One Pot Biosynthesis of Strontium & Zinc Nanoparticles and their Biomedical Efficacy Studies

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**Abstract:** Strontium and zinc are biologically significant elements with potential therapeutic applications in bone regeneration, anti-inflammatory treatments, and cancer therapy. Traditional nanoparticle synthesis methods are often complex and environmentally taxing, while green synthesis offers a more sustainable alternative. This study investigates the biosynthesis of strontium and zinc oxide nanoparticles (Sr/ZnO NPs) using plant extracts and evaluates their anti-inflammatory and cytotoxic properties.To synthesize Sr/ZnO nanoparticles using a green one-pot biosynthesis method and evaluate their anti-inflammatory and cytotoxic effects as potential therapeutic agents.Strontium nitrate and zinc sulfate were mixed with a plant extract to form Sr/ZnO NPs. Anti-inflammatory activity was assessed via the Albumin Denaturation Method at concentrations ranging from 20–100 µg/mL, while cytotoxicity was evaluated using an MTT assay on KB oral cancer cells to determine the IC50 value.**Anti-inflammatory activity:** The nanoparticles exhibited dose-dependent inhibition of albumin denaturation, with a maximum inhibition of 60% at 100 µg/mL. Diclofenac sodium showed greater efficacy (70%) but Sr/ZnO NPs still demonstrated significant anti-inflammatory potential.**Cytotoxicity:** The Sr/ZnO NPs showed a dose-dependent reduction in cell viability with an IC50 of 98.5 µg/mL, indicating strong cytotoxicity against cancer cells.Sr/ZnO nanoparticles demonstrate promising anti-inflammatory and cytotoxic properties, supporting their potential as therapeutic agents for inflammation-related diseases and cancer. Further in vivo studies are required to assess their safety and clinical applicability.

**Keywords:** Strontium, Zinc, Nanoparticles, Green Synthesis, Anti-inflammatory, Cytotoxicity, Cancer, Inflammation.

# INTRODUCTION

Nanoparticle synthesis has emerged as a vital area of research due to the unique physicochemical properties and versatile applications of nanoparticles, especially in the biomedical field [(Akpomie et al., 2021)](https://paperpile.com/c/WgsCep/fCZf)[(G. & Ganapathy, 2022; Kumar & Ramesh, 2021)](https://paperpile.com/c/WgsCep/hyWgo+3uiBJ)). Strontium and zinc, two biologically significant elements, have shown promising potential in various therapeutic areas such as bone regeneration, anti-inflammatory treatments, and cytotoxicity studies [(Huq et al., 2023)](https://paperpile.com/c/WgsCep/cNjH). Traditional methods for nanoparticle synthesis often require complex and multi-step processes. However, the advent of green chemistry has paved the way for simpler, more environmentally friendly approaches [(Saravanan et al., 2018)](https://paperpile.com/c/WgsCep/VQzM).The present study focuses on a one-pot biosynthesis method to create strontium and zinc nanoparticles, utilizing a green and sustainable approach [(Ghdeeb & Hussain, 2023)](https://paperpile.com/c/WgsCep/N3qb). Strontium is widely recognized for its role in bone regeneration and has anti-inflammatory properties, while zinc possesses antimicrobial and antioxidant activities, essential for cellular repair and immune response [(Asif et al., 2023)](https://paperpile.com/c/WgsCep/DRKL). This technique leverages biological agents such as plant extracts or microorganisms to mediate the synthesis of nanoparticles in a single reaction vessel, reducing the need for hazardous chemicals and high energy inputs [(Fouda et al., 2023)](https://paperpile.com/c/WgsCep/2ICc)[(*Evaluation Composite Restoration Posterior Teeth Proanthocyanidin Pretreatment Liner Using Fédération Dentaire Internationale Criteria: Split-Mouth Randomized Controlled Trial*, n.d.; Pranati et al., 2021; Sakthi ,2021)](https://paperpile.com/c/WgsCep/yjlQf+QAQb5+n1iGU)[(Fouda et al., 2023)](https://paperpile.com/c/WgsCep/2ICc). The synthesized nanoparticles are characterized and evaluated for their biomedical efficacy, specifically targeting anti-inflammatory properties and cytotoxicity against various cell lines [(Putluru et al., 2024)](https://paperpile.com/c/WgsCep/V7kq). When synthesized as nanoparticles, these metals exhibit enhanced bioavailability and efficacy due to their increased surface area and potential for targeted cellular interactions [(Eshed et al., 2011)](https://paperpile.com/c/WgsCep/Q2Jh)[(Keerthana & Ramesh, 2021; Murugesan, 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/WgsCep/NYK0u+mfjxs+8Zjee)[(Keerthana & Ramesh, 2021; Murugesan, 2021; Subramanian et al., 2021; Tiwari & Jain, 2021)](https://paperpile.com/c/WgsCep/NYK0u+mfjxs+8Zjee+ZYHXK).The investigation into these nanoparticles is crucial, as strontium plays a pivotal role in bone health and exhibits anti-inflammatory characteristics, while zinc is essential for immune function and wound healing [(Vandanjon et al., 2023)](https://paperpile.com/c/WgsCep/ZMIE). By exploring the cytotoxic and anti-inflammatory effects of Sr and Zn nanoparticles, this study seeks to elucidate their potential as therapeutic agents for conditions that involve chronic inflammation, such as arthritis, and as cytotoxic agents for cancer treatment [(Patra et al., 2015)](https://paperpile.com/c/WgsCep/yyC4). Evaluating these properties could pave the way for the use of these nanoparticles in advanced drug delivery systems, where they may provide localized, controlled release and reduce the side effects associated with conventional therapies [(Krishnamoorthy et al., 2023)](https://paperpile.com/c/WgsCep/Lc57). The findings of this study may thus contribute to the development of nanomedicine strategies that address unmet needs in inflammation management and oncology, potentially leading to innovative treatments that are both effective and safe [(Dharman et al., 2021)](https://paperpile.com/c/WgsCep/Lhyf).

