A review on plant extract mediated green synthesis of zinc oxide and silver nanoparticles and their biomedical applications

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Abstract

In this review, we investigate zinc oxide nanoparticles (ZnO NPs) produced from plant extracts and their subsequent biomedical applications in depth. According to research, a variety of plant extracts are used to produce ZnO nanoparticles. These extracts contain leaves, fruits, seeds, roots, even whole plants. These biological matrices include phytochemicals such as phenolic compounds, alkaloids, flavonoids, and terpenoids. Compounds exhibit bio-reduction mechanisms and function as stabilizing and reducing agents.

Green synthesis of metal nanoparticles and metal oxide nanoparticles from plant extracts is gaining popularity in environmentally friendly development due to its simplicity, low cost, and environmental sustainability benefits over traditional chemical and physical methods. This review article presents data from 85 articles synthesizing Zn O NPs and Ag NPs from various plant parts (e.g. leaves, fruits, flowers, stems, bark, rhizomes, roots, and seeds), with a focus on their biomedical applications. The article also includes 40 data points on antibacterial properties and mechanisms of action.

Our study found that employing plant extracts to produce Zn O and Ag-NPs resulted in outstanding antibacterial and anticancer capabilities due to their biocompability.

Keywords

Nanoparticles, Silver nanoparticles, antibacterial, plant extract, biomedical applications, ZNO NPs

Introduction

In nanotechnology, the goal is to create novel materials on a nanometre scale. Nanomaterials are comprised of small particles with large specific surface area, which results in materials with unexpected surface area, volume, quantum size, and macro tunneling effects when compared to materials with undefined particle sizes [1]. These properties of nanomaterials result in nanomaterials having a broad potential for application due to their unique optical, mechanical, catalytic, and biological properties. Because of their high specific surface area.

Nanoparticles: Types

Silver: Silver nanoparticles have proved to be most effective because of it’s good antimicrobial efficacy against bacteria, viruses and other eukaryotic micro-organisms16,17.

Gold: Gold nanoparticles (AuNPs) are used in immunochemical studies for identification of protein interactions. They are used as lab tracer in DNA fingerprinting to detect presence of DNA in a sample. They are also used for detection of aminoglycoside antibiotics like streptomycin, gentamycin and neomycin.

Alloy: Alloy nanoparticles exhibit structural properties that are different from their bulk samples25. Since Ag has the highest electrical conductivity among metal fillers and, unlike many other metals, their oxides have relatively better conductivity 26, Ag flakes are most widely used.

