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Green Synthesis of Metal Oxide Nanoparticles via Plant Extracts for Biological Applications: A Review

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Abstract

Metal oxide nanoparticles have found their own inevitable place in the field of nanotechnology due to their versatile applications like catalysis, drug delivery, sensors, energy devices, semiconductors, food technology, agriculture and medicine. The use of green synthesis techniques is becoming more and more significant as a practical means of producing nanoparticles that are less hazardous to the environment. It is hopeful for large-scale commercial production because green synthesis methods can yield nanomaterials with lower production costs and energy inputs than conventional synthesis methods. To attain this, plant extracts can be used as precipitating agents for the preparation of metal oxides, by this we can eliminate the usage of hazardous chemicals. Phytochemicals, which are active substances obtained from plants used as reducing and stabilizing agents in the ecologically benign manufacturing of nanoparticles. Furthermore, a cutting-edge green synthesis method that has garnered a lot of scholarly attention is the creation of metal and metal-based hybrid nanoparticles utilizing plants or plant extracts. In this review article we mainly, summarized the synthesis of various metal oxides include zinc oxides, cobalt oxides, iron oxides, magnesium oxides and other nano particles using the plant extract via green synthetic methods and we discussed about some biological applications of these metal oxides.

Keywords: Metal oxides nanoparticles, Sustainable chemistry, Plant extracts, Biological applications

Introduction

The global population seems to be increasing at the same time that industrialization and agriculture do. Uncontrolled uses of pesticides, herbicides, and chlorinated organic poisons, as well as organic hydrocarbon compounds that leak into the environment and contaminate water are some of the effects of this reality. Since nanoparticles molecular activity can have an impact on living things, the most notable aspect of nanotechnology is its application in biology and biological systems, despite the field's apparent advancements in medicine being very amazing. Consequently, the potential for using nanoparticles in illness diagnosis and treatment has been made possible by their special qualities [1].

Nanotechnology in material science refers to the creation of nanoparticles with specific properties by the use of physical or chemical techniques. These materials have unique physical, chemical, thermal, and electrical properties allow them to be used in a broad range of fields, including electronics, agriculture, health care, and environmental management. Using various chemical materials, which are dangerous for people and the environment is one of the challenges in the production of metal oxide nanoparticles [2]. Greener synthesis and bio synthesis of nanoparticles is a significant development method in nanotechnology at the moment [3]. Numerous researchers have documented diverse methods for producing metal oxide nanoparticles using a range of biological sources, including fungi and bacteria [4]. One of the active areas of nano biotechnology study in the current world is the green chemistry approach of plant intermediation [5,6].

Plants are the best source of raw materials for creating metal oxide nanoparticles among the various bio-sources, due to their protein content, availability, simplicity, antioxidant capability, and non-toxicity. Variety of plant extracts can be used as stabilizing, capping, and reducing agents for the production of metal oxide nanoparticles. The application of plant extracts can prove to be highly advantageous as they can function as reducing agents throughout the production process and encourage the development of more biocompatible nanostructures [7,8]. It can be suggested that the application of green technology can reduce the usage of high-risk reagents and solvents [9], as well as increase the energy efficiency and materials in the chemical processes of improvement and design of non-toxic products [10], given that the reaction rate has been observed to be quite fast and that special conditions are not required in this procedure. It has been shown that using plant extracts is more advantageous method to prepare metal oxide nanoparticles [11]. It has long been believed that plants and crops are a rare and reasonably priced source for the synthesis of biological nanomaterials [12]. The MONP's prepared from the green synthesis involves many advantages like enhanced properties (improved stability, bio compatibility), cost effective (inexpensive raw materials, simple synthesis), sustainability (renewable resources, less water) and have versatile application in all fields (**Figure 1**).

Metal oxides are ionic compositions that contain positively charged metal ions and negatively charged oxygen ions, which can function as conductors or semiconductors. One of the best multifunctional materials is semiconductor nanoparticles, which have remarkable physio-chemical properties including high chemical stability, high electrochemical coupling coefficient, broad radiation absorption range, and high light stability [13,14]. Due to this type of properties the researchers are seem to be interested towards nanosized semiconductor metal oxides which are very helpful in creating multifunctional nanoscale optoelectronic and electronic devices and they also mainly used for the gas sensing applications.

From the foregoing discussion, the production of metal oxide nanoparticles using green chemistry principles has gained popularity. The main objectives and alignment of this review about the preparation of metal oxide nanoparticles such as FeO, ZnO, CoO, NiO, CuO, TiO_2 and MgO by using variety of plant extracts and discussion about their biological applications in the fields of anti-cancer, anti-oxidant and others.

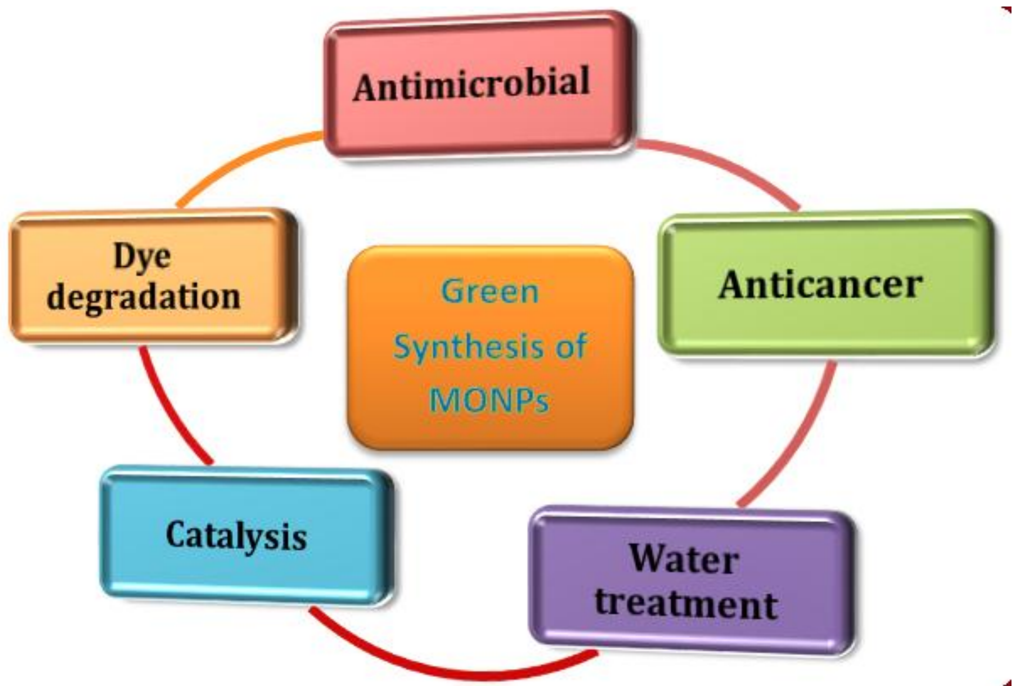

Figure 1 Contribution of MONPs in different field.

