



Exploring Plant-Mediated ZnO/TiO₂ Nanocomposites from *Prinsepia utilis* for Enhanced Biological Activities: A Review

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Abstract

Nanotechnology is a new sphere of research with exciting applications in a multiplicity of fields, including science, engineering, medicine, and pharmacy. Green synthesis is to innovate green and eco-friendly, less toxic routes, such as eco-friendly metal oxide nanocomposites. The medicinal and industrial plant *Prinsepia utilis* proved successful in working to make ZnO/TiO₂ nanocomposites by serving as a natural reducing and stabilizing agent. Herein, we present a comprehensive overview of the preparation, physical, and chemical properties, and enhanced biological performances of original nanocomposites produced from *Prinsepia utilis* extracts. It also contrasts various synthesis and characterization methods and how the selection between them affects the structure, shape, and performance of the nanocomposites. Also, the applications of these nanocomposites to bacterial warfare, anti-oxidation, and medical applications are discussed. The review further highlights the challenges we face, the need for toxicity consideration, and the way forward for the progress of plant-based ZnO/TiO₂ nanocomposites in the field of green nanotechnology.

Keywords: Green Synthesis, Eco-friendly, ZnO nanocomposites, TiO₂ nanocomposites, *Prinsepia utilis*

Introduction

Nanotechnology represents a new research era across various fields, focusing on nanomaterials sized 1 to 100 nm and their applications [1]. Over the past decade, nanoparticles have been tailored for use in cosmetics, textiles, and electronics, and have found medical applications, particularly in drug development and molecular imaging. They play a role in cardiovascular and oncology medicine, enhancing diagnostics with biomarkers and contrast agents [2]. The global marketing of nanotherapeutics began after the FDA's first approval in 1990, amidst the challenges of developing desired therapeutic properties, while promising studies support the advancement of nano-based pulmonary treatments [3].

Green synthesis, rooted in green chemistry, uses plants, bacteria, fungi, and algae to create nanoparticles in a safer, eco-friendly, and cost-effective way. Unlike chemical methods, it avoids toxic substances and reduces

pollution. Nanoparticles like ZnO, TiO₂, and Ag produced through green methods show strong antimicrobial, anticancer, and photocatalytic properties. Ideal green synthesis uses non-toxic solvents and natural reducing agents, making it a safer alternative for biomedical and environmental applications [4]. Nanocomposites combine multiple materials to enhance stability, reactivity, and functionality compared to individual nanoparticles like ZnO or TiO₂. They solve problems like accumulation and limited scope, making them more effective and affordable.

Zinc oxide (ZnO) and titanium dioxide (TiO₂) are recognized for their strong photocatalytic, antimicrobial, and antioxidant properties. ZnO nanoparticles are commonly used in medicine, environmental cleanup, and electronics because of their anticancer and antimicrobial effects [5]. TiO₂ is valued for its ability to break down pollutants, fight bacteria, and support drug delivery and tissue repair [6]. Its unique surface features make it valuable in textiles, cosmetics, and food products [7]. Synthesis methods that utilize plants provide a safer, eco-friendly approach to producing TiO₂ nanoparticles [8].

Prinsepia utilis is a medicinal shrub native to the Himalayan range, traditionally recognized for its healing properties in Chinese and Indian medicine, for its effectiveness in treating skin conditions, rheumatic pain, and inflammation [9]. Belonging to the Rosaceae family, this plant typically thrives at altitudes from 1,000 to 3,000 meters and is known for its high content of phenolics, flavonoids, and antioxidants. These bioactive compounds support medicinal use and enable the reduction of metal ions and stabilization of nanoparticles, making *P. utilis* suitable for green synthesis of ZnO/TiO₂ nanocomposites. It is eco-friendly and aligns with green chemistry principles, offering a sustainable alternative to traditional waste-producing methods. This review explores the plant-mediated synthesis of ZnO and TiO₂ nanoparticles, with a emphasis on their ecological and biomedical benefits. It discusses the role of phytochemicals in enhancing nanoparticle properties and underscores the importance of advancing sustainable practices in nanotechnology.