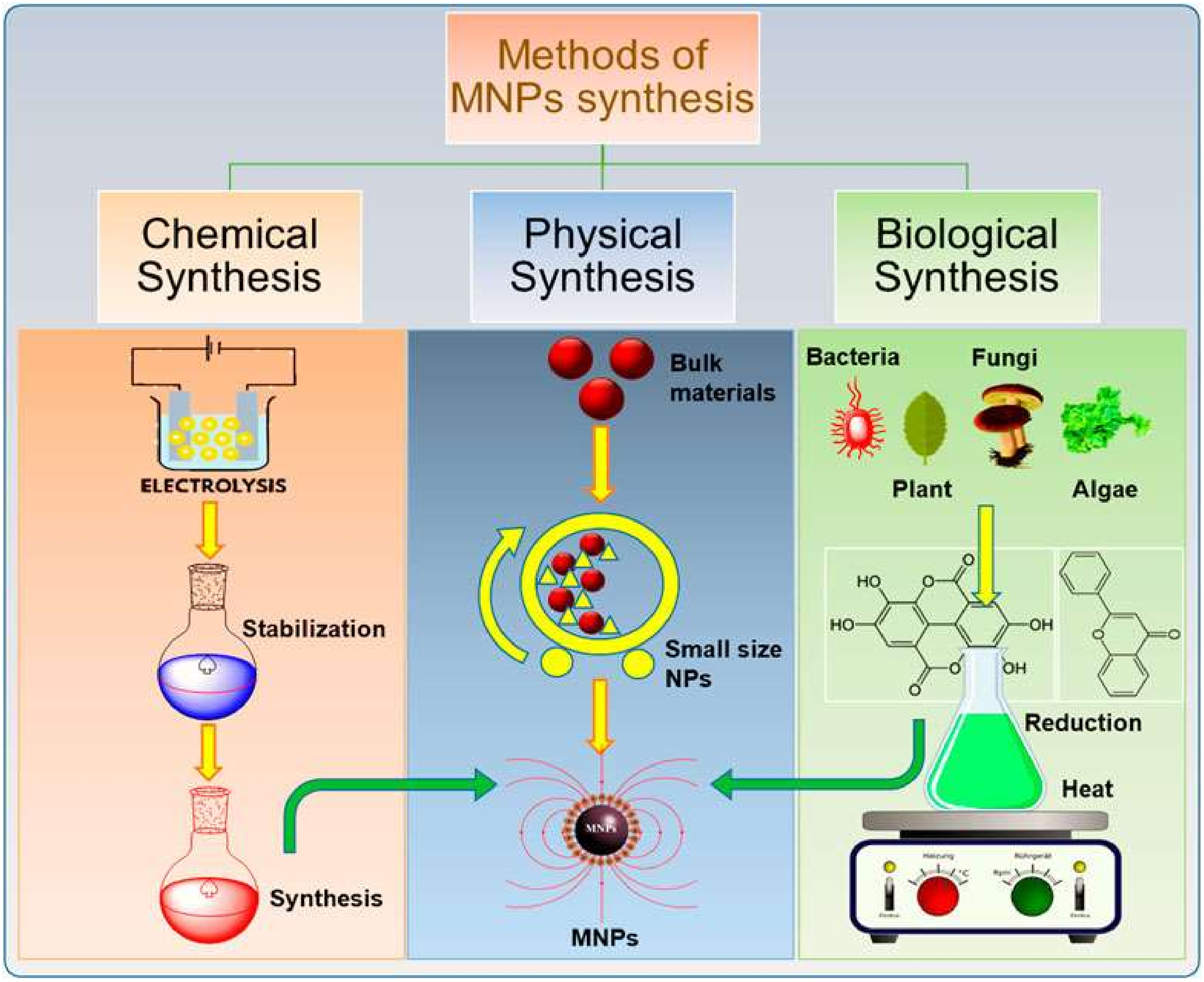
Magnetic: Magnetic nanoparticles like Fe3O4 (magnetite) and Fe2O3 (maghemite) are known to be biocompatible. They have been actively investigated for targeted cancer treatment (magnetic hyperthermia), stem cell sorting and manipulation, guided drug delivery, gene therapy, DNA analysis, and biocompatibility, ultraviolet light absorption, scattering, and antibacterial properties.

Due to the number of Ag-NPs and Zn O NPs applications, the use of environmental-friendly methods for their synthesis becomes increasingly important, particularly since the concept of environmental protection has become embedded in the expectations of the public [3,4]. The term green synthesis refers to fabrication techniques that use microorganisms, enzymes, and natural extracts. Toxic materials should not be utilized in this process, which also uses very little energy. Eco-friendly, environmentally sustainable, and low-cost make it an appealing alternative to traditional physical and chemical methods [5 cu] Plants and extracts are readily available, and the procedure requires only a zinc salt solution and silver nitrate (AgNO3) as a metal precursor.