Metal oxides nanoparticles semiconductors (MONP's)

The semiconductors are the materials which shows the property between the conductor and insulator. The semiconductor was normally an insulator until the electron crosses the valence band to conduction band. The distance between the bands is known as band gap. All semiconductors have a different band gap. Quantum dot semiconductor structures have been of the most motivating materials in optoelectronic devices due to their unique properties such as spiked density of state, low temperature sensitivity, high data transmission rate, low threshold current (**Figure 2**) [15]. The metal oxide nanoparticles (MONP's) can be used as the semiconductors because of its adjustable band gap, MONPs can be used in a wide range of semiconductor applications. MONPs semiconductors have many advantages like low toxicity, cost effectiveness, bio compatibility, energy efficiency and scalability.

One of the best multifunctional materials is semiconductor nanoparticles, which have remarkable physio-chemical properties, which contains positively charged metal ions and negatively charged oxygen ions, which can function as semiconductors [13,14]. The developments of this metal oxide nanoparticles semiconductors will be focusing on the main aspects like refining of synthetic methods, improving the surface functions and by creating a hybrid materials like bimetal oxides, nanocomposites to enhance its efficiency. Nano scale semiconductors showed potent activity, by increasing its surface area, improving their electrical conductivity, and reducing their power consumption [16].

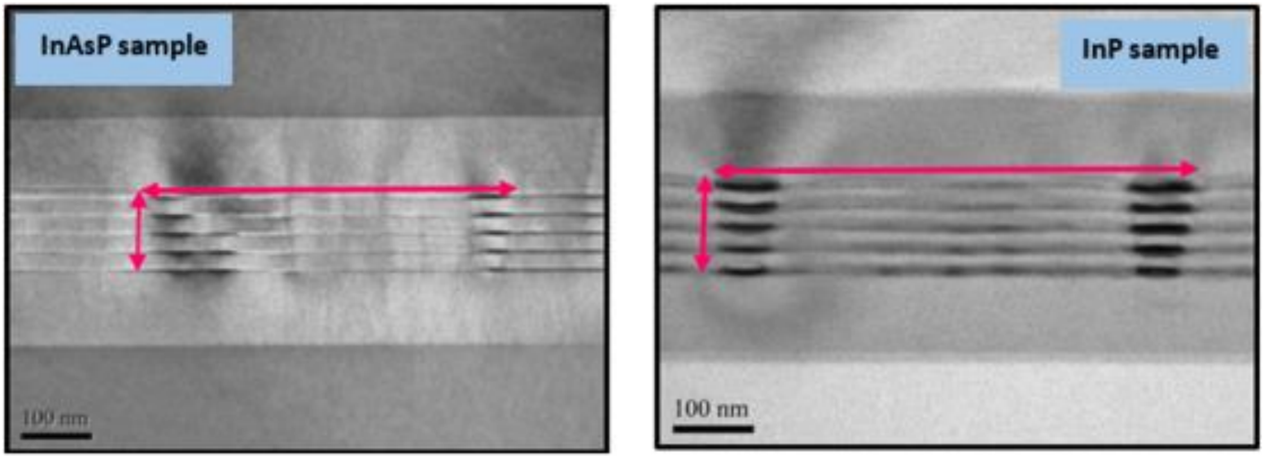

Figure 2 TEM images for the active region of QD samples [15].

This metal oxide nano particles offers unique properties like tunable band gap (very important character of the semiconductor), high surface area, size dependent behavior allows for the significant advancement in semiconductor industry. With the continued innovation and advancements leads to the production of efficient metal oxide nanoparticles semiconductors which dictates the future in the fields of semi conducting technologies, environmental remediation, energy applications, smart sensing systems and some biological applications.

Similarly, recent progress in QD lasers grown in silicon is reviewed, focusing on QD lasers in terms of threshold current density, output optical power, emission wavelengths, and operation temperatures. The future of QD lasers monolithically grown on Si-substrate and their application are also discussed in the literature [17,18]. The scope of III-V compound semiconductors heterogeneously integrated on Si substrates. The commercial success of massively produced integrated optical transceivers based on first-generation innovation is discussed [19].

For uses such as gas detection and catalysis, their huge surface area improves their reactivity and sensitivity. MONPs have special optical qualities that are helpful in optoelectronic devices, like photoluminescence. Recently air pollution grown to be a serious hazard to both people and the environment. Semiconductor metal oxide nanoparticles such as ZnO, TiO_2, CeO_2, SnO_2, In_2O_3, CuO, NiO, WO_3, and Fe_3O_4, are used in the sensing applications for the air pollution [20]. Researchers are seen to be interested towards nanosized semiconductor metal oxides because of their electrical and optical characteristics, which are very helpful in creating multifunctional nanoscale optoelectronic and electronic devices. This chapter highlights the production of metal oxides nanoparticles semiconductors produced form metal oxides in a greener way by using various plant extracts.

Advantages of using plant extracts in nanoparticle synthesis

With the objective to create harmless and environmentally beneficial nano assemblies to address issues impacting the environment or public health, green nanotechnology combines the concepts of green chemistry and ecological engineering. The toxicity and risk of nanoparticles remain a major worry despite significant advancements in the field of nanotechnology. Here, the concept of "green nanotechnology" progressively becomes apparent in order to address the potential risks associated with nanotechnology. Simple, affordable, environmentally safe, and easily accessible raw materials are used in the green synthesis process, which also uses fewer processes and no hazardous chemicals or byproducts (**Figure 3**). The goal of green nanotechnology is to completely remove any harmful materials from the production process. One noteworthy aspect of green nanotechnology is the application of plant-derived phytochemicals as stabilizing and reducing agents during the conversion of metal ions into metallic nanoparticles.

With the help of plant extracts, it is possible to control the synthesis of nanoparticles and obtain well-defined sizes and morphologies in a single step with a high yield. Several bioactive substances can be found in the seeds, leaves, and stems of medicinal plants. These discovered substances include flavonoids, amides, alkaloids, saponins, glycosides, terpenoids, and tannins. These materials serve as reducing and capping agents throughout the nanoparticle production process.

Figure 3 Advantages of green synthesis.

Plants are readily accessible and safe to handle, scientists have placed a great deal of attention on using plant extracts in the creation of nanoparticles. Applications for MONPs (Metal oxide Nanoparticles) are numerous and include drug delivery systems, catalysts, active food packaging materials, parts for nano-biosensor construction, gene transfer systems, antibiotics, antiseptics, disinfectants, and pathogen and pest control solutions, as well as nanoelectronic components. When using plant-mediated methods, biosynthesis proceeds at a faster pace than environmentally when using methods focused on microorganisms, and the resultant nanoparticles (NPs) are more stable and varied in size and shape. Because they are easy to use, inexpensive, and environmentally beneficial for producing large quantities of NPs in a short amount of time, plant extracts are frequently used in the green synthesis of metal-based NPs [21]. In order to create nanoparticles (NPs), extracted phytochemicals are added to metal salt solutions, where they lower the metal ions and connect to the NPs to serve as capping or stabilizing agents. These non-toxic capping agents stop NPs from aggregating. Furthermore, there is better control over the formation of NP crystals using biological methods due their kinetics are slower than those of chemical approaches [22-25].