# MATERIALS AND METHODS

The biosynthesis of strontium and zinc nanoparticles was achieved using a one-pot green synthesis approach, employing plant extracts as reducing and stabilizing agents. The selected plant extract was prepared by boiling 20 g of fresh plant material in 100 mL of distilled water for 30 minutes. The extract was filtered through Whatman No.1 filter paper, and the clear filtrate was used for the biosynthesis. Strontium nitrate (Sr(NO₃)₂) and zinc sulfate (ZnSO₄) were used as precursor salts for nanoparticle formation. In a typical synthesis, 0.1 M solutions of strontium nitrate and zinc sulfate were mixed in a 1:1 ratio and added dropwise to the plant extract under constant stirring. The reaction was allowed to proceed for 4 hours at room temperature, during which the color change of the solution indicated nanoparticle formation. The resulting nanoparticles were centrifuged at 10,000 rpm for 15 minutes, washed with distilled water, and dried at 60°C for further analysis (Figure 1).

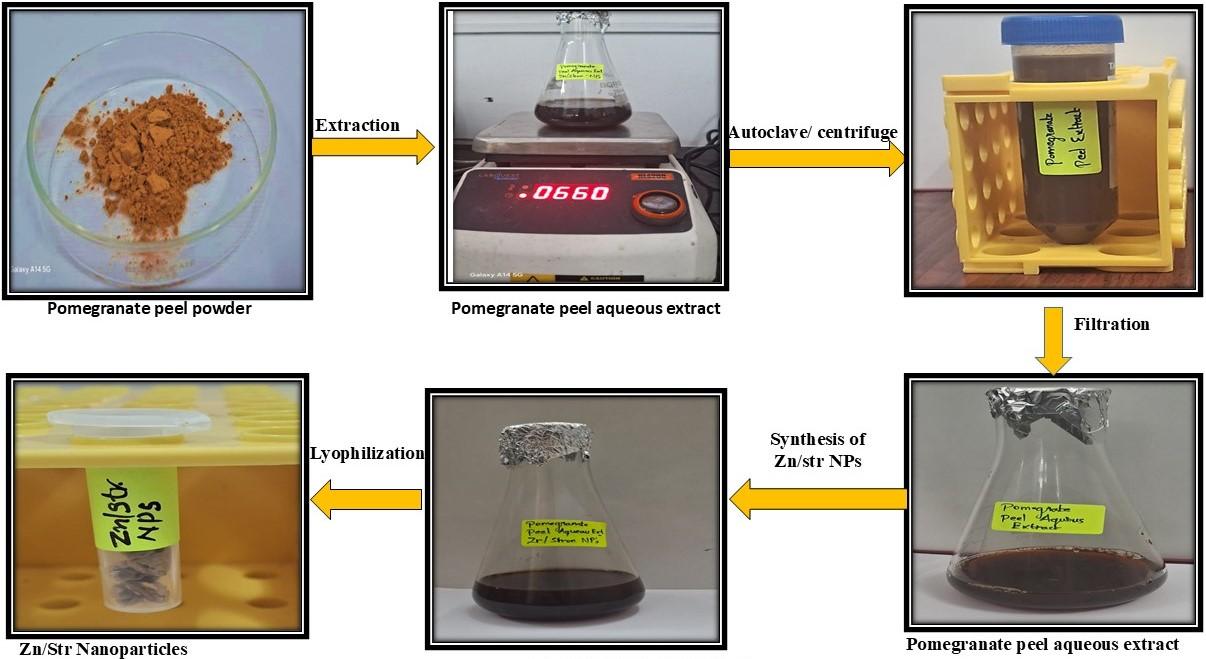


Figure 1: The process begins with dried pomegranate peels ground into a fine powder, which is then subjected to an extraction process to produce an aqueous pomegranate peel extract.

