GO-based biosensors. Carbon nanotubes (CNTs) and graphene oxide (GO) are attractive for this use. Firstly, CNTs and GO have outstanding electrical conductivity, which helps detect biomolecules sensitively. Between biomarkers and recognition elements, their electrical characteristics can transduce particular binding events into detectable electrical signals [1,2]. Secondly, CNTs and GO have a high surface area-to-volume ratio, offering a lot of binding surfaces for biomarker capture. This improves the biosensor's sensitivity. Selective detection of target biomarkers becomes feasible by functionalizing CNTs and GO with particular recognition elements like antibodies or aptamers [3–5].

The label-free detection capability of CNT/GO-based biosensors adds still another benefit. This simplifies the assay process and removes the necessity of extra labeling steps. Moreover, CNTs and GO fit microfabrication methods, which enables integration with miniature devices [6,7]. This makes point-of-care diagnostics portable, and successful detection of several disease biomarkers has been shown by CNT/GO-based biosensors [8–10]. They have shown great sensitivity and specificity for identifying particular tumor markers in cancer diagnosis, thus facilitating early cancer detection and treatment monitoring [11,12]. By identifying cardiac biomarkers linked with heart failure and myocardial infarction, they have also shown promise in diagnosing cardiovascular disease [13–15]. CNT/GO-based biosensors have been applied for fast and sensitive identification of pathogen-associated biomarkers in infectious disease diagnostics, enabling early identification of infectious agents [16]. Furthermore, these biosensors could identify disease-specific biomarkers in neurodegenerative diseases, supporting early diagnosis and disease progression monitoring [17,18].

This review intends to analyze the progress in CNT/GO-based biosensors, emphasizing their fabrication techniques, functionalization approaches, and integration with transducing components to improve sensitivity and selectivity. It examines the particular applications of these biosensors in identifying various disease biomarkers, including those linked to cancer, cardiovascular diseases, infectious diseases, and neurodegenerative disorders. Additionally, the review highlights the superior performance of CNT/GO-based biosensors, such as their high sensitivity, low detection limits, and real-time monitoring capabilities, which contribute to their potential in facilitating early disease diagnosis. Finally, it discusses the challenges and future trajectories in the domain, highlighting the necessity for standardization, scalability, and commercialization to enhance personalized medicine and optimize patient outcomes.

#### 2. Cancer diagnosis

Biosensors using graphene oxide (GO) and carbon nanotubes (CNT) have shown significant potential for cancer detection [19,20]. These biosensors possess exceptional qualities such as high sensitivity, selectivity, and compatibility with biological systems. [21,22]. They can identify specific cancer biomarkers, such as proteins and nucleic acids, in diverse biological specimens, including blood, urine, and saliva [23]. The elevated surface area and superior electrical conductivity of CNTs and GO enhance the immobilization of capture probes that specifically attach to target biomarkers [24,25]. The detection of cancer utilizing a biosensor is depicted in Figure 1. Binding events induce alterations in electrical, optical, or electrochemical signals, facilitating the sensitive detection of cancer biomarkers [26,27]. Liquid biopsy is a non-invasive method utilized for cancer diagnosis and monitoring [28-30]. CNT/GO-based biosensors have been investigated to detect circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) in blood specimens. These biosensors can detect circulating tumor cells (CTCs) or assess genetic modifications in circulating tumor DNA (ctDNA), yielding critical insights regarding tumor existence, advancement, and therapeutic response [31].



Figure 1. Detection of cancer using biosensor.