Synthesis in sustainable chemistry

Plant-mediated green synthesis methods create metal oxide nanoparticles (NPs) of various sizes and shapes using various plant parts, including the seed, fruit, callus, bark, stem, flowers, and leaves [26]. During the creation of nanoparticles, a variety of metabolites included in plant extracts that function as stabilizing and reducing agents. The complexity of the bio reduction process is widely acknowledged. By giving the metal ions electrons, the biomolecules in the extract operate as a reducing agent, causing the metal ions to be reduced to the elemental metal. After the produced atoms function as a nucleation site, nearby smaller particles unite to form larger NPs during a growth phase. To this end, plant extracts can stabilize NPs during the last phase of synthesis, which in turn determines their desirable and energetically stable form. Additionally, a capping agent is added to prevent further growth and keep the particle in the nanoscale region. Therefore, the plant extract’s biomolecules can operate as reducing agents or double as capping agents and reducing agents [27,28] (**Figure 4**).

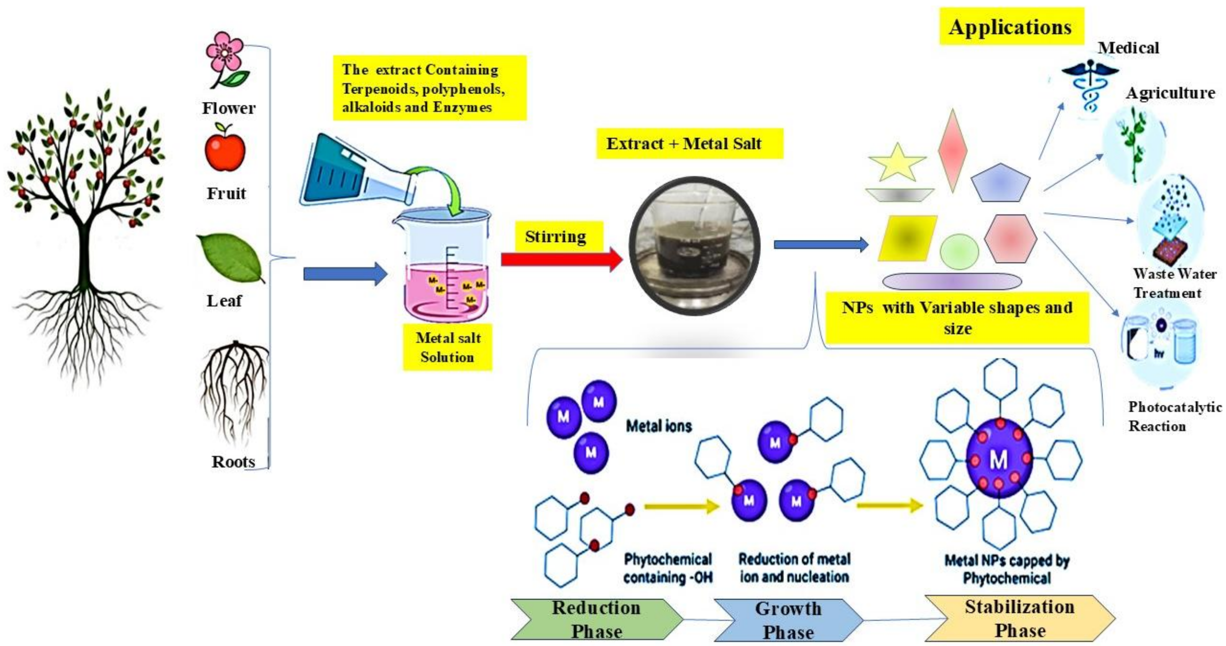

Figure 4 Schematic Synthesis of Metal Oxide from plant extract and its applications.

Synthesis and biological applications of some metal oxide nanoparticles

Iron oxide

Iron oxide has considerable changeable oxidation states, crystal structures, cheap cost, and magnetic properties. It has been one of the transition metal oxides, which has been studied the most [29,30]. In the biomedical fields iron nanoparticles used in magnetic recording media, nonlinear optical systems, magnetic shielding, immunoassays, magnetic targeted site-specific drug delivery, safe labeling of endothelial progenitor cells, environmental remediation, food analysis, microwave absorbers, and electromagnetic interference shielding [31-36]. Only limited studies in the antibacterial properties of iron oxide NPs have been published reported [37,38]. Devi *et al.* [39] explain the green aqueous phase production of iron oxide nanoparticles using *Platanus orientalis* leaf extract, which possessed good anti-microbial activity against *Aspergillus niger* and *Mucor piriformis* and *M. piriformi*. The green manufacture of magnetic iron oxide nanoparticles (Fe_3O_4 NPs) uses leaf extract from *Euphorbia herita*. In particular, polyphenols and alcoholic compounds are important phytochemicals in the production of magnetic iron oxide nanoparticles [40]. When the produced iron oxide nanoparticles were tested for antibacterial activity against a variety of bacterial and fungal pathogens, the results of the investigation were quite encouraging [40].

Iron oxide NP’s like FeO, magnetite (Fe_3O_4) is prepared by the green synthesis (plant extract) have some biological properties that conventionally synthesized FeO NP’s lacks. They have biological properties like, good biocompatibility because greenly produced IONPs are often non-toxic, which qualifies them for use in biological applications. Biological systems frequently tolerate these nanoparticles well, which lowers the possibility of negative effects.

Yusefi *et al*. used the plant peel extract of *Punica Granatum* for the preparation of FeONP's and analyzed its anti-cancer activities in various cancer cell lines like colon (HCT116), breast (MCF7), cervical (HeLa) and lung (A549) cancer cell lines and 2 normal cell lines derived from human colon and kidney (CCD112 and HEK293) [41].

Manimaran *et al*. synthesized the FeONP from the *Pleurotus citrinopileatus* extract (mushroom extract) and evaluated its anti-bacterial and anti-cancer activity. It was discovered that the FeONPs anticancer efficiency (MG-65) was expressed by an IC_{50} value of 55.63 μg/mL [42]. Sriramula *et al*. used the extract of *Aegle marmelos* for the synthesis of FeONP and studied their bacterial properties by using the NP against the bacteria like *E. coli* and *S. aureus* at and compared with Streptomycin and reported that these NP's have good anti-bacterial property [43]. Abdullah *et al*. synthesized the Fe_2O_3, Fe_3O_4-NPs nanoparticles from the *pheonix dactylifera* leaf extract form the green synthesis and the compounds showed good anti-oxidant properties [44]. Ustun *et al*. used the *Ficus Carica* Leaf Extract for the green synthesis of FeO NP's for the application of anti-oxidant studies [154]. Kuldeep Singh *et al.* used the leaf extract of *Coriandrum sativum* L. for the synthesis of FeONP's and studied their anti oxidant property. From their research, iron oxide nanoparticles (50 - 250 mg) showed DPPH radical inhibitory activity from 32.54 to 84.28 %, outperforming ascorbic acid (28.25 to 81.41 %) [45].

Isik *et al*. studied the anti-microbial property of the FeONP derived from the leaf extract of *Centaurea solstitialis* leaves [151]. Devi *et al*. synthesized the FeO NPs from the *P. orientalis* leaf extract for the green synthesis of FeONP. They subjected this NP to the anti fungal activity against Fungi like *A. niger* and *M. Piriformis* which employed as model fungi. But interestingly it shows good anti fungal activity against the *M. piriformis* (later fungus) [46]. Sriramulu *et al*. used the leaf extract of *Aegle marmelos* for the synthesis of FeONP and studied their anti-fungal properties against the fungi like *F. Solani* (12 ± 0.53 mm) compared with fluconazole (7 ± 0.38) at 30 μg/mL and reported that they showed the good anti fungal activity [153]. From the above we revealed that the plant mediated synthesized iron oxide NPs possessed good biological activity.

