

Biomedical Applications of Titanium Dioxide (TiO₂) Nanoparticles

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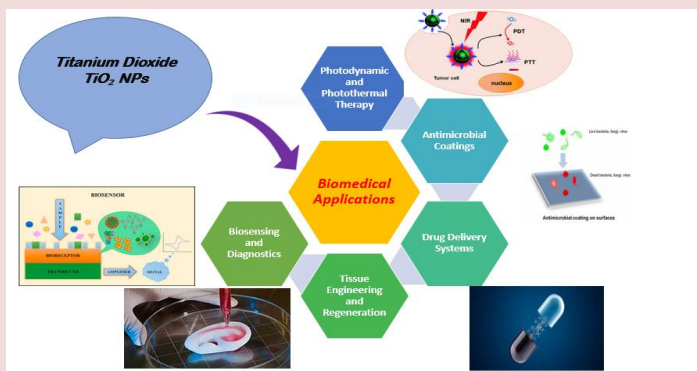
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Abstract

Titanium dioxide (TiO₂) nanoparticles (NPs) have emerged as versatile and promising materials in biomedical applications due to their unique physicochemical properties, including high stability, biocompatibility, photocatalytic activity, and tunable surface chemistry. This review explores their broad spectrum of applications in the biomedical field, emphasizing their role in drug delivery, cancer therapy, antimicrobial coatings, and biosensing. TiO₂ NPs demonstrate significant potential in targeted drug delivery systems due to their ability to conjugate with bioactive molecules, enabling controlled and site-specific therapeutic release. Their photocatalytic properties make them suitable for photodynamic and photothermal therapies, providing effective, minimally invasive treatments for cancer. Furthermore, TiO₂ NPs exhibit strong antimicrobial activity, offering innovative solutions for infection control in medical devices and implants. Recent advancements in TiO₂-based biosensors have facilitated the sensitive and rapid detection of biomarkers, enhancing diagnostic accuracy. Despite their promising applications, challenges such as potential toxicity and long-term biocompatibility must be addressed through rigorous research and development. This paper highlights the current progress and future perspectives of TiO₂ nanoparticles, underscoring their transformative potential in advancing biomedical technologies.



KEYWORDS

Metal oxide, Titanium oxide, Applications, cancer therapy

1. INTRODUCTION

In recent decades, nanotechnology has revolutionized numerous fields, including medicine, by offering novel approaches to disease diagnosis, treatment, and prevention. Among the diverse range of nanomaterials, titanium dioxide (TiO₂) nanoparticles (NPs) have garnered significant attention due to their exceptional physicochemical properties[1]. TiO₂ NPs are characterized by their high surface area-to-volume ratio, chemical stability, non-toxicity, photocatalytic activity, and biocompatibility, making them highly suitable for a wide array of biomedical applications[2]. These nanoparticles can be synthesized in various forms, including anatase, rutile, and brookite crystalline phases, each with distinct properties that can be tailored to meet specific biomedical requirements[3]. One of the primary advantages of TiO₂ NPs lies in their ability to function as multifunctional agents in therapeutic and diagnostic settings[4]. Their surface can be easily modified to conjugate with bioactive molecules, enabling targeted drug delivery systems that reduce off-target effects and enhance therapeutic efficacy[5]. Additionally, the unique photocatalytic properties of TiO₂, particularly under ultraviolet (UV) or near-infrared (NIR) light, allow for their use in photodynamic and photothermal therapies, providing non-invasive and site-specific treatment options for cancer and other diseases[6]. TiO₂ NPs also play a pivotal role in combating microbial infections, a growing concern in clinical settings due to the rise of antibiotic-resistant pathogens. These nanoparticles exhibit strong antimicrobial properties, attributed to the generation of reactive oxygen species (ROS) under light irradiation, which can effectively kill bacteria, fungi, and viruses[7]. As a result, TiO₂ coatings have been extensively studied for application on medical devices, implants, and surgical instruments to prevent biofilm formation and reduce the risk of infection[8]. Moreover, TiO₂ NPs have shown remarkable potential in biosensing applications, where their optical and electronic properties enable the development of sensitive and selective diagnostic platforms[9]. These biosensors can detect a wide range of biomarkers, including

