

# Synthesis and Biomedical Applications of Titanium Dioxide Nanoparticles a Literature Review on Current Advances and Future Directions

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## ABSTRACT

Nanoparticles of Titanium Dioxide (TiO<sub>2</sub>) have also become an essential element of nanomedicine because of their multifunctionality and wide use in medicine. This review compiles current advances in the synthesis, functionalization, and applications of TiO<sub>2</sub> nanoparticles, emphasizing their significance in drug delivery methods. The article begins with an introduction to TiO<sub>2</sub> nanoparticles, focusing on their non-cytotoxicity, photocatalytic properties, and potential medical applications. An approximate study of brightest star-coagulate, hydrothermal, and green combining designs presents the substances and defect of the strategies. The review too demonstrates the various habits by which TiO<sub>2</sub> nanoparticles can authorize the point in a direction drug transfer, the skill of TiO<sub>2</sub> nanoparticles to improve the PDT by way of ROS result and accuracy in the biosensing operation. However, based on the potential applications discussed, the authors critically look at current woes that are associated with toxicity, biocompatibility, and stability issues in biological systems. Of the future directions for TiO<sub>2</sub> nanoparticles pointed out in the review, the two notable ones include other synthesis approach and further application in regenerative medicine. This serves to highlight the need for broader investigations towards the safety characterization and chronic repercussions concurrent with the investigation of the potential of individualized medicine. This literature review not only summarizes the latest development of TiO<sub>2</sub> nanoparticles but also provides a guide to direct subsequent studies to enhance the Biomedical application of TiO<sub>2</sub> nanoparticles.

**Keywords:** Titanium Dioxide Nanoparticles (TiO<sub>2</sub> NPs), Nanotechnology, Nanomedicine, Drug delivery systems, Photodynamic Therapy (PDT), Sonodynamic Therapy (SDT), Antimicrobial applications.

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## INTRODUCTION

Nanotechnology is a relatively new science whose applications entail working at the atomic and molecular level, in an environment measuring between 1 to 100 nm (Pacheco and Aguilar, 2024). This combining several branches of learning training has intrigued plenty consideration for the flexibility of allure uses in subdivisions to a degree farming, strength, fabrics, cure and car. As observed, there are new characteristics at the nanoscale that can offer new approaches and improvements primarily in product utility and effectiveness (Zhou *et al.*, 2024). Nanomaterials include those such as the titanium dioxide nanoparticles, which are widely used in industrial products (Macías-Silva *et al.*, 2024). These

Nanoparticles are employed thanks to their high oxidation states, high refractive index, and remarkably stable chemical nature for various applications including pigments for Paints and Coatings, Photocatalyst for treatment of Wastewater and Food Additive for taste and appearance (Otgonbayar *et al.*, 2024). Nonetheless, existing applications of titanium dioxide nanoparticles are fraught with concerns of the particles' effects on the environment and on life forms (Karnwal *et al.*, 2024).

A multidisciplinary field which finds application in various fields such as agriculture, energy, textiles, medicine and automobiles (Singh and Kaur, 2023). According to the EU regulation, particles with a size between 1 and 100 nm are considered as nanoparticles: however, particles with sizes greater than 100 nm but possibly incorporating themselves into this material class given their possible use. Recent research shows that many metallic nanomaterials, including Copper (Cu), titanium dioxide, Silver (Ag), Zinc (Zn), Iron (Fe) and others have both positive and negative impact in plant growth; however, further study is



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needed with the aim of gathering more information (Faraz *et al.*, 2020).

