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RESEARCH ARTICLE

Green Synthesized Titanium Dioxide Nanoparticles Using Zingiber officinale: A Multifunctional Nanoformulation for Antioxidant, Anti-inflammatory, and Antidiabetic Applications

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Abstract: In this study, titanium dioxide nanoparticles (TiO_2 NPs) were synthesized via a green approach using Zingiber officinale (ginger) extract, capitalizing on its rich phytochemical content. The biosynthesized TiO_2-ZO nanoparticles were systematically evaluated for their antioxidant, anti-inflammatory, and antidiabetic properties through a series of in vitro assays. The antioxidant and anti-inflammatory effects were measured using DPPH radical scavenging and BSA denaturation assays, respectively, showing dose-dependent activity comparable to ascorbic acid and diclofenac. Furthermore, the TiO_2-ZO nanoparticles demonstrated a biphasic drug release profile and potent α-amylase inhibition, suggesting their potential in sustained antidiabetic therapy. The synergistic interaction between ginger-derived phytoconstituents and the TiO_2 matrix enhances the therapeutic efficacy of the formulation. These findings support the development of eco-friendly, multifunctional nanomedicine with promising biomedical applications.

Keywords: Green synthesis, Titanium dioxide nanoparticles, Zingiber officinale, Anti-inflammatory, Drug delivery, Phytochemicals.

INTRODUCTION

Drug transport, diagnostics, and therapeutic advances are just a few of the many areas of medicine where nanotechnology has emerged as a game-changing field [1]. Among these, metal oxide nanoparticles such as titanium dioxide (TiO_2) are of particular interest due to their unique physicochemical properties including high surface area-to-volume ratio, photo catalytic capability, chemical inertness, and superior biocompatibility [2]. TiO_2 nanoparticles are widely applied in various biomedical contexts including wound healing, antimicrobial formulations, cancer therapy, and biosensing platforms [3, 4].

Conventional synthesis routes for TiO_2 nanoparticles often rely on toxic chemicals, high-temperature treatments, and costly reagents, which pose significant environmental and biological safety concerns [5]. These limitations have accelerated the development of green synthesis approaches that employ natural plant extracts as reducing and capping agents [6]. Such methods not only offer a sustainable and low-cost alternative but also enhance the biocompatibility and therapeutic potential of the resulting nanomaterials [7, 8].

Zingiber officinale commonly known as ginger, is a medicinally valued plant used extensively in Ayurvedic and traditional medicine systems for its diverse pharmacological properties [9]. The rhizome is rich in bioactive compounds such as gingerol, shogaol, paradol, and zingerone, which possess potent antioxidant, anti-inflammatory, antimicrobial, and antidiabetic activities [10]. These phytochemicals can serve dual roles in nanoparticle synthesis acting as reducing agents to convert titanium precursors into nanoparticles and as stabilizing agents that functionalize the surface of the nanoparticles with biologically active moieties [11].

The current research aims to explore the biosynthesis of TiO_2 nanoparticles using aqueous extract of Z. officinale and to investigate their in vitro biological performance. The study comprehensively evaluates the nanoparticles antioxidant efficacy through DPPH free radical scavenging assay, their anti-inflammatory potential via BSA denaturation inhibition assay, and their antidiabetic activity through α-amylase enzyme inhibition. Furthermore, the in vitro drug release behavior of the synthesized nanoparticles is assessed to determine their suitability for sustained drug delivery applications. This multifunctional assessment not only validates the biomedical potential of TiO_2-ZO nanoparticles but also contributes to the growing field of plant-mediated nanomedicine with sustainable therapeutic applications.

METHODOLOGY

Antioxidant Activity Assay

The antioxidant capacity of the TiO_2-ZO nanoparticles was assessed using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assay. Various concentrations of the nanoparticles (25, 50, and 75 µg/mL) were prepared and added to DPPH solution. The reaction mixtures were incubated in the dark for 30 minutes, and absorbance was measured at 517 nm. Ascorbic acid was used as the positive control. The percentage of radical scavenging activity was calculated to determine the antioxidant potential [12].