proteins, nucleic acids, and small molecules, with high precision, making them invaluable tools in early disease detection and monitoring[10]. Despite their promising applications, concerns regarding the safety and long-term biocompatibility of TiO₂ NPs remain a significant challenge. Studies have highlighted potential risks associated with their accumulation in biological systems, oxidative stress induction, and inflammation[11]. As a result, rigorous preclinical and clinical studies are necessary to ensure the safe integration of TiO₂ NPs into medical practice[12]. This comprehensive review delves into the current advancements and challenges in the biomedical applications of TiO₂ nanoparticles. It explores their role in drug delivery, cancer therapy, antimicrobial coatings, and biosensing while discussing strategies to overcome limitations and maximize their potential[13]. By addressing these aspects, this work aims to provide a holistic understanding of how TiO₂ NPs can contribute to the development of innovative, effective, and safe biomedical technologies[14].

2. PROPERTIES OF TiO₂ NANOPARTICLES

Titanium dioxide (TiO₂) nanoparticles possess a range of unique properties that make them particularly valuable in biomedical applications. One of their most significant features is their photocatalytic activity, which enables the generation of reactive oxygen species (ROS) upon exposure to specific wavelengths of light[15]. This capability has been extensively leveraged in antimicrobial treatments and cancer therapies, where ROS play a crucial role in effectively damaging pathogens and malignant cells[16]. Another important property of TiO₂ nanoparticles is their biocompatibility. Due to their inert nature and low toxicity when used at controlled concentrations, these nanoparticles are generally well-tolerated by biological systems. This makes them a suitable choice for a variety of therapeutic and diagnostic applications[17]. Additionally, TiO₂ nanoparticles exhibit excellent surface modifiability. Their surfaces can be functionalized with a diverse array of organic and inorganic materials, enhancing their selectivity, targeting efficiency, and overall functionality[18]. This flexibility allows them to be tailored for specific

biomedical purposes, improving their performance in a variety of contexts[19]. Finally, TiO₂ nanoparticles are known for their high stability. They are highly resistant to degradation in physiological environments, ensuring their structural integrity and prolonged effectiveness even under challenging biological conditions[20]. This stability is a key factor in their reliable performance in long-term applications. Together, these properties underscore the immense potential of TiO₂ nanoparticles in advancing biomedical technologies[21].

3. BIOMEDICAL APPLICATIONS

3.1 Photodynamic And Photothermal Therapy

Titanium dioxide (TiO₂) nanoparticles have emerged as a promising tool in advanced cancer treatments, particularly in photodynamic therapy (PDT) and photothermal therapy (PTT). Their ability to interact with light and generate reactive oxygen species (ROS) under UV or visible light is central to their therapeutic potential. This mechanism induces oxidative stress in targeted cells, leading to cell death, which is especially advantageous for treating cancer due to its selective action[22, 23]. In **Photodynamic Therapy (PDT)**, TiO₂ nanoparticles serve as efficient photosensitizers. Upon light activation, they produce ROS that selectively destroy cancerous cells while minimizing damage to surrounding healthy tissues. This selectivity not only improves treatment efficacy but also reduces adverse side effects, making PDT a safer alternative to conventional cancer therapies[24]. In **Photothermal Therapy (PTT)**, functionalized TiO₂ nanoparticles play a pivotal role in converting light energy into heat. By absorbing specific wavelengths of light, these nanoparticles produce localized heat capable of ablating tumor tissues with high precision[25]. The functionalization

of TiO₂ nanoparticles enhances their light absorption properties and allows for targeted delivery to tumor sites, thereby increasing the therapeutic efficiency of PTT. Together, these therapies showcase the versatility of TiO₂ nanoparticles as a multifunctional platform in the fight against cancer[26].