Recent studies proved that Titanium Dioxide nanoparticles (TiO<sub>2</sub>) are among the most commonly used nanomaterials in various commercial fields (Kaur *et al.*, 2024). USGS also expects that around 10,000 tonnes of titanium dioxide nanoparticles were used in application including paints, coatings, solar cells, cosmetics, and cement during 2014 out of about 1.31 million tonnes of titanium dioxide pigments produced globally. Estimated production of titanium dioxide pigment in the U.S by year, 2021 stood at 1.1 million tonnes; nevertheless, it remains a net exporter of the product although import of titanium mineral concentrates. For instance, there is an increase in titanium pigment exports in 2021 lifts from its exported declined in 2020, while the current production from China is expected at about 3.7 million tonnes of titanium dioxide pigment (Habib *et al.*, 2023). Titanium dioxide nanoparticles are favorable materials since they possess high oxidation capability, high refractive index, low cost, high chemical stability and the presence of oxygen vacancies in the lattice structure (Alameen *et al.*, 2024). These characteristics are what make TiO<sub>2</sub> nanoparticles most suitable and appreciated in different applications. They are used in the optical industry as semiconductors because they have a wide direct bandgap; electronically and ionically they can be tuned to meet the needs of sensors and electronics (Bisht and Das, 2024).

In terms of physical forms, titanium dioxide occurs naturally in three polymorphic structures: rutile anatase and brookite, rutile and anatase, and rutile, anatase, and brookite. Both forms have different crystalline structures associated with the various performances of each form. For instance, TiO<sub>2</sub> nanoparticles are used as pigments and the main ingredient in products that are used in food additives and cosmetics due to their brightness and good texture (Dongre and Peshwe, 2020). The use of titanium dioxide nanoparticles is not limited to being a pigment; the particles are employed in photocatalytic degradation of pollutants in wastewaters, and antimicrobial properties in diverse products; are also being considered for potential uses in nanomedicine (Krishnan and Shrivastav, 2021). As the market trends for these nanoparticles increase, so does the worries over their effects on the ecosystem and health. More efforts are needed in order to depict the effects of extended utilization of TiO<sub>2</sub> nanoparticles and to guarantee the appropriate measures being taken by various sectors (Huang *et al.*, 2024).

### Synthesis of TiO<sub>2</sub> Nanoparticles

The preparation of Titanium Dioxide (TiO<sub>2</sub>) nanoparticles has attracted considerable interest because of their characteristics and uses including in medicine, environment, and materials. There are many approaches used in the synthesis of TiO<sub>2</sub> nanoparticles which are unique in their advantages and disadvantages. This overview will briefly describe the major synthesis approaches

for nanomaterials in the three categories; Physical, chemical and biological. Figure 1 illustrates various methods for the synthesis of Titanium Dioxide (TiO<sub>2</sub>) nanoparticles (Mude, 2023).

### Physical Methods

The physical techniques for synthesis of Titanium Dioxide (TiO<sub>2</sub>) nanoparticles include the advantage of using each of these physical methods of synthesis will be discussed below. These methods are crucial for producing nanoparticles with specific sizes, shapes, and properties suitable for diverse applications, particularly in the biomedical field (Table 1) (Aboualigaledari and Rahmani, 2021).

TiO<sub>2</sub> nanoparticles preparation is possible by physical techniques which includes various methods with strengths in their application. Ball milling is another of the conventional methods where bulk TiO<sub>2</sub> is reduced into increasingly fine nanoparticles by physical impacts. It raises the specific surface area of the material, and can manage the particle size according to aims, making it perfect utilized in photocatalytic procedures and environmental procedure. Another is pyrolytic, that is high temperature thermal degradation of titanium precursors in an inert medium. With assist of this technique, it paves the way to control the size and the formation of the nanoparticles for wastewater treatment and air purification (Sheikh and Mude, 2024).

To synthesize nanoparticles, this method requires the hydrolysis and polycondensation of titanium alkoxides forming gel, which is then dried and calcined. As will be discussed, this method provides very high control over crystallite size, shape, and phase, which is vital for photocatalytic purposes and for increasing biocompatibility. Hydrothermal synthesis involves heating of fluids containing TiO<sub>2</sub> at high pressure for the purpose of growing nanoparticles of TiO<sub>2</sub>. This approach results information of highly ordered nanoparticles with sharp size distribution; high antibacterial characteristics making it suitable in biomedicine for instance in drug delivery systems. All of the above mentioned physical methods collectively enhances the multifunctional applicability of TiO<sub>2</sub> Nanoparticles and found more application in environmental and biomedical field (Mude, 2023).