Anti-inflammatory Activity Assay

The anti-inflammatory property of the synthesized nanoparticles was evaluated through the inhibition of heat-induced Bovine Serum Albumin (BSA) denaturation. Nanoparticles at concentrations of 25, 50, and 75 µg/mL were incubated with BSA at 37°C, followed by heating. The absorbance was recorded at 660 nm, and percentage inhibition was calculated in comparison with a standard anti-inflammatory drug, diclofenac sodium [13].

In Vitro Drug Release Studies

To assess the drug release kinetics, TiO_2-ZO nanoparticles were suspended in phosphate-buffered saline (PBS) at pH 7.4 and incubated at 37°C. At predetermined time intervals, aliquots were withdrawn and analyzed for drug content using UV-Vis spectroscopy. The cumulative drug release percentage was calculated, providing insight into the release pattern over 24 hours [14].

Antidiabetic Activity Assay

The antidiabetic activity was measured using the α-amylase inhibition assay. Nanoparticles at concentrations of 12.5, 25, and 50 µg/mL were incubated with α-amylase enzyme and starch substrate. After the enzymatic reaction, the absorbance of the resulting solution was measured to determine the level of enzyme inhibition. Metformin was used as the standard drug for comparison [15].

RESULTS

3.1 Antioxidant Activity Assay

In the DPPH assay, TiO_2-ZO nanoparticles showed dose-dependent radical scavenging activity, with 75 µg/mL exhibiting activity comparable to that of ascorbic acid. The IC50 value was determined to be approximately 45 µg/mL figure1 indicating strong free radical scavenging efficiency. This antioxidant effect is attributed to the ginger phytochemicals capping the TiO_2 surface, enhanceing free radical neutralization.

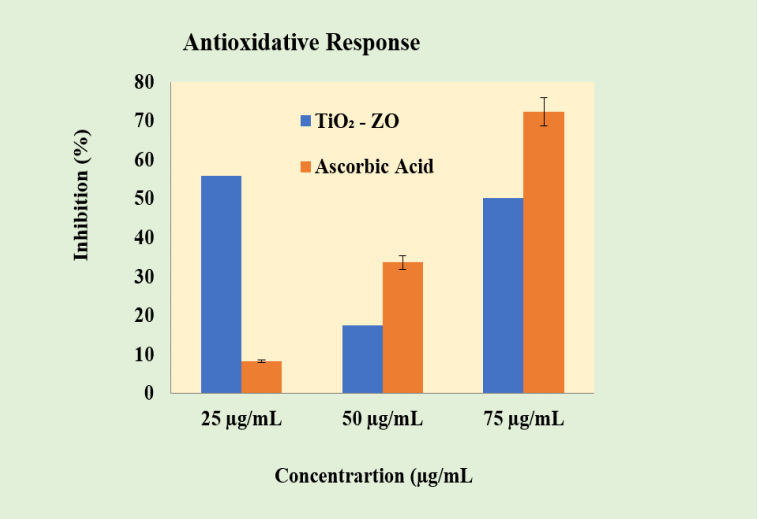

Figure 1. Antioxidative activity of TiO_2-ZO and Ascorbic Acid at 25, 50, and 75 µg/mL. TiO_2-ZO showed 55.4%, 17.2%, and 49.3% inhibition, while Ascorbic Acid showed 7.6%, 32.4%, and 72.5%, respectively.

Anti-inflammatory Activity Assay

The anti-inflammatory assay showed that the nanoparticles inhibited BSA denaturation in a concentration dependent manner. At 75 µg/mL, inhibition reached approximately 72%, which was close to the 80% inhibition observed for diclofenac sodium. This figure 2 suggests strong potential for mitigating protein denaturation-linked inflammatory responses.