3.2 Antimicrobial Coatings

Titanium dioxide (TiO₂) nanoparticles are increasingly utilized in antimicrobial coatings due to their potent photocatalytic activity. When exposed to light, TiO₂ nanoparticles generate reactive oxygen species (ROS), which disrupt microbial cell walls, membranes, and DNA[27]. This photocatalytic mechanism effectively inhibits the growth and survival of a wide range of pathogens, including bacteria, viruses, and fungi[28]. One of the key applications of TiO₂-based antimicrobial coatings is in the prevention of biofilm formation on medical devices and implants. Biofilms, which are complex communities of microorganisms adhering to surfaces, pose a significant challenge in clinical settings as they are highly resistant to conventional treatments[29]. By integrating TiO₂ nanoparticles into the surface coatings of medical devices such as catheters, surgical instruments, and implants, biofilm formation can be effectively mitigated. This not only reduces the risk of device-associated infections but also enhances the longevity and safety of these devices in biomedical applications[30]. These coatings, which are durable and highly effective under physiological conditions, represent a valuable advancement in infection control strategies, particularly in hospital environments where the risk of healthcare-associated infections is high. Below is Table 01 in which different type of Titanium oxide along with there use in Antimicrobial activity is shown.

Table 01: Different type of Titanium oxide along with use in Antimicrobial Coating

Serial No	Name of Material	Morphology	Applications	References
01	Titanium Dioxide (TiO ₂)	Nanoparticles	Antimicrobial Coating	[31]
02	TiO ₂ -ZnO Composite	Nanorods	Antibacterial Surface	[32]
03	TiO ₂ -Ag Nanocomposite	Nanotubes	Antiviral Protective Coating	[33]
04	TiO ₂ -PVA Hybrid	Thin Films	Antimicrobial Packaging	[34]
05	TiO ₂ -CuO Composite	Nanoparticles	Self-cleaning Surfaces	[35]
06	Doped TiO ₂ (N-TiO ₂)	Porous Structures	Water Purification Coatings	[36]
07	TiO ₂ -SiO ₂ Composite	Core-Shell Structures	Anti-biofilm Coating	[37]
08	TiO ₂ -Graphene Oxide Hybrid	Nanosheets	Antibacterial Wound Dressings	[38]
09	TiO ₂ -Zeolite Composite	Mesoporous Structures	Food Preservation Coatings	[39]
10	TiO ₂ -Polymer Nanocomposite	Fibrous Networks	Medical Device Coatings	[40]
11	TiO ₂ -Fe ₂ O ₃ Hybrid	Hollow Microspheres	Air Purification via Photocatalysis	[41]
12	TiO ₂ -Au Nanoparticles	Spherical Nanostructures	Antiviral Textile Coatings	[42]
13	TiO ₂ -Carbon Nanotube Blend	Nanorod Bundles	Self-disinfecting Surfaces	[43]
14	TiO ₂ -Cu Nanoparticles	Porous Thin Films	Hospital Sterilization Coatings	[44]
15	TiO ₂ -Al ₂ O ₃ Composite	Nanoaggregates	Food Preservation	[45]

3.3 Drug Delivery Systems

Titanium dioxide (TiO₂) nanoparticles have shown great promise in drug delivery systems due to their unique physicochemical properties. Their high

surface area and ability to bind to a variety of molecules make them ideal carriers for controlled and targeted drug release[46]. The mechanism primarily involves the nanoparticles acting as vehicles to deliver therapeutic agents with precision, minimizing off-target effects and enhancing drug efficacy[47]. One of the major applications of TiO₂ nanoparticles in drug

delivery is the delivery of chemotherapeutic agents directly to tumor sites[48]. By functionalizing the nanoparticles, they can be engineered to specifically target cancer cells, reducing systemic toxicity and improving the therapeutic index of anticancer drugs[49]. Additionally, TiO₂ nanoparticles are utilized in **pH-responsive drug release systems**, taking advantage of the acidic microenvironment of tumors[50]. In such systems, the nanoparticles release their payload in response to the lower pH of the tumor site, ensuring that the therapeutic agents are delivered exactly where they are needed while remaining stable in normal physiological

conditions[51]. Recent advances in this field have focused on functionalizing TiO₂ nanoparticles with specific ligands, which further enhance their selectivity and bioavailability[52]. These functionalized nanoparticles can bind to receptors on the surface of target cells, ensuring precise delivery of the therapeutic agents. This not only improves drug efficacy but also reduces side effects, making TiO₂ nanoparticles a versatile platform for next-generation drug delivery systems[53]. Below is Table 02 Consist of Different type of Titanium Oxide along with their use in Drug delivery System.