Another advantage is the potential for multiplexed detection, allowing simultaneous analysis of multiple cancer biomarkers [32-34]. By integrating different capture probes specific to distinct biomarkers, CNT/GO-based biosensors can detect and quantify multiple analytes in a single assay. Multiplex biomarker detection employs modern techniques such as microarrays, multiplexed enzymelinked immunosorbent assay, mass spectrometry, and biosensors to recognize many targets at once [35]. Techniques use unique probes, spectral signatures, or chemical interactions to provide high-throughput and specific detection [36]. This multiplexed approach improves diagnostic accuracy and efficiency by providing a comprehensive profile of the disease [37]. CNT/GO-based biosensors are also well-suited for pointof-care cancer testing due to their portability, rapid response, and ability to detect low analyte concentrations [38]. They can be integrated into portable devices or wearable sensors, enabling real-time and on-site cancer diagnosis. By continually monitoring physiological or chemical signals from the body, wearable sensors can identify cancer biomarkers. These devices detect cancer-related markers in physiological fluids such blood, saliva, perspiration, or interstitial fluid by using cutting-edge materials and technology [39]. Point-of-care testing facilitates early detection, personalized treatment, and improved patient outcomes, particularly in resource-limited settings [40-42]. Furthermore, CNT/GO-based biosensors have been investigated for cancer imaging and visualization. Functionalized CNTs or GO can act as contrast agents in various imaging techniques such as photoacoustic imaging, fluorescence imaging, and magnetic resonance imaging (MRI) [43-46]. These biosensors enhance sensitivity and specificity in cancer imaging, aiding in tumor localization, staging, and monitoring [47,48]. It's important to note that while CNT/GO-based biosensors hold promise for cancer diagnosis, further research and development are necessary to optimize their performance, validate their clinical utility, and ensure integration into routine clinical practice [49,50]. The field of biosensors is rapidly evolving, and recent advancements may have occurred since my knowledge cutoff. Therefore, referring to the latest scientific literature and

research updates is recommended for the most recent progress in CNT/GO-based biosensors for cancer diagnosis.

#### 3. Infectious disease diagnosis

Biosensors based on CNT/GO have shown great promise as tools for diagnosing infectious diseases. These biosensors allow for the quick and accurate identification of particular biomarkers linked to contagious agents using the unique qualities of graphene oxide (GO) and carbon nanotubes (CNTs). They can identify various biomarkers that indicate the presence of pathogens or host immune responses, such as proteins, nucleic acids, and other molecular targets [51,52]. Figure 2 shows how infectious diseases are detected. The high sensitivity and selectivity of CNT/GO-based biosensors is one of their main benefits. They improved sensitivity results from the effective capture of biomarkers made possible by the high surface area-to-volume ratio of GO and CNTs [53-55]. Accurate diagnosis is also ensured by functionalizing CNTs and GO with particular recognition elements, like aptamers or antibodies, which allow for the selective detection of target biomarkers. Multiplexed detection is another significant characteristic of CNT/GO-based biosensors [56-58]. These systems enable the simultaneous detection of multiple infectious disease biomarkers by attaching multiple capture probes to the biosensor. This feature allows for thorough disease profiling and improves diagnostic efficiency and accuracy [59,60].



Figure 2. Infectious disease detection.

Ongoing research efforts in this field focus on enhancing the sensitivity, stability, and scalability of CNT/GO-based biosensors for infectious disease diagnosis. Additionally, there is a concerted effort to address challenges related to standardization, validation, and the integration of these biosensors into routine clinical practice.

#### 4. Neurological disorder diagnosis

The use of CNT/GO-based biosensors in diagnosing neurological conditions, such as Parkinson's and Alzheimer's diseases, has shown encouraging results [61,62]. These biosensors can detect Specific biomarkers closely linked to the pathophysiology of these disorders, such as alpha-synuclein and amyloid-beta proteins. Amyloid-beta plaques and tau protein tangles are two characteristics of Alzheimer's disease found in the brain [63,64]. Amyloid-beta peptides or tau

proteins in blood or cerebrospinal fluid can be detected by CNT/GO-based biosensors, allowing for the early diagnosis and tracking of Alzheimer's disease progression. Similarly, Lewy bodies, which are aggregates of alpha-synuclein proteins, are a hallmark of Parkinson's disease [65,66]. **Figure 3** shows a schematic diagram for detecting neurological diseases using a biosensor based on CNT/GO. One possible diagnostic tool for Parkinson's disease is biosensors based on carbon nanotubes and graphene oxide that detect alpha-synuclein in blood and cerebrospinal fluid. Initiating effective treatments, tracking disease progression, and enhancing patient outcomes depend on early and accurate diagnosis of neurological disorders [67–69]. The creation of biosensors based on carbon nanotubes and graphene oxide that selective detection of biomarkers linked to these diseases, which could lead to earlier diagnoses and more tailored treatments. Clinical translation of these biosensors for neurological disorder diagnosis will be advanced by ongoing research and validation studies [70–73].