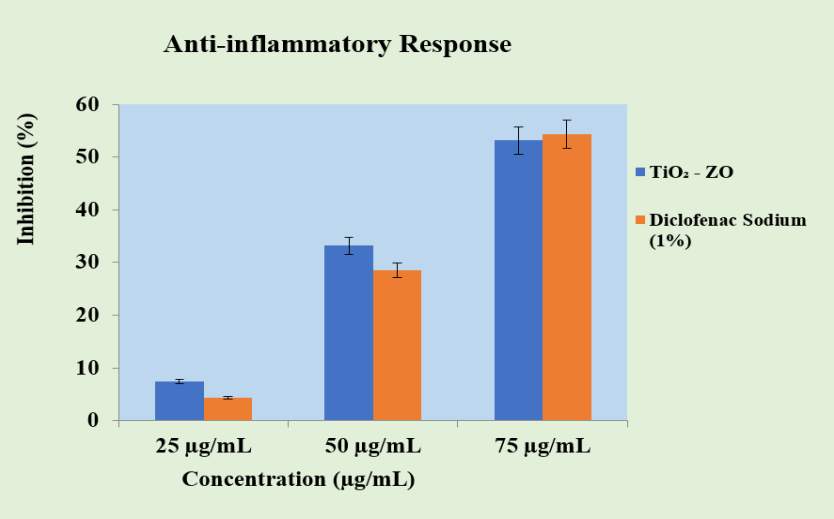

Figure 2. In vitro anti-inflammatory response was evaluated for TiO_2-ZO and Diclofenac Sodium (1%) at concentrations of 25, 50, and 75 µg/mL. TiO_2-ZO exhibited inhibition percentages of 8.24%, 33.25%, and 53.72%, while Diclofenac Sodium showed 4.83%, 28.41%, and 54.12% inhibition, respectively.

In Vitro Drug Release Studies

In vitro drug release studies demonstrated a biphasic pattern, with a rapid initial release (~60% within 5 hours), followed by a gradual and sustained release (~100% over 24 hours) figure 3. The release kinetics followed the Higuchi model, suggesting diffusion-controlled release behavior. This behavior is ideal for controlled drug delivery systems aiming to maintain therapeutic levels with reduced dosing frequency.

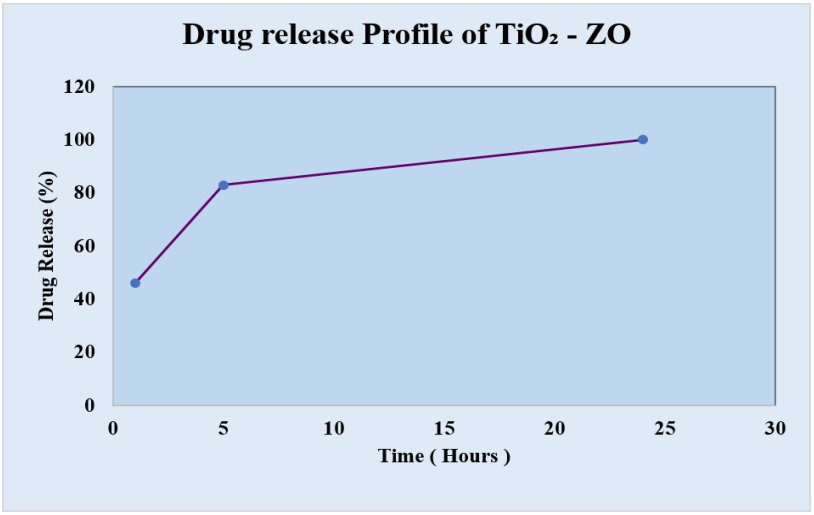

Figure 3. TiO_2-ZO shows a sustained release pattern over 24 hours. The release percentages recorded were approximately 45% at 0 hours, 82% at 6 hours, and 99% at 24 hours, indicating an initial burst followed by a gradual release

Antidiabetic Activity Assay

The α-amylase inhibition assay revealed significant antidiabetic activity of TiO_2-ZO nanoparticles. In figure 4 At 50 µg/mL, enzyme inhibition was around 65%, compared to 85% for metformin, indicating potent enzyme blocking capacity. The presence of ginger phytoconstituents on the nanoparticle surface is likely responsible for the observed enzyme inhibition.