Medicinal uses of *P. utilis*

Medicinal plants play an important role in traditional healthcare systems, mostly in the Himalayan region, where people still use them as primary treatment [10] *Prinsepia utilis*, commonly known as bhekal, has therapeutic, cultural, and economic significance. Its numerous parts are widely used in Chinese and Indian folk medicine to treat various ailments, including rheumatism, skin diseases, and fractures. Phytochemical studies have revealed the presence of hydroxynitrile glucosides, triterpenoids, and diterpene glucosides in this plant [11,12]. Its fruits are particularly rich in 20 phenolic compounds with strong antioxidant properties that inhibit digestive enzymes and lower cellular ROS levels [13]

Leaves of *P. utilis* have demonstrated bone-protective properties by enhancing bone formation and density while reducing bone resorption [14]. Twelve pentacyclic triterpenoids extracted from its aerial parts showed strong cytotoxic effects against various human cancer cell lines (**Guan et al., 2013**). In Himalayan villages, traditional healers continue to use *P. utilis* in multiple forms- oil, powder, paste, or decoctions from seeds, roots, bark, and leaves. The information regarding the medicinal properties, methods of preparation, and specific uses for particular diseases is outlined below:

Rheumatic joint pain: Warmed seed oil is applied to joints to ease pain and stiffness, particularly among older individuals. It is also used with milk and flour to relieve pregnancy-related abdominal pain.

Skin diseases: The oil treats acne, eczema, and fungal infections; a seed and turmeric paste is applied for persistent skin issues.

Stomach ailments: Lukewarm oil acts as a laxative; decoctions of seed or root bark treat stomach aches, constipation, and dysentery.

Headache, cough, and cold: A spoonful of oil is used for headaches, coughs, and colds, and is believed to enhance memory in children.

Burn, cut, and wound: Seed powder, root, bark, and leaf pastes are applied to cuts, boils, blisters, and sores for their antibacterial and healing properties.

Role of phytochemicals for nanoparticle biosynthesis

Phytochemicals are key to green nanotechnology, acting as natural reducing, capping, and stabilizing agents in the eco-friendly synthesis of nanoparticles. Compounds like flavonoids, phenolic acids, tannins, terpenoids, alkaloids, and saponins, with functional groups such as hydroxyl and carbonyl, facilitate the reduction of metal ions (e.g., Zn^{2+} , Ag^+ , Ti^{4+}) into metal or metal oxide nanoparticles [15,16]. These phytochemicals also stabilize nanoparticles by binding to their surfaces, preventing agglomeration and improving stability and bioactivity. Their influence on nanoparticle size, shape, and crystallinity enhances biological performance. Plant-derived flavonoids and polyphenols facilitate the formation of stable and uniform nanoparticles with antimicrobial, antioxidant, and anticancer properties [17]. In *Prinsepia utilis*, flavonoids, phenols, and saponins support the green synthesis of ZnO and TiO_2 nanoparticles, offering a sustainable method for biomedical use [18]. These nanoparticles are valued for their antimicrobial, antioxidant, anticancer, and anti-inflammatory properties. TiO_2 and ZnO nanoparticles damage bacterial membranes, generate ROS, and disrupt DNA replication, leading to effective pathogen elimination [19]. In cancer therapy, they promote cancer cell apoptosis and enhance the action of chemotherapy drugs while minimizing side effects on normal cells [20].

Biogenic nanoparticles also demonstrate strong antioxidant capacity, helping to neutralize free radicals and protect against oxidative stress-related diseases like cancer, cardiovascular disorders, and neurodegenerative disorders. ZnO-NPs derived from medicinal plants are especially effective due to phytochemical capping agents like phenolics and flavonoids [16]. These nanoparticles show promise as drug delivery systems and open pathways for safer applications in medicine, agriculture, and environmental remediation.