### Chemical Methods

There are several chemical methods to synthesize titanium dioxide nanoparticles, and each method has its own benefits and properties. These stages generally consist of one or more stages of ageing, one or two stages of drying, and thermal decomposition to form anatase TiO<sub>2</sub>. Closely related to the control of particle size and morphology are factors, such as temperature, and the amount of water used in the course of hydrolysis (Alameen *et al.*, 2024).

Another method is the hydrothermal synthesis in which high pressure and high temperature is applied to encourage crystallization in the presence of water. Compared to other

sol-gel procedures, this technique enables the synthesis with greater control of the size and form of the particles. On the other hand, solvothermal method utilize nonaqueous solvents allowing syntheses at high temperature while controlling the resulting nanostructures (Saka *et al.*, 2022). Another effective method of synthesizing TiO<sub>2</sub> nanoparticles involves Chemical Vapor Deposition (CVD) and Physical Vapor Deposition (PVD). Also known as Chemical Vapor Deposition these techniques entail the reduction of vapors that have precursors on the substrates then subjecting them to favorable conditions to create thin films or nanostructures with particular morphology (De Matteis *et al.*, 2020). Further, nanoporous TiO<sub>2</sub> layers are synthesized on titanium substrates through electrochemical anodization techniques, which change the surface properties of the material to a very large extent (Mani *et al.*, 2021).

Finally, sonochemical and microwave assisted synthesis are modern approaches that use ultrasonic waves and microwave irradiation to increase the rate of various processes and the homogeneity of nanoparticles. Unfortunately, these techniques are reported to be efficient in providing TiO<sub>2</sub> nanoparticles with desirable photocatalytic properties<sup>23</sup>. All of these chemical methods plays an important role in enhancing the versatility and potential application of TiO<sub>2</sub> nanoparticles in areas such as catalysis, photovoltaic and environmental treatment (De Matteis *et al.*, 2020) (Figure 2).

### Chemical Methods

Titanium Dioxide (TiO<sub>2</sub>) nanoparticles can be synthesized through various chemical methods, each with unique mechanisms and outcomes.

#### Hydrolysis Method

The main procedure for synthesising is the hydrolysis of titanium alkoxides, especially Titanium Tetraisopropoxide (TTIP) in the presence of water and alcohol. The process commences by forming titanium hydroxides and followed by polycondensation to build a gel network. Crystalline TiO<sub>2</sub> nanoparticles are produced after aging, drying and calcination. This method gives control over particle size and shape based on the controllable factor which include temperature and concentration of precursors (ÖZTÜRK and ÇITAK, n.d.-a).

#### Precipitation Method

In this approach, TiO<sub>2</sub> is synthesized by precipitating titanium salts from a solution; the precipitating agent used is an alkali hydroxide. Titanium is also to be precipitated from the solution it dissolves in, by an agent such as sodium or ammonium hydroxide from titanium chloride or titanium sulfate. This method is easy and can easily be scaled up, however, specific particle characteristics such as pH and temperature may need to be closely monitored (Aboualigaledari and Rahmani, 2021).

Photo/Thermo Reduction Method: In this process, light or thermal energy is used to decompose titanium precursors into TiO<sub>2</sub> nanoparticles. For instance, titanium oxysulfide when undergoes thermal treatment in an inert environment it releases TiO<sub>2</sub>. On the other hand, photo-reduction methods entail the use of reducing agents to reduce titanium precursors – in this case applying UV-light will result in formation of TiO<sub>2</sub> nanoparticles.

### Biomedical Applications of TiO<sub>2</sub> Nanoparticles

Titanium Dioxide (TiO<sub>2</sub>) Nanoparticles (NPs) have attracted increasing research interest in the recent past because of their photocatalytic properties, biocompatibility, and low toxicity. These attributes make TiO<sub>2</sub> NPs as potential candidates for several biomedical destinations, especially in drug delivery, Photodynamic Therapy (PDT) and Sonodynamic Therapy (SDT).