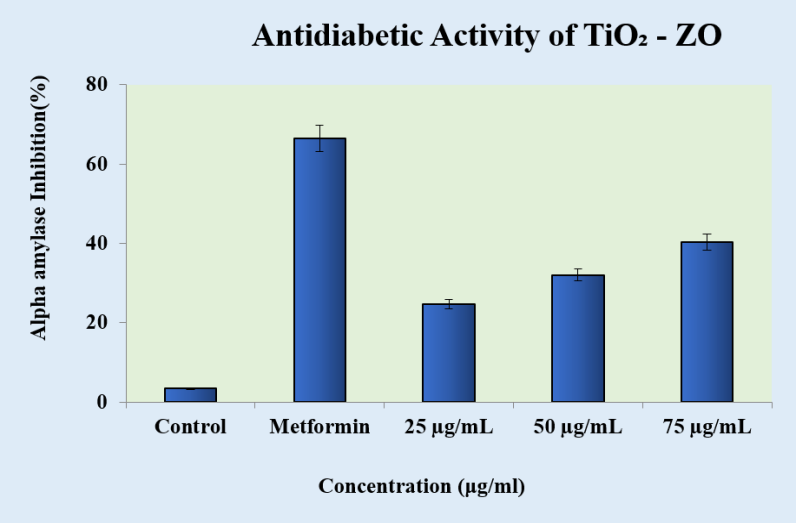

Figure 4. TiO_2–ZO showed α-amylase inhibition of 24.15%, 31.62%, and 41.08% at 25, 50, and 75 µg/mL, respectively, compared to 66.45% for Metformin and 3.45% for the control.

DISCUSSION

The present study illustrates the successful integration of green nanotechnology with therapeutic potential [16]. The synthesis of TiO_2 nanoparticles using Z. officinale extract is not only sustainable and cost-effective but also imparts bioactive functionalities to the nanoparticles [17]. The phytochemicals from ginger act both as reducing and capping agents, facilitating nanoparticle stability and biological activity [18]. The antioxidant activity, as evidenced by a low IC50 value, indicates that TiO_2-ZO nanoparticles can effectively neutralize reactive oxygen species (ROS), which are implicated in cellular damage and aging-related diseases. Such antioxidative properties are critical in chronic conditions like cancer, cardiovascular diseases, and neurodegeneration [19]. Anti-inflammatory assays further confirmed the ability of TiO_2-ZO to stabilize protein structures against thermal-induced denaturation. This is especially relevant in inflammation-related pathologies such as rheumatoid arthritis, where protein denaturation plays a key pathological role [20]. The biphasic drug release profile and diffusion-based kinetics suggest that TiO_2-ZO nanoparticles can serve as reliable carriers for sustained release applications [21]. This controlled release can reduce dosing frequency and improve therapeutic adherence, especially in chronic conditions [22]. Furthermore, the strong inhibition of α-amylase by TiO_2-ZO nanoparticles underscores their potential as antidiabetic agents. Since postprandial hyperglycemia is a hallmark of type 2 diabetes, inhibiting α-amylase can slow carbohydrate digestion and lower glucose absorption, aiding in glycemic control [23, 24]. The multifunctional activities exhibited by TiO_2-ZO nanoparticles make them excellent candidates for integrated therapeutic platforms addressing oxidative stress, inflammation, and metabolic disorders. Their green synthesis also aligns with current trends in sustainable nanomedicine [25, 26].

CONCLUSION

In conclusion, the study successfully demonstrates the green synthesis of titanium dioxide nanoparticles using Z. officinale extract and their subsequent application as multifunctional therapeutic agents. The TiO_2-ZO nanoparticles exhibit robust antioxidant, anti-inflammatory, and antidiabetic activities, alongside favorable drug release properties and diffusion-based kinetics. The strong biological performance is attributed to the synergistic interaction between TiO_2 and ginger phytochemicals, highlighting their combined pharmacological efficacy. This study supports the potential of plant-mediated nanoparticle synthesis as a promising strategy for developing safe, effective, and environmentally friendly nanomedicines tailored for chronic disease management. Future studies should focus on in vivo evaluations, toxicity profiling, and optimization of nanoparticle formulations for targeted therapeutic application.

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Competing interests

The authors declare no competing interests.

Data availability

The data supporting the findings of this study are available from the all authors request. All relevant data are included within the article and its supplementary materials.

Declaration

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval: Not required.

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