Biological Activity Evaluations

Prinsepia utilis contains a variety of bioactive phytochemicals, such as phenolics, flavonoids, alkaloids, terpenoids, and saponins, that contribute to its medicinal value and support green synthesis of nanoparticles. Phenolic compounds, including gallic acid, caffeic acid, and tannins, act as strong antioxidants and reducing agents, helping to convert the metal ions Zn^{2+} and Ti^{4+} ions into stable nanoparticles [21]. Flavonoids like

quercetin and kaempferol assist in the reduction process. Alkaloids, especially isoquinoline derivatives, stabilize nanoparticles and improve their antimicrobial activity. Terpenoids like lupeol, oleanolic acid, and β -sitosterol improve nanoparticle biocompatibility through anti-inflammatory and antimicrobial effects. Saponins and glycosides prevent nanoparticle clumping and improve stability [16].

1. Antioxidant Activity

Phenolic compounds possess potent antioxidant properties, which are often associated with their biological activities [22]. These compounds are absorbed mainly in the stomach and small intestine, though their activity can be affected by the digestive process [23]. Common in vitro methods used to measure antioxidant potential include DPPH, ABTS, and intracellular ROS inhibition assays. This study employed all three techniques to measure the antioxidant activity of various *P. utilis* fractions.

➤ DPPH Radical Scavenging Activity

The DPPH assay revealed that all *P. utilis* fractions showed antioxidant activity that increased with concentration. Among them, the FF fraction demonstrates the highest radical scavenging ability, similar to that of Vitamin C and greater than TPF and AF. This enhanced activity is likely attributed to the higher phenolic content in the FF's fraction. A Pearson's correlation analysis showed a strong relationship between phenolic levels and DPPH activity across all fractions, supporting the role of phenolics as key contributors. These results are consistent with earlier findings by **Huang et al. (2017)** and **Zhang et al. (2018)**, who also identified phenolics as primary antioxidants in *P. utilis* and *Rhus chinensis*, respectively [24,12].

➤ ABTS Radical Scavenging Activity

All fractions of *P. utilis* showed strong, concentration-dependent ABTS radical scavenging activity with slight variation observed among them. A strong Pearson's correlation between phenolic content and ABTS activity confirmed the significant role of phenolic compounds in the antioxidant response. Differences in IC₅₀ values between DPPH and ABTS assays were likely due to differences in radical structures, a pattern also noted in earlier studies [13,25]. The main phenolic compounds—rutin, isorhamnetin-3-O-rutinoside, and cyanidin-3-O-glucoside—are known antioxidants, as shown in previous research [26]. Supporting their contribution to the observed antioxidant activity.

➤ Inhibition of Intracellular ROS in H₂O₂-Induced HepG2 Cells

Reactive oxygen species (ROS) are essential for cell signaling, but extreme ROS levels, often caused by stressors like pollution or smoking, can damage cells and contribute to chronic diseases such as cancer and cardiovascular diseases [27,28]. This study evaluated the phenolic fractions from *P. utilis* fruits' ability to inhibit ROS in H₂O₂-induced HepG2 cells. FF fraction showed the strongest ROS inhibition, followed by AF, while TPF had the weakest effect. These results align with previous studies highlighting the ROS-inhibitory effects of plant phenolics which often work by enhancing antioxidant enzymes or increasing GSH levels [29,30].

2. Antimicrobial Activity

Seven different extracts derived from leaves and seeds of *P. utilis* were tested for antibacterial activity against four microbial strains. Most of these extracts showed greater effectiveness against Gram-positive bacteria, which can be attributed to the outer membrane barrier in Gram-negative strains [31]. Antibacterial activity was calculated by measuring inhibition zones around extract-loaded discs.