Figure 3. Schematic diagram of neurological disease detection using CNT/GO based biosensor.

#### 5. Glucose monitoring in diabetes management

One exciting development in diabetes management is using biosensors based on carbon nanotubes and gonads (CNTs/GO). These biosensors provide an alternative to the invasive and time-consuming finger-prick test for monitoring glucose levels. They reduce patient pain and infection risk by detecting glucose in non-invasive bodily fluids such as saliva, sweat, or tears rather than blood [74–76]. Thanks to their distinct electrical characteristics, CNTs and GO make it possible to track glucose levels in real-time. Changes in electrical conductivity or other sensing mechanisms provide quick feedback on glucose fluctuations, enabling patients to make timely adjustments to their diabetes management. Wearable devices like smartwatches, patches, or contact lenses can incorporate these biosensors, allowing for more accessible and convenient continuous glucose monitoring [77,78]. Patients can benefit greatly by having their glucose profiles monitored continuously throughout the day. Glucose detection using CNT/GO-based biosensors is exact and sensitive—**Figure 4** displays glucose monitoring for diabetes management. Accurate readings

are guaranteed by functionalizing the biosensor surface with molecules or enzymes specific to glucose, increasing sensitivity and selectivity [79,80]. Patients can then better manage their diabetes as a whole because they can control their blood glucose levels through dietary, exercise, and medication choices [81]. However, there are still challenges to address in the field. Researchers are actively working on improving sensor stability, calibration, and long-term performance to enhance the reliability, accuracy, and durability of CNT/GO-based biosensors [82,83].



Figure 4. Glucose monitoring in diabetes management.

Standardization and regulatory approval are also vital for the widespread adoption of these biosensors in clinical practice. Despite these challenges, CNT/GObased biosensors hold significant potential to transform diabetes management by providing non-invasive, real-time glucose monitoring [84,85]. Continued research and development efforts aim to overcome the current limitations and pave the way for their integration into routine clinical care.

#### 6. Cardiovascular diseases detection

The promising diagnosis of cardiovascular disease is CNT/GO-based biosensors. In this discipline, biosensors have many advantages. Accurately identifying cardiovascular disease biomarkers, including cardiac troponins, CRP, and BNP, which expose heart muscle damage, inflammation, and heart failure [86–88], they expose to diagnosis and track cardiovascular disease, CNT/GO-based biosensors measure biomarkers in blood or other non-invasive samples. Figure 5 shows cardiovascular disease detection methods. High sensitivity and selectivity are CNT/GO biosensor strengths [89,90]. They can detect low cardiovascular biomarker concentrations in complex biological matrices, enabling early cardiac event detection and precise disease progression monitoring. Early intervention and treatment may improve patient outcomes. The detection and monitoring of cardiovascular disease using CNT/GO-based biosensors from blood or saliva samples is easy and patientfriendly. Eliminating invasive treatments helps biosensors lower patient discomfort and improve monitoring [91-94]. Real-time tracking of CNT/GO-based biosensors would help management of cardiovascular diseases. Their dynamic character and rapid biomarker feedback help to enable quick medical interventions and treatment plan modifications related to cardiovascular diseases.



Figure 5. Detection technique of various cardiovascular disease.