Thakur *et al.* [47] developed magnetic iron nanoparticles from Chenopodium glaucum (CG) and it act as an efficient and recyclable heterogeneous catalyst for one-pot synthesis of xanthene derivatives, yielding products with high yields (up to 97 %) and excellent purity (crystalline form) within a short timeframe (6 min) using microwave irradiations (at 120 W) (**Figure 5**).

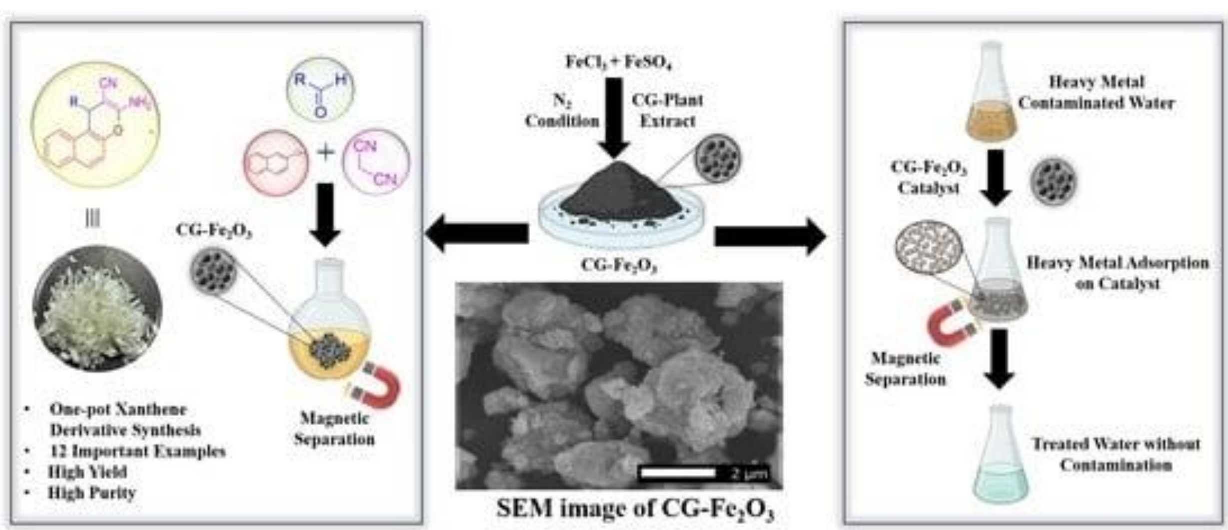

Figure 5 Schematic representation of development of magnetic iron nanoparticles from Chenopodium glaucum (CG) [47].

Zinc oxide nanoparticles (ZnONPs)

Zinc oxide nanoparticles (ZnO NPs) have garnered the most attention among all the metal oxides utilized to create nanoparticles (NPs) because of their appealing characteristics, extensive uses, and environmentally benign makeup [48,49]. Zinc oxide (ZnO) is a kind of semiconducting metal oxide that has garnered interest in the last 2 to 3 years because of its enormous potential for use in biomolecular, microelectronics, optics, biomedical systems, and antimicrobial agent manufacture [50,51]. The structure of bacterial cell membranes can be disrupted by these NPs adhering to them [52]. Because the chemical processes involved in the synthesis of nanomaterials produce a large number of hazardous by products, antibacterial agents produced using novel chemical or physical methods result in the direct absorption of several toxic chemical species onto the surface and may have poor consequences for therapeutic purpose [53,54]. Since green synthesis methods don't require the use of hazardous chemicals, they are an economical and environmentally beneficial alternative to chemical procedures. In order to employ plants as antimicrobial agents and comprehend the underlying mechanisms of their antibacterial properties, numerous investigations on plants have been conducted [55]. Because of their biocompatibility, zinc oxide nanoparticles have been approved by the Food and Drug Administration (FDA) in the United States and are mostly utilized in the food industry for packaging purposes aimed at extending the shelf life of food [56]. ZnONPs have a high surface area to volume ratio, they are utilized in a number of agromedicinal applications, including those that are antibacterial, antifungal, anti-inflammatory, anti-cancerous, and antidiabetic [57].

The effectiveness of plant extracts in the biogenic synthesis of ZnONPs has been shown for a range of compounds that they include [58]. Nyctanthes arbor-tristis flower extract boosted antifungal and antibacterial properties of ZnONPs against 5 pathogenic fungus and many bacterial species, according to a study by Jamdagni *et al*. [59]. Given this, every plant extract listed in **Tables 1** and **2** has been employed to improve the antibacterial or anticancer properties of these ZnONPs. One significant member of the Fabaceae family is Sutherlandia frutescens (Sf), often known as bush cancer tea [60-62]. It is a powerful and versatile medicinal plant native to Southern Africa. According to Kumar *et al*. [63], *Justicia wynaadensis* aqueous leaf extract was used in the biosynthesis of the hexagon-shaped wurtzite nanoparticles. ZnONPs that have been biosynthesized have been tested for their antimitotic qualities using Allium cepa. The findings show that treatment with ZnO-NPs increases chromosomal aberrations, which in turn reduces the number of dividing cells [63]. The green synthesis of ZnO NPs, and Ag/Ag2O/ZnO NCs using polar and apolar extracts of C. vulgaris offers a sustainable and versatile method for producing nanoparticles with customizable properties (**Figure 6**). The impact of the synthesis environment and the nanomaterials' characteristics on cytotoxicity was evaluated by examining reactive species production and their effects on mitochondrial bioenergetic [64].