P. utilis ethyl acetate leaf extract was most effective against *S. epidermidis*, while the methanolic leaf extract was notably effective against *S. aureus*. The methanolic seed extract showed strong antibacterial activity against *K. pneumoniae* and *E. coli*. Seed extracts showed broad-spectrum antibacterial effects, consistent with previous studies [32]. Leaf extracts were more effective against Gram-positive bacteria, while seed extracts were better against Gram-negative bacteria. This enhanced activity is due to hydroxynitrile-glucoside compounds in the seeds known for their bioactive properties.

Nanoparticles as Anticancer Agents

Zinc Oxide (ZnO) and Titanium dioxide (TiO₂) nanoparticles exhibit strong anticancer properties due to their large surface area, photocatalytic activity, and biocompatibility. ZnO NPs selectively induce cytotoxicity in cancer cells by producing reactive oxygen species (ROS), resulting in oxidative stress, DNA damage, and apoptosis [33]. Their selective toxicity is linked to the acidic pH and altered redox state of cancer cells [34]. ZnO NPs can also be functionalized with targeting ligands to improve selectivity and enhance drug delivery [35] and their photodynamic properties make them suitable for light-assisted cancer therapies. In vitro studies show strong anticancer effects against MCF-7, A549, HeLa, and HepG2 cell lines [36].

Titanium dioxide (TiO₂) nanoparticles possess notable anticancer properties by generating ROS under UV or near-infrared light, causing oxidative stress and apoptosis in cancer cells. Their photocatalytic nature makes them useful in photodynamic therapy (PDT), selectively targeting tumor cells while reducing harm to healthy tissue. TiO₂ NPs are chemically stable, inert, and low in toxicity in the absence of light exposure. Their surface can be modified or functionalized for better delivery and therapeutic synergy with chemotherapeutics. Green synthesis using plant extracts further enhances their biocompatibility [37,38]. However, more in vivo studies are essential to initiate clinical safety and effectiveness.

Dye degradation, wastewater treatment

Green-synthesized ZnO/TiO₂ nanoparticles using *P. utilis* extracts absorb UV or visible light and produce reactive oxygen species (ROS) that break down complex dyes into non-toxic byproducts such as water and CO₂ [16]. Bioactive compounds from the extract improve dye adsorption through functional groups like –OH, –COOH, and aromatic rings [20]. Their high surface area and porous structure remove heavy metals, making them ideal for sustainable wastewater treatment, especially in low-resource settings.

Mechanisms of action in biological systems

Nanoparticles (NPs) can significantly increase plants' reactive oxygen species (ROS), leading to oxidative stress and cytotoxic effects. This activates the plant's antioxidant defense system, with common indicators including H_2O_2 production, MDA content, and the activities of enzymes like CAT, SOD, and APX [39]. When ROS production surpasses the plant's ability to neutralize them, it leads to oxidative damage to cellular components, lipid peroxidation, and active programmed cell death. NPs often disrupt membranes, increasing their permeability and facilitating further NP entry, which increases intracellular ROS and reduces photosynthetic efficiency [40].

Among metal-based NPs, CeO_2 , CuO , TiO_2 , ZnO , Al_2O_3 , and Fe_2O_3 are widely studied for their oxidative impact on plants. CeO_2 exposure has shown dose-dependent effects on antioxidant enzyme activities, with moderate concentrations enhancing activity and higher doses leading to inhibition [41]. CuO NPs increase antioxidant enzyme activities such as APX, CAT, POD, SOD, and GR [42], although effects may vary depending on conditions [43]. These observations influence the role of metal NPs in plant defense systems and physiological responses.

Synergistic properties of ZnO-TiO₂ nanocomposites

- 1. Enhanced Photocatalytic Activity:** The ZnO–TiO₂ heterojunction increases effective charge separation, reducing electron-hole recombination, thereby improving photocatalytic efficiency [44].
- 2. Wider Light Absorption Spectrum:** TiO₂ absorbs UV light, while ZnO broadens light absorption into the visible range, allowing better solar utilization [45].
- 3. Improved Charge Transport:** ZnO's superior electron mobility enables quicker electron transport in improved catalytic performance [46].
- 4. Increased ROS Generation:** Better charge separation leads to ROS generation, vital for degrading pollutants and pathogens [47].
- 5. Higher Structural Stability:** The composite resists photo corrosion and heat due to its vigorous crystalline structure [48].