Synthesizing Zn O NPs was achieved by reacting plant extracts with zinc salt solution, representing a green method to synthesize Zn O NPs. The leaves, peels, roots, flowers, fruits, and seeds of plants have been shown to act as reduction as well as stabilization agents when synthesizing Ag-NPs and Zn O NPs, according to several studies. In contrast to chemically synthesized Ag-NPs and Zn O NPs, the green synthesis of those nanoparticles shows more effective antibacterial activity [8,9]. Nano biotechnology application combines silver and zinc oxide nanoparticles made by biosynthesis for the antimicrobial application, offering insight toward better health, a cleaner environment, and the prevention of infectious diseases [10,11]. Metal /Metal oxide nanoparticles derived from plants have increasingly been recognized as therapeutic agents against various cancers. In addition to killing cancer cells, anti-cancer agents can also kill healthy cells when used as a treatment [12]. Ideally, a perfect medicine would be selective, specific to the target site, strong (100 mg/day), safe, and effective with minimal food/drug interactions, with an easily adjustable dose frequency, and without blood level monitoring. Scientists are attempting to develop an anti-cancer agent that is stable, specific to the target region, biocompatible, inexpensive, and simple to replicate [13]. Hence, this review focus on the medical applications of two nanoparticles which are silver nanoparticles and zinc oxide nanoparticles in antibacterial and anticancer potency of the plant-mediated synthesis of these nanoparticles based on the results of recently published studies (2014 to 2022). The application of MNPs and MONPs leads to better efficacy and minimal toxicity of novel antimicrobial and anticancer drugs.

Synthesis Of ZNO NPs and Ag NPs

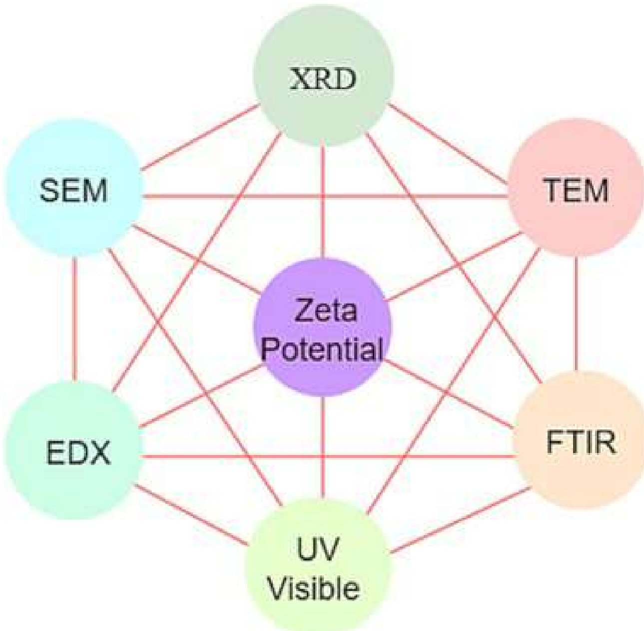
For the synthesis of Zn O-NPs, various techniques, including chemical, physical, and biological methods, are used. Chemical methods include precipitation, coprecipitation, colloidal, sol-gel processing, water-oil microemulsion, hydrothermal synthesis, cellulo thermal, and sono chemical and polyol methods [40]. Physical methods include a range of techniques, such as arc plasma, thermal evaporation, physical vapor deposition, ultrasonic irradiation, and laser ablation.The green technique is a biological approach that utilizes plant extracts to synthesize zinc oxide nanoparticles (Zn O NPs). The present methodology has several benefits compared to conventional approaches, including simplicity, environmental sustainability, cost efficiency, and replicability. Recent research has investigated the environmentally friendly production of zinc oxide nanoparticles (Zn O NPs) using several plant extracts. These extracts include royal jelly, Cassia fistula, Melia azadarach, and Limonium bruinosum L. chaz. The dimensions and morphology of the generated zinc oxide nanoparticles (Zn O NPs) exhibit variability contingent the specific plant extract used (Fig.