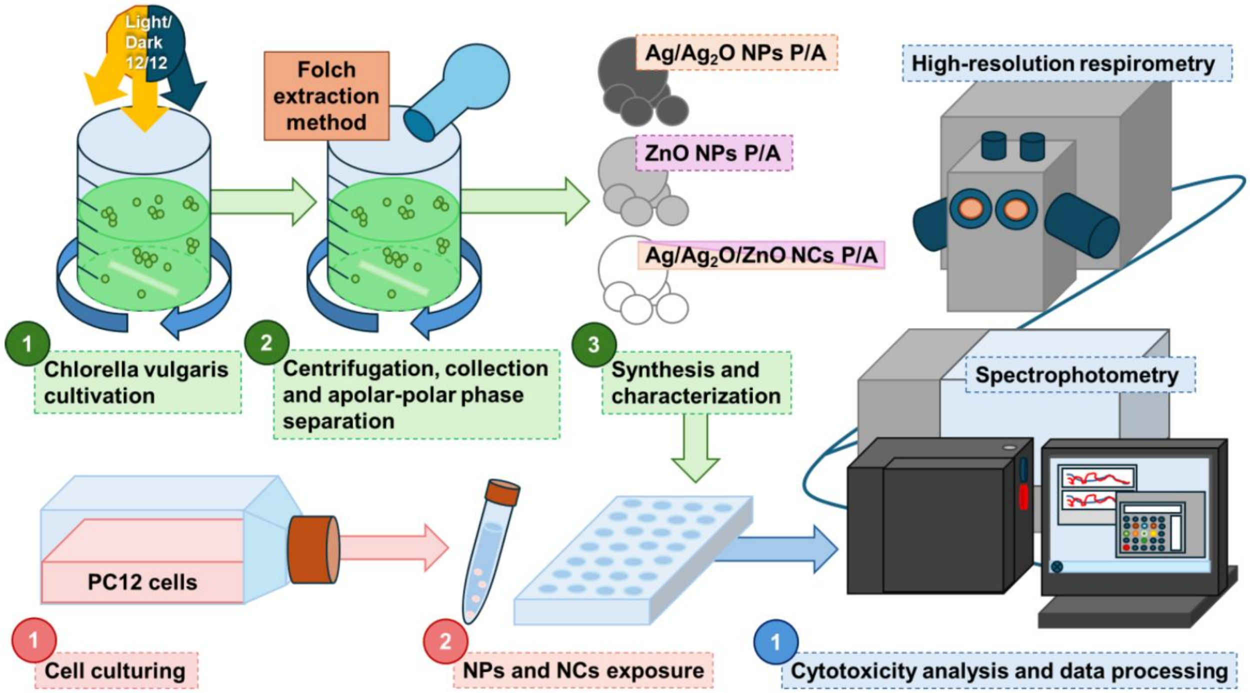

Figure 6 Scheme of the experimental activity involving green synthesis and characterization of metallic NPs using Chlorella vulgaris extracts, as well as tests on PC12 cells using spectrophotometric assays and respirometry analysis [64].

Various zinc oxide nanoparticles (ZnONPs) can be effectively synthesized using various plant extracts [65-67]. Hydroxyl groups can form complexes with zinc, which is one of the ways suggested by which these biomolecules may function in the production of nanoparticles [68]. Therefore, by choosing plant species that contain the proper kind and quantity of biomolecules, it is possible to hypothesize a green synthetic method to produce ZnONPs without having to worry about the negative effects that traditional synthetic procedures have on the environment. Anti-cancer and anti-oxidant activity of the zinc oxide nanoparticles prepared by using various plants were given in **Tables 1** and **2**.

Table 1 Antioxidant studies for ZnO Nanoparticals prepared from plant extract.

S. No	Plant extract	Assay	Concentration	References
1	*Artocarpus gomezianus*	DPPH	10.8 mg mL^{-1}	[69]
2	*Coccinia abyssinica*	DPPH	127.74 µg mL^{-1}	[70]
3	*Polygala tenuifolia*	DPPH	1 mg mL^{-1}	[71]
4	*Cassia fistula*	DPPH	2853 µg mL^{-1}	[72]
5	*oat extract*	DPPH	0.88 ± 0.03 µg mL^{-1}	[73]
6	*Myristica fragrans*	ABTS, DPPH	400 µg mL^{-1}	[74]
7	*Aegle marmelos*	ABTS, DPPH	5.75 - 6.78, 4.45 - 5.05 mg mL^{-1}	[75]
8	*Scutellaria baicalensis*	DPPH	43 µgmL^{-1}	[76]
9	*Tecoma castanifolia*	DPPH	100 µgmL^{-1}	[77]
10	*Trianthema portulacastrum*	DPPH	500 µg mL^{-1}	[78]

Table 2 Anticancer activity of ZnO Nanoparticals prepared from plant extract.

S. No	Plant extract	Cancer cell	IC_{50} value	References
1	*Elaeagnus angustifolia*	HUH-7 and HepG2	29.8 μg mL^{-1} 21.7 μg mL^{-1}	[79]
2	*Anchusa italica*	Vero cells	142 μg mL^{-1}	[80]
3	*Rosa canina*	(A549) cells	> 0.1 mg mL^{-1}	[81]
4	*Citrullus colocynthis*	3T3 cells	0.258 mg mL^{-1}	[82]
5	*Pongamia pinnata*	MCF-7	50 μg mL^{-1}	[83]
6	*Ziziphus nummularia*	HeLa	200 μg mL^{-1}	[84]
7	*Mangifera indica*	A549 cell lines	25 μg mL^{-1}	[85]
8	*Costus pictus*	DLA cells	50 μg mL^{-1}	[86]
9	*Anacardium occidentale*	Hu02	50 μg mL^{-1}	[87]
10	*Gracilaria edulis*	SiHa cells	35 μg mL^{-1}	[88]

Cobalt oxide nanoparticles

By virtue of the participation of the 3^{rd} orbital, cobalt has various oxidation states and multi-electronic valences [89]. The most stable cobalt oxides are CoO and Co_3O_4, which are both stable at normal temperature [90]. Gas sensors, drug delivery, energy storage, solid-state sensors, electrochromic devices, magnetic resonance imaging, heterogeneous catalysts, solid-state sensors, and lithium batteries are only a few of the numerous applications [91,92]. In addition to the environmentally friendly synthesis of Co_3O_4 NPs and their biological uses, a number of chemical and physical approaches for their synthesis have been reported [93,94]. In this study, Co_3O_4 NPs were synthesized using the green approach, which is a simpler, more economical, and ecologically friendly method. The Co_3O_4 NPs were prepared by using *Aspalathus linearis* leaf extract, *Punica granatum* peel, and *Calotropis procera* latex [95,96]. The textile dye effluents were observed to exhibit photodegradation when tricobalt tetraoxide (Co_3O_4) was produced using *Punica granatum (P. granatum)* seed extract [97].

Abbasi *et al*. used the *Rhamnus virgata* leaves extract for the synthesis of CoONPs and subjected this NPs for anti cancer activity studies against the various human cancer cell lines. From this study they reported that CoONPs demonstrated potent anticancer activity against human hepatoma HUH-7 (IC_{50}: 33.25 µg/mL) and hepatocellular carcinoma HepG2 (IC_{50}: 11.62 µg/mL) cancer cells in their *in vitro* cytotoxic experiments [98]. Govindasamy *et al*. reported the green synthetic technique for the synthesis of CoONPs from the *Psidium guajava* Leaves Extracts, these NP from the *P. guajava* have reduced the cell viability of MCF 7 and HCT 116. MTT assay of *P. guajava* cobalt oxide nanoparticles showed an excellent cytotoxic effect against MCF 7 and HCT 116 cells compared to normal cells [99]. Shanmuganathan *et al*. used the seed extract of *Curcuma longa* for the synthesis of CoONPs and to find their anti-cancer potential. They have reported that CL-Cobalt oxide nanoparticles demonstrated anticancer activity against MDA-MB-468 cancer cell lines, with an IC_{50} value of 150.8 µg/mL [100]. Their anti-bacterial potential in the gram-negative bacteria: Klebsiella pneumoniae, *Escherichia coli* and gram-positive bacteria: *Bacillus subtilis*, *Staphylococcus aureus*. Anupong *et al*., used the CoO prepared from the orange peel aqueous extract and studied their bacterial activity against the CoNPs showed exceptional antibacterial action against the following bacterial pathogens: *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis* and found that they have good anti-bacterial properties [101].