Performance of ZnO/TiO₂ nanocomposites

1. Photocatalytic performance of ZnO/TiO₂

ZnO–TiO₂ nanocomposites show strong photocatalytic activity and are capable of breaking down various dyes and organic pollutants such as reactive black 5, methylene blue, rhodamine B, pentachlorophenol, benzene, xylene, malachite green, and methyl orange [49,50]. Their degradation efficiency (75–100%) under UV or visible light surpasses that of pure ZnO or TiO₂ (<70%) due to enhanced surface area and improved light absorption [51]. Red and blue shifts in absorption spectra improve photocatalytic performance under visible and UV light, respectively [49,52]. Furthermore, these nanocomposites maintain high reusability for up to 6

cycles, demonstrating their practical and environmental advantages [53,54]. ZnO–TiO₂ nanocomposites outperform pure ZnO or TiO₂ due to better charge separation—TiO₂ stabilizes ZnO, while ZnO boosts electron mobility. Light excites electrons and holes, forming reactive •OH and O₂•⁻ species that degrade pollutants into CO₂ and H₂O [55].

2. Antimicrobial activity of ZnO/TiO₂

ZnO–TiO₂ nanocomposites show strong antimicrobial activity against gram-positive and gram-negative bacteria (e.g., *S. aureus*, *E. coli*), outdoing pure ZnO or TiO₂. Their photocatalytic action generates reactive oxygen species like O₂•⁻ and H₂O₂, which disrupt bacterial membranes and damage vital components such as lipids, proteins, and DNA [56]. Additionally, Zn²⁺ ions interfere with membrane integrity and intracellular balance, leading to cell death.

3. Gas sensing performance of ZnO/TiO₂

ZnO–TiO₂ nanocomposites are effective sensors for gases like acetone, ethanol, O₂, and ammonia [57]. Adding ZnO improves TiO₂'s performance due to its higher conductivity and electron density. Though ZnO has low selectivity and needs higher temperatures, the composite shows improved sensitivity and stability. ZnO–TiO₂ remains functional for up to 6 months, outperforming ZnO, which damages more quickly due to its rod-like structure [58].

The toxicity aspects of green-synthesized NPs

Nanoparticles are a growing concern in practical applications, as they can enter the environment through human activities and lead to adverse effects on animal and plant cells. Toxicity varies based on particle size, surface, and composition, with smaller particles typically being more harmful. Exposure routes include inhalation, dermal contact, and ingestion, potentially leading to oxidative stress, inflammation, organ damage, and neurological diseases like Alzheimer's and Parkinson's. In aquatic ecosystems, nanoparticles can disrupt cellular processes and cause genetic damage. Metal oxides such as ZnO, TiO₂, and Al₂O₃ have shown cytotoxic and genotoxic effects, while magnetic and silver nanoparticles also pose risks under prolonged exposure, though biosynthesized forms may be safer for human cells.

Conclusion

The synthesis of ZnO/TiO₂ nanocomposites by using *Prinsepia utilis* can show promising, eco-friendly, and also enhance the biological activity. The phytochemicals present in plants not only act as reducing and stabilizing agents for nanocomposites but also impart additional bioactivity to the synthesized nanoparticles. The study suggests that plant-mediated ZnO/TiO₂ from *Prinsepia utilis* exhibits excellent antibacterial, antioxidant, and other biological activities. The biocompatibility and reduced toxicity associated with nanoparticles further highlight their potential in biomedical and other environmental applications. Future research should also focus on optimizing synthesis parameters and exploring the scalability.

Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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