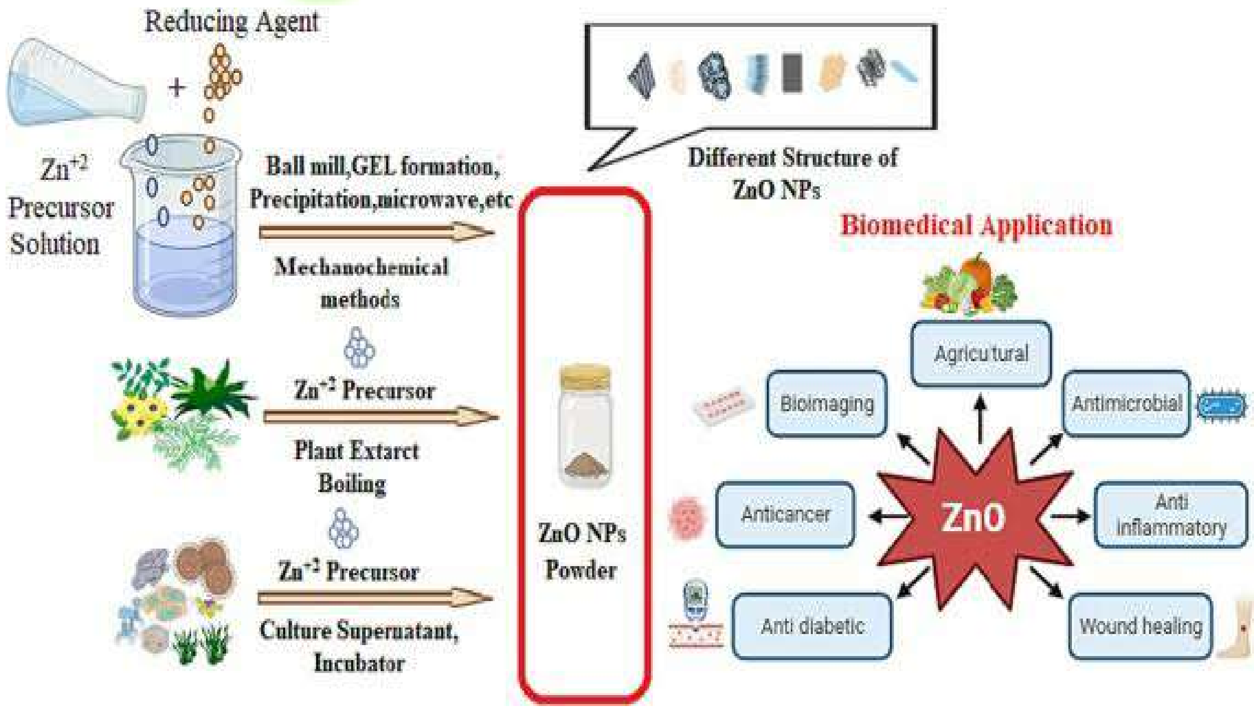


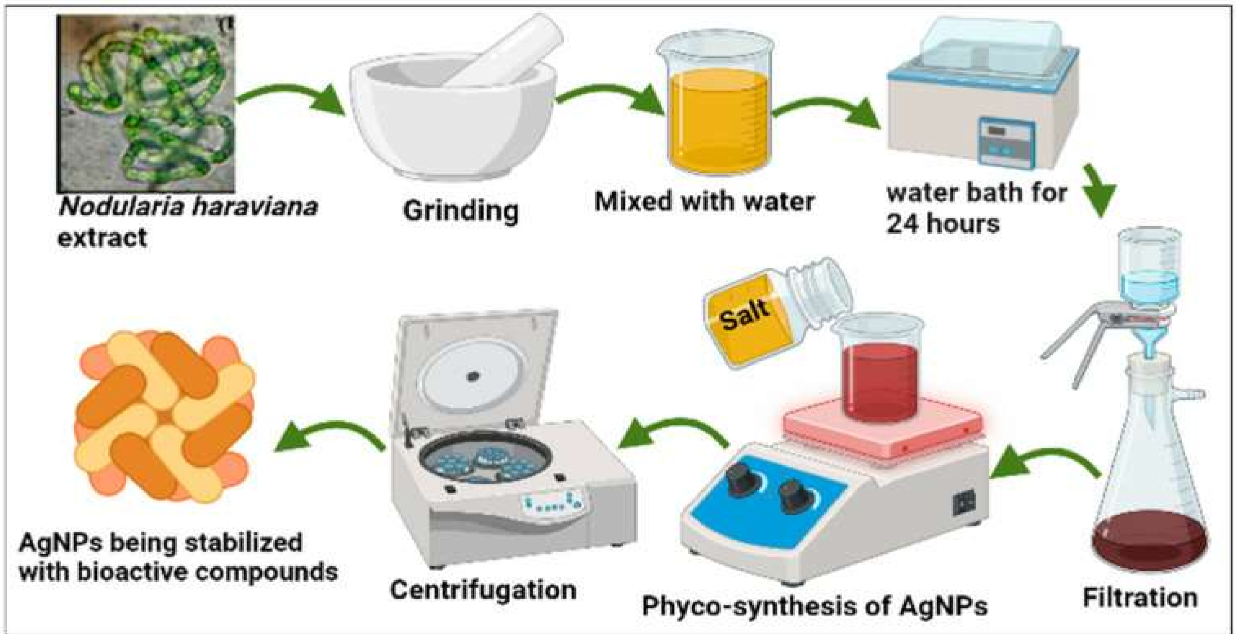
1)