#### Drug Delivery Systems

The drug delivery systems can use TiO<sub>2</sub> nanoparticles as nanocarriers. These profiles enable the drugs to be loaded easily and to be released in the correct location in the human body. This capability is useful especially for disease such as cancer and epilepsy for which localized drug delivery is important (Joseph *et al.*, 2024). For instance, León *et al.* (2017) synthesised a PEG-TiO<sub>2</sub> NPs – 2ME system that consists of PEG coated TiO<sub>2</sub> NPs embedded with 2-Methoxyestradiol, an antitumor drug. The alteration of TiO<sub>2</sub> NPs was established through characterization techniques that included IR and Raman spectroscopy hence showing an improved relation between the drug and the carrier. This work underscores the call for change in the TiO<sub>2</sub> NPs to enhance their drug transport function, which forms a rich research direction for targeted anti-cancer treatments (León *et al.*, 2017).

Similarly, the incorporation of gold nanoparticles (Au) into TiO<sub>2</sub> NPs has been explored to enhance their therapeutic efficacy. Deepagan *et al.* (2016) discussed the fabrication of hydrophilized Au-TiO<sub>2</sub> nanocomposites for SDT, which enhances the production of ROS under ultrasound irradiation. This combination does not only overcome the shortcomings of TiO<sub>2</sub> NPs but also improves their anticancer activities dramatically (Deepagan *et al.*, 2016).

#### Photodynamic Therapy and Sonodynamic Therapy

The photocatalytic characteristics of TiO<sub>2</sub> NPs make them suitable for use in PDT. Yin *et al.* (2013) gave a detailed analysis of the biomedical uses of TiO<sub>2</sub>, its relationship with improving the treatment methods, especially in cancer therapy. The study also stressed on surface alteration of TiO<sub>2</sub> NPs because it affects its activities and therapy benefits in PDT (Fei Yin *et al.*, 2013). Also, Ziental *et al.* (2020) reviewed on two presentations of SDT and PDT of TiO<sub>2</sub> NPs where they can produce ROS when exposed to UV light (Ziental *et al.*, 2020). The utility of TiO<sub>2</sub> NPs in the treatment of malignant tumor and antibacterial resistant bacteria indicates it's a potential application in pharmaceuticals

particularly in oncology and antibiotic resistance. It has been established that modifications to the material composition, for example introducing oxygen-deficient TiO<sub>2-x</sub> layers, increases charge carrier separation and ROS formation, thus increasing therapeutics efficiency (Han *et al.*, 2018).

### Advanced Hybrid Nanoparticles

The use of hybrid nanocomposites has therefore been advanced as a promising approach to improve the therapeutic effect of TiO<sub>2</sub> nanoparticles. Ren *et al.* (2015) also described hydrogenated black TiO<sub>2</sub> nanoparticles that can absorb NEAR INFRARED light which is very beneficial to the common Titanium dioxide that only operates under UV light. The systematic assessment of their safety and efficacy also add to their potential in clinical applications (Ren *et al.*, 2015).

Deepagan *et al.* (2016) further studied modification of gold nanoparticles to TiO<sub>2</sub> through SDT to occur ROS generation. According to them, their nanocomposites did not only increase the efficacy of therapy but also were able to show eradication of tumor *in vivo*, meaning that there is a possibility of increasing the efficiency of TiO<sub>2</sub> when using it with other materials (Deepagan *et al.*, 2016).

### Antimicrobial Applications

The antibacterial activity of TiO<sub>2</sub> nanoparticles has also been investigated with major emphasis on wound dressing application. About chitosan formulations containing TiO<sub>2</sub> nanoparticles, Hu *et al.* (2019) explained that TiO<sub>2</sub> nanoparticles might improve antibacterial effects that could improve the outcomes for wound healing. This work enriches the opportunity of using TiO<sub>2</sub> nanoparticles to advance material for tissue engineering and wound healing applications (Hu *et al.*, 2019).

## TOXICITY AND SAFETY CONSIDERATIONS

Titanium Dioxide (TiO<sub>2</sub>) nanoparticles are considered promising due to their characteristics and wide usability in different fields, especially the medical field. However, there are questions on the safety and the toxicity impact of these nanoparticles that is an important issue so often nanoparticles are used in products frequently consumed by people such as food, cosmetic products, and medical services.