Moreover, the use of CNT/GO-based biosensors aligns with the principles of personalized medicine. By providing real-time monitoring and precise quantification of cardiovascular biomarkers, these biosensors facilitate tailored treatment plans and patient-specific interventions, optimizing patient outcomes. While ongoing research and development are still needed, CNT/GO-based biosensors hold great promise for the detection and monitoring of cardiovascular diseases. Continued collaboration among researchers, clinicians, and industry partners is essential to further refine the technology, establish robust validation protocols, and ensure the successful integration of these biosensors into routine clinical practice [95].

#### 7. Challenges and future directions

In the field of CNT/GO-based biosensors, there are several challenges that need to be addressed for their widespread adoption, standardization, scalability, and commercialization. These challenges include:

#### 7.1. Standardization of fabrication processes

One of the key challenges is the standardization of fabrication processes for CNT/GO-based biosensors. Variations in synthesis methods, functionalization techniques, and sensor assembly can lead to inconsistent performance and hinder reproducibility. Establishing standardized protocols and quality control measures is crucial to ensure consistent and reliable biosensor performance across different laboratories and manufacturing facilities.

#### 7.2. Sensor stability and longevity

The stability and longevity of CNT/GO-based biosensors are important factors for their practical implementation. The performance of these biosensors should be maintained over extended periods, ensuring reliable and accurate detection of cardiovascular biomarkers. Addressing issues related to sensor degradation, biofouling, and long-term stability will be crucial for their successful commercialization.

#### 7.3. Scalability and manufacturing processes

For wide-scale adoption, CNT/GO-based biosensors need to be manufactured in large quantities using scalable and cost-effective processes. It is important to develop manufacturing techniques that can produce biosensors with consistent quality, while also ensuring affordability and accessibility for healthcare settings.

#### 7.4. Integration with point-of-care devices

The integration of CNT/GO-based biosensors with portable and user-friendly point-of-care devices is a significant challenge. These biosensors need to be compatible with miniaturized and low-power electronics, enabling their integration into handheld or wearable devices. This integration would facilitate on-site testing, remote monitoring, and real-time data analysis, thereby enhancing their clinical utility. Point-of-care (POC) cancer detection technologies include i-STAT for Prostate-specific antigen assessment, Lateral Flow Assays for visual biomarker detection, and wearable microneedle biosensors for noninvasive monitoring.

#### 7.5. Regulatory and commercialization aspects

The regulatory landscape and commercialization pathways for CNT/GO-based biosensors need to be addressed. Meeting regulatory requirements, obtaining necessary certifications, and navigating the complex commercialization process are critical steps for bringing these biosensors to the market and making them available for widespread clinical use.

#### 7.6. Additional challenges

Robust clinical validation studies are essential to demonstrate the efficacy, accuracy, and clinical relevance of CNT/GO-based biosensors for cardiovascular disease detection and monitoring. Collaboration between researchers, clinicians, and industry partners is crucial for conducting large-scale clinical trials, validating the biosensor performance, and refining the technology based on feedback from end-users.

Future directions in the field of CNT/GO-based biosensors should focus on addressing these challenges. Collaborative efforts among researchers, regulatory agencies, and industry partners are necessary to establish standardized protocols, optimize manufacturing processes, ensure sensor stability, and navigate the regulatory and commercialization landscape. By overcoming these challenges, CNT/GO-based biosensors can become valuable tools for cardiovascular disease diagnosis and management in clinical settings.

#### 8. Conclusion

In conclusion, CNT/GO-based biosensors have shown significant potential in various areas of medical diagnosis, including cancer, infectious diseases, neurological disorders, diabetes management, and cardiovascular diseases. These biosensors offer advantages such as high sensitivity, selectivity, multiplexed detection, and real-time monitoring. They can detect specific biomarkers associated with different diseases, enabling early diagnosis, treatment monitoring, and

personalized medicine approaches. The non-invasive sampling methods and compatibility with portable devices make them suitable for point-of-care testing and resource-limited settings. However, further research and development are necessary to optimize their performance, validate their clinical utility, and integrate them into routine clinical practice. The field of biosensors is rapidly evolving, and staying updated with the latest scientific literature and research advancements is crucial for the most recent progress in CNT/GO-based biosensors for medical diagnosis.

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