Green synthesis of zinc oxide nanoparticles.

Zinc oxide nanoparticles (ZnO NPs) have garnered considerable attention as viable contenders for a range of biomedical applications owing to their favorable attributes, such as biocompatibility, minimal toxicity, and cost-effectiveness [54–56]. These compounds have robust biological properties and have been used in several sectors for their antibacterial, anticancer, antioxidant, antiinflammatory, and wound-healing properties [57]. Synthesizing zinc oxide nanoparticles (ZnO NPs) by environmentally friendly methods includes utilizing many plant components, including leaves, stems, bark, roots, rhizomes, fruits, flowers, and seeds. The plant extracts mentioned in the statement consist of several phytochemicals such as lupeol, ursolic acid, oleanolic acid, sitosterol, rutin, leucocyanidin, anthocyanins, proanthocyanidins, and glycosides of kaempferol and quercetin. These phytochemicals have reducing properties [58]. Plant-based synthesis techniques have several benefits compared to traditional physicochemical approaches. This method effectively mitigates the utilization of dangerous substances that provide potential health hazards to both the ecosystem and individuals [59]. Green synthesis produces metal and metal oxide NPs, and these phytochemicals are considered vital in their production [60]. The effects of temperatures between 20 and 100 ◦C on the formation and size of ZnO NPs were also studied by Singh et al. [61]. There was an increase in ZnO NPs production at higher temperatures, but the particles grew more slowly and were smaller due to the short reaction response time during synthesis. Several scientific investigations have shown biological substrates to be the only possible raw materials for NP biosynthesis [62]. The chemical process during green synthesis is complicated, making it difficult to measure and quantify. Bacteria that can be reproduced (such as lactic acid-generating bacteria) have become increasingly intriguing in bacterial-mediated NP synthesis because of their ability to produce a wide range of enzymes and non-pathogenic characteristics. Lactic acid bacteria, which are Gram-positive, possess a robust cell wall layer consisting of proteins, polysaccharides, lipoteichoic acid, and teichoic acid.


XRD
SEM
TEM
Zeta Potential
EDX
FTIR
UV Visible


Reducing Agent
Zn+2 Precursor Solution
Ball mill,GEL formation, Precipitation,microwave,etc
Mechanochemical methods
Different Structure of ZnO NPs
Biomedical Application
Zn+2 Precursor
Plant Extarct Boiling
Zn+2 Precursor
Culture Supernatant, Incubator
ZnO NPs Powder
Agricultural
Bioimaging
Antimicrobial
Anticancer
ZnO
Anti inflammatory
Anti diabetic
Wound healing



Formulation and characterization of metallic zinc oxide nanoparticles

Energy dispersive x ray [EDX]