### Toxicity of TiO<sub>2</sub> Nanoparticles

**Reproductive Toxicity:** Research also shows that exposure to TiO<sub>2</sub> nanoparticles is detrimental to reproductive health. It could concentrate in the reproductive system, cause reduced sperm mobility, increased DNA fragmentation and potentially had adverse effects on offspring formation through increased oxidative stress and inflammation (Minghui *et al.*, 2023).

**Neurotoxicity:** Recent reports on the impact of TiO<sub>2</sub> NPs indicated they could exert neurotoxicity through the generation of oxidative stress, and neuroinflammation. These particles can cross BBB and may otherwise affect the neurons and cause several neurological disorders (Zhang *et al.*, 2023).

**Carcinogenic Potential:** The International Agency for Research on Cancer (IARC) classifies TiO<sub>2</sub> as a Group 2B carcinogen, indicating it is possibly carcinogenic to humans. This classification stems from studies showing lung tumors in rats exposed to high levels of TiO<sub>2</sub> particles (Zhang *et al.*, 2023).

**Oxidative Stress Mechanism:** Specifically, the primary toxic mechanism in the antidotal treatment for lithium ingestion is oxidative stress. The precise outcome that is observed is in line

**Table 1: Various synthesis methods used in nanotechnology, highlighting their descriptions, advantages, and applications across different fields.**

| Synthesis Method       | Description                                                                                              | Key Advantages                                       | Applications                                       | Ref                            |
|------------------------|----------------------------------------------------------------------------------------------------------|------------------------------------------------------|----------------------------------------------------|--------------------------------|
| Milling Techniques     | Mechanical grinding of bulk TiO <sub>2</sub> into nanoparticles using high-energy collisions.            | Increases surface area; customizable particle size.  | Photocatalysis, environmental remediation.         | (Hameed and Abdulrahman, 2023) |
| Pyrolysis              | Thermal decomposition of titanium precursors at high temperatures in an inert atmosphere.                | Precise control over size and morphology.            | Wastewater treatment, air purification.            | (ÖZTÜRK and ÇITAK, n.d.-a)     |
| Sol-Gel Method         | Hydrolysis and polycondensation of titanium alkoxides to form a gel, followed by drying and calcination. | Cost-effective; fine control over properties.        | Photocatalytic applications, biocompatibility.     | (Owens <i>et al.</i> , 2016)   |
| Hydrothermal Synthesis | Growth of nanoparticles in aqueous solutions under high temperature and pressure.                        | Produces highly crystalline nanoparticles; scalable. | Antibacterial applications, drug delivery systems. | (Dunne <i>et al.</i> , 2015)   |

with the size, form, and surface chemistry of the nanoparticles (Skocaj *et al.*, 2011).

**Environmental Concerns:** While TiO<sub>2</sub> exhibits low acute toxicity to aquatic organisms, long-term exposure can result in sub-lethal effects that may disrupt ecosystems (Skocaj *et al.*, 2011).

## CHALLENGES AND CONSIDERATIONS

### Toxicity and Biocompatibility

Titanium Dioxide (TiO<sub>2</sub>) Nanoparticles (NPs) have garnered significant attention due to their widespread applications in various industries, including biomedical fields. However, concerns regarding their toxicity and biocompatibility have emerged, necessitating a thorough examination of their effects on human health and the environment.

### Toxicological Mechanisms

Different toxicities caused by TiO<sub>2</sub> NPs can be explained by direct or indirect effects of their interaction, which can be detected through oxidative stress, inflammation and genotoxicity. Research shows that TiO<sub>2</sub> NPs when introduced can cause formation of ROS, which are potent promoters of cell damage and inflammation. For example, the *in vivo* photo-transformation has shown that TiO<sub>2</sub> NPs can deposit in the lungs, liver, and reproductive system and cause inflammation and oxidative stress (Zhang *et al.*, 2023).