The synthesized CoONPs by using the plant extract acted as a good anti-fungal agent [10]. Anuradha and Raji synthesized the CoONP from the *Senna auriculata* flower extract to use them as a new anti-fungal agent

[101]. Kavica *et al*. [102] synthesized the CoONP’s with the help of *Ziziphus oenopolia* leaf Extract as the anti-fungal agent and they proved it by using it as an anti-fungal agent against the fungi like *Candida albicans*, *Candida vulgaris*, *Aspergillus niger* and *Aspergillus flavus*. Various functional groups present in *Psidium guajava* leaf extracts are used to stabilize the synthesis of cobalt oxide nanoparticles (**Figure 7**). The anti-bacterial activity of was evaluated against Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli* with a 7 to 18 mm inhibitory zone. The photocatalytic activity was evaluated using green synthesized *P. guajava* cobalt oxide nanoparticles and observed 79 % of dye degradation [45].

Khalil *et al*. [100] *Sageretia thea* (Osbeck) for the synthesis of CoO nano particles and subjected it to various biological studies includes anti-oxidant study. They reported that they have good scavenging activity against DPPH's capacity to scavenge free radicals, moderate lowering power and antioxidant capability.

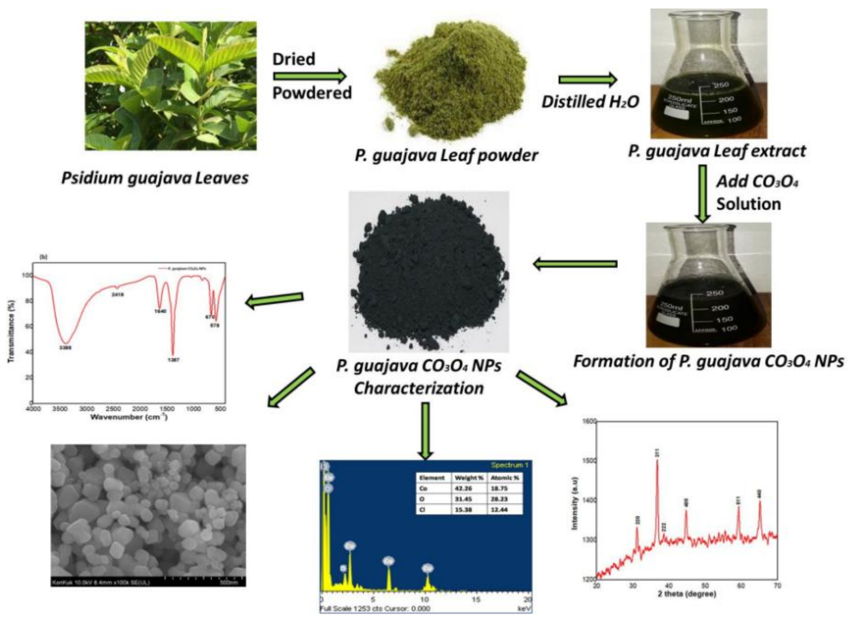

Figure 7 Synthesis route of cobalt oxide nanoparticles using *Psidium guajava* leaf extracts [45].

Nickel oxide nanoparticles

Among the various nanomaterials available today are nickel oxide nanoparticles (NiONPs) are important one due to their remarkable stability, remarkable qualities, as well as their many uses—gas sensors, electrochromic devices, solar energy absorbers, and magnetic recording devices—have garnered them a lot of attention. In addition, compared to other metal oxide nanoparticles, NiONPs are extraordinarily affordable, non-toxic, and very stable conductive materials with a broad band gap of 3.6 - 4.0 eV. NiONPs have a significant role in environmental protection because of their efficacious removal of both organic and inorganic contaminants. In the biological field nickel oxide nanoparticles were used in magnetic resonance imaging (MRI) enhancement, magnetic storage data, ferro fluids for biological sample impurity elimination, medication administration, catalysis, pigments, and sensors [106,107]. Further they are acted in supercapacitors [108], magnetic [109], electrochemical performance [110], photocatalyst studies [111], antimicrobial studies [112], and water treatment [113]. Chemical precipitation [108], solvothermal [109], thermal-decomposition [110], precipitation-calcinations [111], and microwave-assisted hydrothermal procedures [112] are some of the techniques used to create NiO nanoparticles.

Uddin *et al.* [103] synthesized the NiONP’s from the native medicinal plant Berberis balochistanica (BB) leaf extract was used to create nickel oxide nanoparticles (NiONPs). In the production of BB@NiONPs, the extract from BB leaves has multi functions in the NiO synthesis as a potent reducing, stabilizing, and capping agent. Iqbal *et al*. [104] used the extract of *Rhamnus triquetra* for the synthesis of NiO nano particles and examine their biological character of the NiONPs. Raj *et al*. [105] used the leaf extract of *Coriandrum sativum* for the synthesis of NiONP's but they used the micro wave assisted technique for this method. Lingaraju *et al*. [113] used the extract from the *Euphorbia heterophylla* (L.) as the reducing agent for the NiO synthesis. Through a green synthetic process, nickel oxide nanoparticles (NiO NPs) were created from an extract of *E. heterophylla* (L.) leaves that functioned as a capping and reducing agent.

Because of its inexpensive precursors and fast preparation time, the plant-extracted microwave method (MM) technique has garnered substantial interest in the fabrication of homogenous, nano-sized functional materials at this moment [114-116]. In addition to being an efficient photocatalyst for the removal of dyes and organic contaminants from waste water, NiO nanoparticles are well-known for their antibacterial activity against a variety of bacterial infections [117]. The green techniques for synthesizing NiONPs using *Moringa oleifera* plant extract were published by Ezhilarasi *et al*. [118] which showed potent antibacterial properties against bacterial pathogens and effective cytotoxic activities against HT-29 cancer cells. In the green synthesis of copper-doped nickel oxide nanoparticles using okra plant extract by the sol-gel process reported by the Ghazal *et al.* [119] which showed good biological activity.

Copper oxide

Due to their superior potentials and numerous uses in biology and medicine, copper oxide nanoparticles, or CuONPs, are of pronounced attention to humans [120-122]. CuONPs have been synthesized using a range of techniques, including the sol-gel method [123], hydrothermal method [124], chemical reduction method [125], precipitation method [121], and sonochemical method [122]. CuONPs simplicity and distinctive optical, electrical, and therapeutic qualities have made them extremely important [126]. When integrated into optical, sensors, electrical, plastics, coatings, textiles, and sensors, CuONPs operate as an antimicrobial, antibiotic, antifungal, and antifouling agent [127,128]. Numerous research publications on the green synthesis of CuONPs utilizing plant leaf extract, including those from *Calotropis gigantea* [133], *Albizia lebbeck* [132], *Gloriosa superba* L. [130], *Garcinia mangostana* [129], *Eclipta prostrata* [131], and *Azadirachta indica* [134], have been published.