The X-rays given out by the NPs while being

bombarded by an energetic electron beam are measured. Each element's

atomic structure produces distinctive peaks in the X-ray spectrum since

the rays are created according to the elements' properties. The ratio of

the quantity of X-rays

Zeta potential

Zeta potential is a method used to assess the surface charge of NPs in colloidal solution. The Zeta potential quantifies the electric potential at the border of the double layer of counter ions that form around NPs due to their surface charge. Particle size, concentration, temperature, solvent, and ionic strength also have a role in determining the Zeta potential. Zeta potentials in the 25–40 mV range are typically considered stable, whereas those more significant than 60 mV are highly stable to NPs in solution energy is the unit of measurement.

SEM

The scanning electron microscope (SEM) is a method of high

resolution surface imaging used to learn about the nano- and microscale structures of objects using an electron beam [124]. Because of their higher magnification and greater field of view, SEM images may be used to evaluate the topology of the surface of Zn O NPs [125]. This method relies on eye inspection for morphological identification [126]. The detector produces and records signals when Zn O NPs are subjected to electron beams. The signal may infer the Zn O NPs' shape, orientation, and crystalline structure [127]. SEM's application in characterizing biosynthesized Zn O NPs for size and shape are provided.

X-ray diffraction

The purity of a Zn O sample and its hexagonal wurtzite structure may be established with the use of X-ray diffraction. X-ray diffraction (XRD) has promising applications in the investigation of nanostructures because the breadth and shape of reflections provide insight into the materials' underlying structure (e.g., crystallite sizes.

Fourier Transform Infrared spectrometer (FTIR)

FTIR is an abbreviation for "Fourier Transform Infrared." Absorption of electromagnetic radiation between 400 and 4000 cm− 1 allows for the collection of FTIR spectra. The FTIR spectrometer gathers data across a large spectrum. The ability of Zn O nanoparticles to absorb electromagnetic waves of varying frequencies and intensities facilitates the characterization of individual functional groups and chemical structures. shape [128].

Transmission electron microscope (TEM)

Transmission electron microscopy (TEM) is often used to characterize the physical characteristics of NPs. That is what Fohen cong and company say. According to the paper, TEM provided a clear picture of the particles' sizes and shapes at a very high resolution. To characterize NPs, TEM is a valuable technique. The synthesized zinc oxide was found to have an average size of 7.4 1.2 nm

BIOMEDICAL APPLICATIONS

Antimicrobial properties

Compared to other metal oxides with antibacterial capabilities, Zn O nanostructures have been more harmful to bacteria and less reactive towards human cells in recent decades [141–143]. This is because Zn O nanostructures have an excellent antibacterial mechanism based on the production of reactive oxygen species (ROS) that kills bacterial cells [144–148]. Reactive oxygen species (ROS) have gained considerable interest as a possible strategy for warding off human infectious illnesses [149]. The use of reactive oxygen species (ROS) technology, employs agents that are easily reproducible, environmentally benign, highly portable, cost-efficient, and capable of inducing the biological synthesis of Zn O nanostructure

Anti-inflammatory properties

Inflammatory responses are upregulated by pro-inflammatory cytokines such as IL-1, IL-1β, and TNF-α, ultimately resulting in inflammation. It is well-recognized that they can stimulate the differentiation and proliferation of mast cells. The activation of nuclear factor kappa B (NF-KB) initiates the transcription of certain genes that promote cellular proliferation, thereby amplifying the inflammatory response [161]. The caspase-1 enzyme functions as an IL-1β converting enzyme, facilitating the conversion of inert cytokines such as pro-IL-1β and pro-IL-18 into their active counterparts [162]. Mast cells are recognized for their significant involvement in immunoregulatory processes associated with immunological diseases since they release diverse inflammatory mediators, including histamines, chemokines, leukotrienes, and cytokines. Additionally, they elicit allergic inflammatory reactions by stimulating the production of Ig E antibodies by B-lymphocytes [163]. The zinc oxide nanoparticle (Zn O NP) has inhibitory effects on the activated caspase-1 enzyme in mast cells and the nuclear factor kappa B (NF-KB) signaling pathway

Antioxidant properties

Zn O-NPs have promising medical applications for treating a wide range of diseases brought on by oxidative stress. When too many free radicals exist in the body, antioxidant molecules may neutralize them. The capacity of zinc oxide nanoparticles (Zn O NPs)to increase the body's antioxidant system has been proven in conditions where the body creates excess free radicals. Because of their ability to damage biomolecules within the cell and cause oxidative stress [175], avoiding exposure to free radicals is recommended.