Table 02: Titanium oxide and their Applications in Drug Delivery System

Serial No	Name of the Material	Morphology	Application	References
1	Titanium Dioxide (TiO ₂)	Nanoparticles	Controlled Drug Release	[54]
2	TiO ₂ -PEG Nanocomposite	Mesoporous Nanoparticles	Targeted Drug Delivery	[55]
3	TiO ₂ -Doped Hydroxyapatite	Porous Microspheres	Bone Tissue Engineering and Drug Delivery	[56]
4	TiO ₂ -Polylactic Acid (PLA) Hybrid	Nanotubes	Cancer Therapy Drug Carriers	[57]
5	TiO ₂ -Graphene Oxide Hybrid	Nanosheets	Chemotherapeutic Drug Delivery	[58]
6	TiO ₂ -Polymer Nanocomposite	Fibrous Structures	Sustained Release of Antibiotics	[59]
7	TiO ₂ -ZnO Nanocomposite	Hollow Nanoparticles	Multi-drug Delivery Platforms	[60]
8	Doped TiO ₂ (N-TiO ₂)	Nanorods	pH-Sensitive Drug Delivery Systems	[61]
9	TiO ₂ -Silica Composite	Core-Shell Nanoparticles	Dual-Drug Delivery Systems	[62]
10	TiO ₂ -Curcumin Hybrid	Nanoparticles	Anti-inflammatory Drug Delivery	[63]
11	TiO ₂ -Chitosan Composite	Thin Films	Wound Healing and Drug Release	[64]
12	TiO ₂ -Cerium Oxide Hybrid	Porous Nanostructures	Antioxidant Drug Delivery	[65]
13	TiO ₂ -Alumina Nanocomposite	Mesoporous Films	Protein and Peptide Drug Delivery	[66]
14	TiO ₂ -CNT (Carbon Nanotube) Blend	Tubular Nanostructures	Gene Therapy Delivery Systems	[67]

3.4. Tissue Engineering And Regeneration

Titanium dioxide (TiO₂) nanoparticles have gained prominence in tissue engineering and regenerative medicine due to their ability to mimic the natural extracellular matrix. Their surface properties and biocompatibility promote cell adhesion, proliferation, and differentiation, making them an ideal material for scaffold development in tissue regeneration[69]. One key application is in **bone regeneration**, where TiO₂ nanoparticles enhance osteoblast activity and mineralization. The nanoparticles provide a bioactive surface that facilitates the deposition of hydroxyapatite, a key component of bone tissue, thereby accelerating the healing process and improving bone strength[70, 71]. In **cartilage repair**, TiO₂-based scaffolds provide structural support to damaged cartilage tissues. These biocompatible scaffolds not only promote chondrocyte adhesion but also ensure the mechanical integrity required for cartilage regeneration[72]. Advancements in this field have led to the development of **composite scaffolds** that combine TiO₂ nanoparticles with polymers such as collagen or chitosan. These hybrid scaffolds are both bioactive and biodegradable, offering the dual benefits of supporting tissue regeneration and degrading naturally over time as the new tissue forms[73]. Such innovations have paved the way for creating more effective and tailored solutions in tissue engineering[74].

3.5 BIOSENSING AND DIAGNOSTICS

Titanium dioxide (TiO₂) nanoparticles have garnered significant attention in the field of biosensing and diagnostics due to their unique optical and electrochemical properties. These properties enable the sensitive detection of various biomolecules, making TiO₂ a valuable component in advanced biosensing technologies[10]. TiO₂ nanoparticles exhibit high surface area, excellent biocompatibility, and unique