Copper oxide nanoparticles (CuONPs) are synthesized at ambient temperature (27 °C) using leaf extracts from *Acanthospermum hispidum* and *Eupatorium odoratum*. CuONPs generated alone from *Eupatorium odoratum* extract showed a good anti-bacterial activity with *S. aureus*, *B. cereus*, and *E. coli* [135]. It has been investigated how biosynthesized CuONPs can limit the growth of gram-positive and gram-negative bacterial strains [136]. *Tecoma castanifolia* leaf extract was used to create phyto-synthesised CuONPs, which demonstrated consistent bactericidal efficacy and potential utility in biomedical applications [137]. Redox processes involving copper oxide NP can produce ROS such hydrogen peroxide (H_2O_2), superoxide anions (O_2•-), and hydroxyl radicals (•OH). Because of their high reactivity, these ROS have the ability to oxidatively damage lipids, proteins, and DNA in cells. Fenton-like reactions, in which hydrogen peroxide and copper ions combine to form hydroxyl radicals, can be catalyzed by copper. These highly reactive radicals have the potential to seriously harm biological components. Oxidative stress, which is brought on by the production of ROS, can interfere with regular cellular processes and ultimately cause cell lysis and death [138]. Copper oxide nano particles was used in the various biological applications [139], CuO-NiO nanocomposite through microwave–hydrothermal-assisted green synthesis offers several advantages [140] (**Figure 8**).

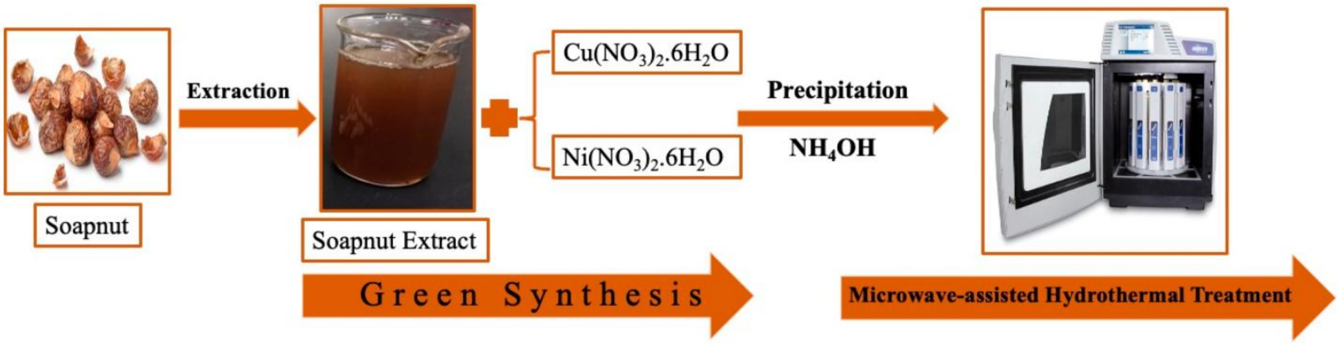

Figure 8 Synthetic method of CuO-NiO nanocomposites [140].

Titanium dioxide

Due to its exceptional surface chemistry, great chemical firmness, non-toxicity, and clean photocatalytic nature with excellent morphologies, titanium dioxide (TiO_2NPs) has proven to be a highly valuable material in a variety of fields, particularly in the biomedicine field [141-143]. TiO_2NPs are a substance that is environmentally friendly and has extraordinary biological activity, such as antibacterial [144], antioxidant [145], anti-parasitic [146], and anticancer [147] properties. TiO_2 usefulness is limited by 2 intrinsic properties: A large bandgap and quick electron-hole pair recombination [148,149]. TiO_2 is a stable, recyclable, non-toxic substance with strong catalytic qualities [150].

Goutam *et al*. used the leaf extract from *Jatropha curcas* L. for the synthesis of TiO_2NP's. Here the leaf extract used as the reducing agent which reduces the metals and forms the respective metal oxide and also acts as capping and satbilixing agent in the process [151]. Pushpamalini *et al*. used the 4 different leaves extract for the synthesis of TiO_2NP's to find which extract having the good photo catalytic applications. They used the extracts of *Piper betel*, *Ocimum tenuiflorum*, *Moringa oleifera* and *Coriandrum sativum* [152]. In the synthesis of TiO_2NP's using the solgel process, the ethanolic extracts of *Camellia sinensis*, *Syzygium aromaticum*, and *Equisetum arvense* functioned as surfactants, altering the growth mechanism and stabilizing the nanoparticles. *E. arvense* produced the greatest results, resulting in the creation of high-quality, quasi-spherical, non-aggregated TiO_2 nanoparticles with a size range of 20 - 50 nm. The creation of structurally and morphologically uniform nanoparticles was made easier by these extracts [153]. Nevertheless, NaOH is a dangerous chemical compound. Currently, *Cinnamomum tamala*, *Cicer arietinum* L., and *Carpobrotus acinaciformis* can be used as an alternative for the manufacture of TiO_2 nanoparticles [160-162]. However, another plant from Indonesia called *Averrhoa bilimbi* can also be used to synthesize TiO_2 NPs. It has been specifically noted that *Averrhoa bilimbi* fruit has some phytochemical elements [163] that may function as a weak base source. From the literature we know that the titanium nanoparticles possessed good biological activity (**Table 3**). The green synthesis of TiO_2 NPs using non-toxic food-grade TiO_2 and blueberry extract proved cost-effective and aligned with sustainable practices. These TiO_2 NPs demonstrated remarkable photocatalytic activity, achieving approximately 94 % degradation of MG dye within 30 min under direct sunlight and complete degradation within 60 min (**Figure 9**) [164].

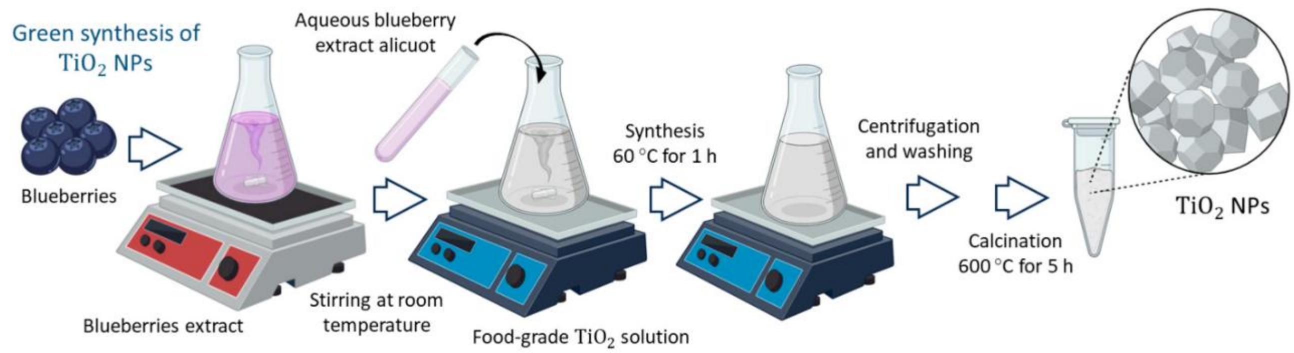

Figure 9 Schematic representation of the green synthesis protocol for TiO_2 NPs using blueberry (*Vaccinium corymbosum*) extract.

Table 3 Biological activity of TiO_2 Nanoparticles prepared from various plant extracts.