Anticancer properties

Cancer is a complex group of illnesses defined by the uncontrolled proliferation of aberrant cells, which may give rise to the formation of tumors capable of infiltrating adjacent organs and inducing significant detrimental consequences in affected individuals, possibly resulting in mortality [197]. According to [198], cancer was identified as the second most prevalent cause of mortality in the United States in 2019, with an estimated annual diagnosis rate of around 2 million individuals. The provision of pharmaceutical substances without charge [203,204]. The generation of a substantial quantity of reactive oxygen species (ROS) in cancerous cells in comparison to healthy cells leads to an increased ROS concentration, subsequently resulting in impaired mitochondrial function and triggering the intrinsic mitochondrial apoptotic pathway (Fig. 8) [205]. Nanoparticles (NPs) possess the capability of functionalization, which allows them to target malignant cells selectively. Cells may be targeted by attaching various molecules, such as aptamers, proteins, or antibodies, allowing particular binding to nanoparticles (NPs). The increased cellular penetration and DNA binding of the complex might perhaps be ascribed to the robust Zn O bond.

Antifungal activity

The antifungal mechanism was elucidated based on the capacity of Zn O nanoparticles (NPs) to penetrate the fungal membrane by diffusion and endocytosis. Within the cytoplasm, the presence of Zn O nanoparticles (NPs) disrupts the normal functioning of mitochondria, hence triggering the generation of reactive oxygen species (ROS) and the subsequent liberation of Zn2+ ions. The excessive generation of reactive oxygen species (ROS) and the accumulation of zinc ions (Zn2+) led to permanent DNA harm and the demise of cells [218,219]. The enhanced antifungal efficacy seen when combining biogenic Zn O NPs with antifungal medicines, such as nystatin, fluconazole, terbinafine, and itraconazole, may be related to their synergistic mode of action. This can be explained by the fact that these antifungal agents and Zn O NPs have distinct cellular targets, leading to an augmentation in antifungal effectiveness [220]. The objective of combination treatment is to mitigate toxicity by decreasing the regular dosages of pharmaceuticals and enhancing the antifungal efficacy of traditional antifungal activities.

Challenges and prosperity

Despite a wide range of manufactured Zn O nanostructures with different shapes, sizes, and architectures, a precise understanding of the mechanics behind their production throughout the stated techniques is still needed. While some progress has been made in studying the impact of synthesis conditions on structure and morphology, much work still needs to be done to fully comprehend the effects of synthesis parameters on structure, particle size, and morphology. Insufficient surface passivation, charge recombination at the interface, and lack of long-term stability have resulted in a low electron injection efficiency, leading to low current density and efficiency in the solar device based on Zn O. Possible solutions include using organic and inorganic substances to improve surface passivation and enhance electronic interaction via surface modification. The need for additional investigation lies in the inadequate management of the characteristics of individual building blocks and the need for more consistency in device-to-device replication.

Conclusion

Scientists are now focusing on improving the environmentally friendly production of Zn O nanoparticles and Ag O for various medicinal uses. The Zn O nanoparticles synthesized using green methods have been highly valued because they are environmentally benign, biocompatible, and more cost-effective than those produced using chemical and physical techniques. The diverse range of plant extracts, including phytochemicals like flavonoids, terpenoids, polyphenols, tannins, and alkaloids, is a promising resource for the environmentally friendly production of Zn O nanoparticles.

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