### Neurotoxicity

Recent studies provide evidence that TiO<sub>2</sub> NPs have neurotoxic effects. Some of these nanoparticles are believed to pass through the blood brain barrier and cause neurotoxic effects. In animal

models' exposure has shown neuro inflammation and cognitive impairments. In addition, and more specifically, epidemiological investigations have pointed to positive association between exposure to TiO<sub>2</sub> and incidence of neurological diseases suggesting the necessity for further research on this compound's negative impacts on brains health after longer periods of exposure (Xuan *et al.*, 2023).

### Reproductive Toxicity

The toxicity of TiO<sub>2</sub> NPs has also influenced the reproductive health of other living organisms as well. Studies show that these nanoparticles can get sequestered in reproductive organs and decimate sperm factors such as efficiency and DNA integrity in male samples. In female rats, exposure has been linked with ovarian cell suicide and hormonal imbalances. Considering the proved genotoxicity profiles of TiO<sub>2</sub> NPs, the observed reproductive toxicities would be largely attributable to the oxidative stress caused by these nanoparticles (Mude, 2023).

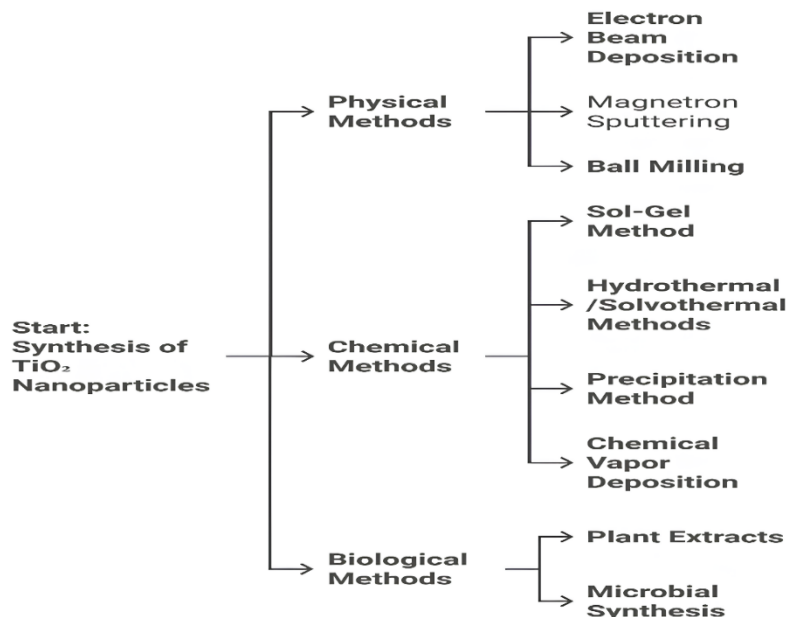
### Stability and Functionalization

#### Regulatory Oversight

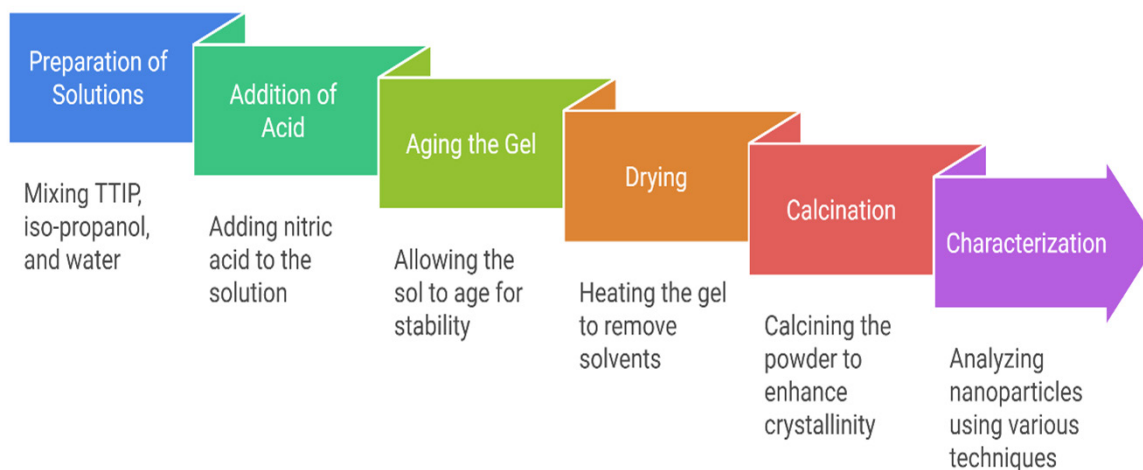
Regulatory bodies like the European Food Safety Authority (EFSA) have deemed certain uses of TiO<sub>2</sub> unsafe, particularly as a food additive. Ongoing evaluations aim to align regulations with emerging scientific evidence regarding nanomaterials (Sheikh *et al.*, 2024).