S. No	Plant extract used	Type of TiO_2 NP prepared	Biological property	References
1	*Acorus calamus*	AA@TiO_2 NP	Anti-microbial	[154]
2	*Mentha arvensis*	MA@TiO_2 NP	Anti-microbial	[155]
3	*Trigonella foenum-graecum*	TFG@TiO_2 NP	Anti-microbial	[156]
4	*Luffa acutangula*	LA@TiO_2 NP	Anti-microbial	[157]
5	*Cynodon Dactylon*	CD@TiO_2 NP	Anti-cancer	[158]
6	*Coleus aromaticus*	CA@TiO_2 NP	Anti-cancer	[159]
7	*Ledebouria revoluta*	LR@TiO_2 NP	Anti-cancer	[163]
8	*Tulbhagia violacea*	TV@TiO_2 NP	Anti-cancer	[165]
9	*Psidium guajava*	PG@TiO_2 NP	Anti-oxidant	[166]
10	*Laurus nobilis*	LN@TiO_2 NP	Anti-oxidant	[167]
11	*Malva parviflora*	MP@TiO_2 NP	Anti-oxidant	[168]
12	*Wrightia tinctoria*	WT@TiO_2 NP	Anti-oxidant	[169]
13	*Azadirachta indica*	AI@TiO_2 NP	Anti-bacterial	[170]
14	*Lippia adoensis*	LA@TiO_2 NP	Anti-bacterial	[171]
15	*Tinospora cordifolia*	TC@TiO_2 NP	Anti-bacterial	[172]
16	*Morus alba*	MA@TiO_2 NP	Anti-bacterial	[173]
17	*Caricaceae papaya*	CP@TiO_2 NP	Anti-fungal	[174]
18	*Trianthema portulacastrum, Chenopodium quinoa*	TP@TiO_2 NP/CQ@TiO_2 NP	Anti-fungal	[175]
19	*C. pulcherrima.*	CP@TiO_2 NP/	Anti-fungal	[176]
20	*juniperus phoenicea* (L.)	JP@TiO_2 NP	Anti-fungal	[177]

Magnesium oxide

MgONPs have drawn more attention because of their outstanding applicability, particularly in the biomedical field, remarkable nontoxicity, and great stability under hard conditions. In addition, MgONPs have a number of advantageous physicochemical properties, including a broad surface area, strong ionic character, oxygen vacancies, and an uncommon crystal shape that facilitates easy interaction with a variety of biological systems. Moreover, it has been applied in biomedicine to cure stomach discomfort, regenerate bone, relieve heartburn, and in several other therapeutic applications, including medications, coated capsules, bio labeling, blood collection vessels, and many more [178].

They have enhanced biocompatibility, biodegradability, high stability, cationic capacity, and redox capabilities in addition to MgONPs characteristics. As a result, they have developed into a compelling substance to fight bacteria and get around problems with removing microbial biofilms and antibiotic resistance [179,180]. The production of reactive oxygen species (ROS), direct interaction with the bacterial cell wall, and the start of intracellular abnormalities like macromolecular interactions (between proteins and DNA) are some of the ways by which it exhibits its antibacterial efficiency [181]. Regarding their synthesis, there are numerous physical and chemical methods for obtaining MgONPs. But in recent years, the greener synthesis has gained favor over the other techniques because the NPs it produces are more stable, safe for the environment, affordable, and non-toxic. **Figure 10** provides an explanation of the primary biosources and synthesis methods [182].

Regarding this, Kumar *et al*. [181] showed how to create MgONPs by using an extract from *Camellia sinensis* (tea leaves) as a reducing agent. In this instance, the polyphenols required to support the reduction of the metal salt precursor are provided by the tea leaf extract. The produced nanoparticles (NPs) had an average particle size of 65 ± 5 nm and a spherical shape. Extracts from 4 different widely used plants, including *Aloe vera*, *Echeveria elegans*, *Sansevieria trifasciata*, and *Sedum morganianum*, were evaluated for their ability to facilitate the “green synthesis” of MgO nanoparticles [182]. Various biological activities of the plant mediated synthesized Magnesium oxide nanoparticles have discussed in **Table 4** and the obtained data confirmed its biological activity.

Figure 10 Readily available plants used for the synthesis of MgONPs by the “green chemistry” method [182].

Table 4 Biological activity of MgO Nanoparticles prepared from various plant extracts.

S. No	Plant extract used	Type of MgO NP prepared	Biological property	References
1	*Ocimum americanum*	OA@MgO NP	Anti-microbial	[183]
2	*Citrus aurantium*	CA@MgO NP	Anti-microbial	[184]
3	*Carica papaya*	AP@MgO NP	Anti-microbial	[185]
4	*Pisonia grandis R. Br.*	PG@MgO NP	Anti-microbial	[186]
5	*Costus pictus D. Don*	CP@MgO NP	Anti-cancer	[187]
6	*Caccinia macranthera*	CM@MgO NP	Anti-cancer	[188]
7	*Oryza sativa L. indica*	OS@MgO NP	Anti-cancer	[189]
8	*Andrographis paniculata*	AP@MgO NP	Anti-cancer	[190]
9	*Artemisia abrotanum Herba*	AB@MgO NP	Anti-oxidant	[191]

S. No	Plant extract used	Type of MgO NP prepared	Biological property	References
10	*Piper nigrum*	PN@MgO NP	Anti-oxidant	[192]
11	*Piper betle*	PB@MgO NP	Anti-oxidant	[193]
12	*Magnolia champaca*	MC@MgO NP	Anti-oxidant	[194]
13	*Pisidium guvajava (P. guvajava)/ Aloe vera (A. vera)*	PG@MgO NP/AV@MgO NP	Anti-bacterial	[195]
14	*Moringa oleifera*	MO@MgO NP	Anti-bacterial	[196]
15	*Mangifera indica, Azadirachta indica and Carica papaya*	MI@MgO NP/AI@MgO NP/ CP@MgO NP	Anti-bacterial	[197]
16	*Lawsonia inermis*	LI@MgO NP	Anti-bacterial	[198]
17	*Pisonia alba*	PA@MgO NP	Anti-fungal	[199]

Conclusions

Form this chapter we can conclude that in what ways phytochemical mediated synthesized metal oxide nanoparticles semiconductors prove them as the efficient biological candidates. Researchers have been paying a lot of attention to nanotechnology lately, particularly in the field of materials science. Moreover, it was determined that there are numerous ways to synthesize NPs chemically and physically, they are also expensive, require high temperatures and pressures, and have an adverse effect on the environment. Among the various synthesis method, green synthesis method is renowned for producing nanoparticles in a fast, easy, safe, affordable, and environmentally friendly manner. The employment of non-toxic solvents and effective production techniques is a significant benefit of green synthesis. Furthermore, the green produced metal or metal oxide nanoparticles have been successfully used in a variety of biomedical applications, including drug delivery, tissue engineering, cancer therapy, and even bioimaging. Utilizing plants or plant extracts has a synergistic impact that is advantageous since it can reduce the amount of toxicity of the compounds.

Research on the factors is still necessary because the plant extracts have the potential to affect the produced materials polydispersity. Furthermore, the majority of these green synthesis methodologies are still in the research phase, necessitating the resolution of their remaining problems such as controlling crystal formation, shape, and size, as well as the stability and aggregation of nanoparticles. When it comes to metal nanoparticles, those made by plants and/or plant extracts are more stable than those made by other creatures.

While many investigations found that metal NPs were less dangerous when the right dosage, size, and distribution are used. However, the challenges like scalability, stability and environmental impact falls in the place, by addressing them and solving these metal oxide nano particles can be the best candidate for the biological applications. Thus, future research still needs to pay close attention to the ecologically sustainable synthesis of nanoparticles and their biological uses.

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