photocatalytic activity, which collectively facilitate their use in biosensing applications. Their optical properties, such as fluorescence quenching and photoabsorption, and electrochemical capabilities, such as electron transfer, enable precise detection of biomolecules[75]. When functionalized with specific recognition elements (e.g., antibodies, enzymes, or DNA probes), TiO₂ nanoparticles can selectively bind target molecules, producing detectable signals for diagnostic purposes[76]. TiO₂ nanoparticles are widely used in glucose sensors to monitor blood sugar levels in diabetic patients. Their photocatalytic properties enhance the oxidation of glucose, resulting in amplified electrochemical signals that improve the sensitivity and accuracy of glucose measurements[77]. In diagnostic devices, TiO₂ nanoparticles are employed to detect DNA sequences, proteins, and specific biomarkers associated with various diseases. For example, nanostructured TiO₂ substrates can enhance the immobilization of biomolecules, improving the stability and sensitivity of assays. This application is critical in early disease detection, such as cancer diagnostics, where identifying biomarkers at low concentrations is crucial[78]. Recent advances in nanotechnology have further elevated the performance of TiO₂-based biosensors. The development of nanostructured TiO₂, such as nanotubes, nanorods, and mesoporous structures, has led to significant improvements in signal amplification and sensitivity[79]. These nanostructures provide a larger active surface area and facilitate better interaction with target molecules. Additionally, the incorporation of TiO₂ nanoparticles with other nanomaterials, such as graphene or gold nanoparticles, has resulted in hybrid sensors with synergistic properties, further enhancing detection capabilities[80]. Overall, TiO₂ nanoparticles continue to revolutionize biosensing and diagnostics, paving the way for more accurate, reliable, and efficient diagnostic tools. Their integration into portable and point-of-care devices holds great promise for improving healthcare outcomes through early disease detection and management[81].

4. FUTURE PERSPECTIVES

To address existing challenges and enhance the biomedical utility of titanium dioxide (TiO₂) nanoparticles, future research must explore several key areas to unlock their full potential in medical applications. These efforts will help overcome current limitations while broadening their scope for clinical use. Surface functionalization is a critical area for improving the biocompatibility and functionality of TiO₂ nanoparticles. Developing advanced coatings and functional ligands can enable more precise targeting in therapeutic applications, reducing off-target effects and enhancing efficacy. Biocompatible polymers, peptides, and antibodies could be used to improve the nanoparticles' interaction with biological environments, facilitating their use in targeted drug delivery and diagnostics. Functionalization also aids in minimizing potential toxicity, ensuring safer biomedical applications. Multifunctionality is another promising direction, focusing on integrating TiO₂ nanoparticles with other nanomaterials such as gold, graphene, or magnetic nanoparticles. These combinations can produce synergistic effects that enhance the nanoparticles' optical, electronic, and therapeutic properties. For example, coupling TiO₂ with gold can amplify its photothermal effects, while integration with graphene can improve conductivity and mechanical strength, making these hybrid materials more versatile for applications like biosensing, imaging, and cancer therapy. Advancements in light activation strategies are essential for expanding the therapeutic applications of TiO₂ nanoparticles. Traditional TiO₂-based photodynamic therapies rely on ultraviolet (UV) light activation, which has limited tissue penetration and potential for causing damage to surrounding tissues. Future research should prioritize the development of visible and near-infrared (NIR) light activation methods to achieve deeper tissue penetration with reduced side effects. This can significantly enhance the effectiveness of TiO₂ nanoparticles in photodynamic and photothermal therapies, particularly for treating cancers and other deep-seated diseases. Comprehensive *in vivo* studies are indispensable for accelerating the clinical translation of TiO₂-based biomedical technologies. While *in vitro* experiments have demonstrated promising results, the safety, biodistribution, and long-term effects of TiO₂ nanoparticles need thorough evaluation in living organisms. These studies should focus on understanding

toxicity, clearance mechanisms, and efficacy in realistic physiological conditions, providing essential data for regulatory approval and clinical adoption. Regenerative medicine offers a significant frontier for the application of TiO₂ nanoparticles, particularly in tissue engineering and scaffolding. While TiO₂ scaffolds are already used for bone regeneration, expanding their use for soft tissue engineering is a promising avenue. Research should aim to optimize the mechanical properties, porosity, and biocompatibility of TiO₂-based scaffolds to support the growth and differentiation of soft tissue cells. Functionalization with biomolecules or growth factors could further enhance their regenerative capabilities, opening new possibilities in wound healing, vascular tissue engineering, and organ repair. By focusing on these strategic areas, future research can overcome the current limitations of TiO₂ nanoparticles and unlock their full potential for diverse biomedical applications. These efforts will not only improve their performance and safety but also pave the way for innovative therapies and diagnostic tools that can transform modern medicine.