### Dermal Exposure

TiO<sub>2</sub> nanoparticles used in sunscreens as UV filters are safe for topical application only on intact skin and there are concerns



**Figure 1:** Different Methodes to synthesis of TiO2 Nanoparticles.



**Figure 2:** Synthesis of TiO<sub>2</sub> Nanoparticles.

related to inhalation exposure from aerosolized products. Hazards associated with the inhalation are as follows, Lung toxicity and inflammation.

### Need for Further Research

There is a pressing need for comprehensive toxicological studies to better understand the absorption, distribution, excretion, and long-term effects of TiO<sub>2</sub> nanoparticles in humans. Current methodologies for assessing nanomaterial risks are still being developed.

### Precautionary Measures

Until more conclusive data are available, it is recommended to use TiO<sub>2</sub> nanoparticles with caution, particularly in applications involving inhalation or prolonged exposure (Sheikh *et al.*, 2024).

### Future Directions

The future of Titanium Dioxide (TiO<sub>2</sub>) Nanoparticles (NPs) in biomedical applications is poised for significant advancements, driven by innovative synthesis approaches and the exploration of expanded applications. As researchers continue to investigate the unique properties of TiO<sub>2</sub> NPs, several promising directions emerge that could enhance their effectiveness and versatility in medical settings (Figure 3).

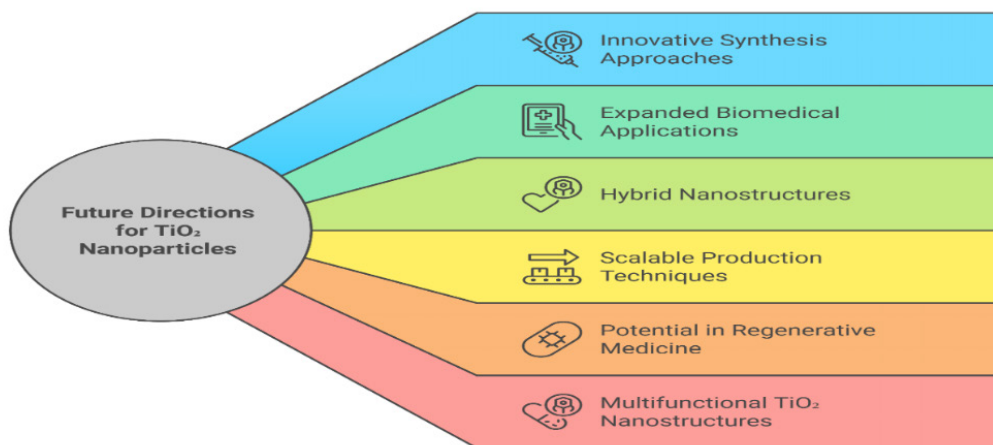
Specifically, the first area of research interest involves the synthesis of heterogeneous nanocomposites containing TiO<sub>2</sub> (Krishnan and Shrivastav, 2021). This approach is designed to take advantage of the existence of many components that could form multifunctional platforms where several thermo-therapeutic needs can be met at once. For example, incorporating TiO<sub>2</sub> with metallic NPs such as gold or silver can boost the photothermal performance which make these core/shell structures very useful for localized cancer treatments. Gold-coated TiO<sub>2</sub> NPs have shown better photothermal properties which enable targeted heat generation that can effectively kill tumor cells when the surface of the nanoparticles accumulates on the tumor site while at the

same time sparing the surrounding healthy tissue. It has been focusing on the application of these materials in biosensing and drug delivery systems since stability and performance are critical aspects (ÖZTÜRK and ÇITAK, n.d.-b).

Another important aspect for the future of TiO<sub>2</sub> NPs in biomedicine is the scalability of particle manufacture. In most cases, currently used synthesis methods carry certain problems tied to reproducibility and cost of the processes, the latter of which might be a crucial obstacle when it comes to application of the methods. In this regard, various modified methods, which are referred to as green synthesis methods, have been proposed to reduce the synthesis and production problems associated with the nanomaterials (ÖZTÜRK and ÇITAK, n.d.-b). These methods help in achieving required properties of TiO<sub>2</sub> NPs while reducing toxic products in agreement with current nanotechnology trend for green synthesis. Microfluidic synthesis is another recent method that allows a rational control of reaction conditions at the micro scale as well as allows short time product formation, and scale-up process of the nanoparticles with high quality (Huang *et al.*, 2024).

In view of the biocompatibility and bioactivity of TiO<sub>2</sub> NPs, much attention has been given to them as therapeutic agents for bone tissue engineering, wound healing and stem cell applications. TiO<sub>2</sub>-polymers have adjustable mechanical strength and microarchitectures, and their incorporation into biodegradable polymers can improve cell attachment and viability. In the context of wound healing, the antibacterial properties of TiO<sub>2</sub> NPs recommend their use as components added into dressings that minimise infections during the healing process through stimulating cell migration and proliferation (De Matteis *et al.*, 2020).

Furthermore, functionalized TiO<sub>2</sub> NPs could be used as carriers of growth factors or genes amineralized to stem cells in stem cell therapy. This targeted delivery system could greatly increase the treatment benefit of stem cell therapies for different



**Figure 3:** Future direction for TiO<sub>2</sub> Nanoparticle.

ailments, benefiting the patients that receive such treatment. For example, multifunctional TiO<sub>2</sub> NPs might be designed to release chemotherapeutic agents and at the same time to perform PTT or PDT. Such a two-pronged strategy might increase treatment effectiveness against tumors and reduce the side effects of using traditional therapies (Macías-Silva *et al.*, 2024).

## CONCLUSION

The emphasis made on the ongoing research on Titanium Dioxide (TiO<sub>2</sub>) Nanoparticles (NPs) revealed these materials' great promise and possibilities for their application in the biomedical field such as drug delivery systems, PDT, as well as for biosensing systems. This literature synthesis aims to highlight the progress in the synthesis and functionalization of TiO<sub>2</sub> NPs particularly in relation to potential medical applications of the material. As exciting as they are, there are key issues that need to be address such as toxicity effects, biocompatibility, and stability when put into biological environment. Thus, these issues require more study so that the application of TiO<sub>2</sub> NPs in clinical practice will not endanger public health. Thus, the further investigation of these challenges should be made a priority for future studies based on the advancement of novel synthesis methods and the growing potential of TiO<sub>2</sub> NPs in regenerative medicine. Thus, the synthesis of the new generation of multifunctional nanocomposites based on TiO<sub>2</sub> with other materials can improve the therapeutic activity and minimize the potential toxic effects. Moreover, the production of common safety measures and tests procedures, as well as the creation of the legal framework, is critical due to the progress in nanotechnology. Thus, this review not only indicates the direction of the development of TiO<sub>2</sub> NP but also offers direction for further investigations of their biomedical uses. Thus, filling the existing gaps in the literature and promoting the interdisciplinary approach, this study will pave the way for enhanced use of TiO<sub>2</sub> nanoparticles in nanomedicine

with the purpose of developing new therapy protocols that can help to solve unmet needs of the modern health care system.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**TiO<sub>2</sub>:** Titanium Dioxide; **NPs:** Nanoparticles; **PDT:** Photodynamic Therapy; **SDT:** Sonodynamic Therapy; **ROS:** Reactive Oxygen Species; **PEG:** Polyethylene Glycol; **Au-TiO<sub>2</sub>:** Gold-Titanium Dioxide Nanocomposites; **CVD:** Chemical Vapor Deposition; **PVD:** Physical Vapor Deposition; **USGS:** United States Geological Survey.

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