5. CONCLUSION

Titanium dioxide (TiO₂) nanoparticles have emerged as a versatile and promising material in the realm of biomedical applications. Their unique physicochemical properties, including high biocompatibility, photocatalytic activity, and optical characteristics, make them suitable for a wide range of medical uses. These applications span cancer therapies, antimicrobial coatings, biosensing, and tissue engineering, showcasing their immense potential in advancing healthcare technologies. One of the most significant applications of TiO₂ nanoparticles is in cancer therapies. Their photocatalytic properties enable their use in photodynamic therapy (PDT) and photothermal therapy (PTT). In PDT, TiO₂ nanoparticles generate reactive oxygen species (ROS) upon light activation, leading to the targeted destruction of cancer cells. This approach minimizes damage to surrounding healthy tissues compared to conventional cancer treatments. Efforts to improve light penetration using visible and near-infrared (NIR) wavelengths have further enhanced the efficacy of TiO₂-based PDT, making it a promising tool for treating deep-seated tumors. Additionally, their ability to be functionalized with targeting ligands, such as peptides or

antibodies, enables the precise delivery of therapeutic agents, paving the way for more personalized cancer treatments. In the fight against infections, TiO₂ nanoparticles have proven to be effective antimicrobial agents. Their photocatalytic generation of ROS disrupts microbial cell membranes and DNA, making them highly effective against a broad spectrum of pathogens, including bacteria, fungi, and viruses. This property has led to their incorporation into antimicrobial coatings for medical devices, implants, and hospital surfaces, reducing the risk of healthcare-associated infections. Moreover, the long-lasting antimicrobial activity of TiO₂ nanoparticles under light exposure makes them an excellent candidate for sustainable and self-disinfecting surfaces. The field of tissue engineering has also benefited from the unique attributes of TiO₂ nanoparticles. They are widely used in the development of scaffolds for bone regeneration due to their excellent mechanical strength, biocompatibility, and osteogenic properties. These scaffolds provide a supportive framework for cell attachment, proliferation, and differentiation, facilitating the repair of damaged bone tissue. Beyond bone applications, recent research is exploring their potential in soft tissue engineering, such as vascular and skin tissue regeneration. Functionalization with bioactive molecules or growth factors can further enhance their regenerative capabilities, expanding their use in complex tissue engineering applications. Despite their many advantages, challenges remain in the widespread clinical adoption of TiO₂ nanoparticles. Toxicity concerns, particularly the generation of ROS and their interaction with healthy cells, need to be thoroughly addressed through careful design and functionalization. Coating TiO₂ nanoparticles with biocompatible materials or polymers can mitigate these effects, improving their safety profile. Additionally, the scalability of TiO₂ nanoparticle production for clinical use is an ongoing challenge. Developing cost-effective and reproducible synthesis methods that meet regulatory standards is essential for translating laboratory research into practical medical applications. Advances in material engineering and functionalization techniques continue to push the boundaries of TiO₂ nanoparticle applications. By combining TiO₂ with other nanomaterials such as gold, graphene, or magnetic nanoparticles, researchers are creating hybrid systems with enhanced properties, such as improved light absorption, stronger antimicrobial

activity, and multifunctionality. These advancements enable TiO₂ nanoparticles to be tailored for specific medical applications, ranging from precision therapies to real-time diagnostics. With continued research and development, TiO₂ nanoparticles are poised to play a pivotal role in the future of medicine. Their integration into innovative treatment modalities and medical devices holds the potential to revolutionize healthcare by enabling more effective, targeted, and personalized treatments. As researchers overcome the current challenges and expand their applications, TiO₂ nanoparticles are likely to become a cornerstone of next-generation biomedical technologies.

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Conflicts of interest

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