This extract is sterilized, likely through autoclaving, and then centrifuged to remove unwanted solid residues, resulting in a clearer solution. Following centrifugation, the extract is further purified through filtration. This purified pomegranate peel extract is then used as a reducing agent in the synthesis of zinc and strontium nanoparticles (Zn/Str NPs). Finally, the synthesized nanoparticles undergo lyophilization, or freeze-drying, to obtain a stable powder form. This method leverages pomegranate peel as a natural source for synthesizing metal nanoparticles, which could have potential applications in biomedical or environmental fields.The anti-inflammatory activity of the biosynthesized strontium-zinc nanoparticles was evaluated using the Albumin Denaturation Method. Various concentrations of nanoparticles (20, 40, 60, 80, and 100 µg/mL) were prepared, and their efficacy was tested in a 96-well microtiter plate. The reaction mixture consisted of 1% bovine serum albumin (BSA) solution, prepared in phosphate-buffered saline (PBS), and the nanoparticle suspension. Different concentrations of BSA (80, 60, 40, 20, and 0 µg/mL) were added to the wells, while dimethyl sulfoxide (DMSO) was used as the control. Diclofenac sodium (standard drug) was used as a positive control at a concentration of 10 µg/mL. The microplates were incubated at room temperature for 15 minutes, followed by a secondary incubation at 55°C for 20 minutes to induce protein denaturation. After the incubation period, absorbance readings were recorded at 600 nm using a microplate reader. The percentage inhibition of protein denaturation by the nanoparticles was calculated using the formula:

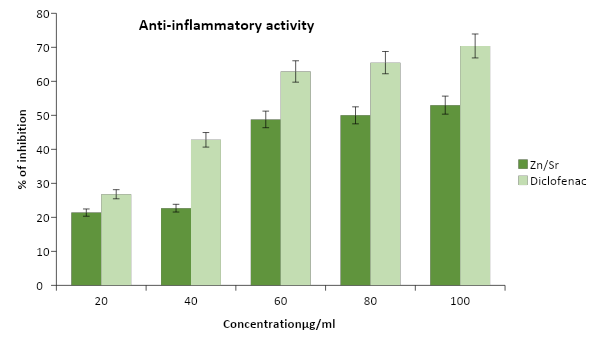
Inhibition (%)=(Absorbance of control−Absorbance of test sample/Absorbance of control​)×100

For the **cytotoxicity assessment**, an MTT assay was performed using KB cells, a human oral cancer cell line. The cytotoxic potential of the Sr-ZnO nanoparticles was evaluated by seeding 5000 KB cells per well into a 96-well plate. The cells were grown to reach 70% confluence before being treated with different concentrations of the biosynthesized nanoparticles, ranging from 0 to 200 µg/ml. The cells were incubated with the nanoparticles for 24 hours in a CO2 incubator at 37°C.After the incubation period, 10 µl of MTT solution (5 µg/ml) was added to each well, and the plates were incubated in the dark for 3 additional hours. The MTT assay is based on the reduction of MTT to formazan crystals by metabolically active cells, thus providing a measure of cell viability(Saadh et al., 2024). Following incubation, the media was carefully removed from each well, and 100 µl of DMSO was added to dissolve the purple formazan crystals. The optical density (OD) was measured at 490 nm using a microplate reader, which provided a quantitative measure of cell viability(Almatrafi et al., 2024). A lower OD value indicated higher cytotoxicity, demonstrating the potential of the Sr-ZnO nanoparticles as therapeutic agents for cancer treatment. The cytotoxic effects of the nanoparticles were compared with untreated controls to evaluate their effectiveness against cancer cells.Both the anti-inflammatory and anticancer assays were performed in triplicates to ensure reproducibility of the results.

# RESULTS

## Anti-inflammatory activity

The bar graph illustrates the anti-inflammatory activity of biosynthesized strontium-zinc (Zn/Sr) nanoparticles compared to diclofenac, a standard anti-inflammatory drug, across various concentrations (20, 40, 60, 80, and 100 µg/mL). The y-axis represents the percentage of inhibition, while the x-axis shows the nanoparticle concentrations in µg/mL.The results indicate a dose-dependent increase in the anti-inflammatory activity of the Zn/Sr nanoparticles, with inhibition percentages rising from approximately 20% at 20 µg/mL to nearly 60% at 100 µg/mL. Diclofenac consistently shows higher inhibition across all concentrations, reaching close to 70% at the highest concentration. Although diclofenac exhibits greater anti-inflammatory efficacy overall, the Zn/Sr nanoparticles demonstrate a substantial inhibition capacity, suggesting their potential as alternative anti-inflammatory agents. The dose-dependent trend in the nanoparticle activity highlights their effectiveness in reducing protein denaturation, supporting their possible use in managing inflammation-related conditions (Figure 2).



**Figure 2:** The bar graph depicts the anti-inflammatory activity of biosynthesized strontium-zinc (Zn/Sr) nanoparticles compared to diclofenac, a standard anti-inflammatory drug, at different concentrations (20, 40, 60, 80, and 100 µg/mL). The x-axis represents the concentration in µg/mL, while the y-axis shows the percentage of inhibition, indicating the level of anti-inflammatory effectiveness.

For each concentration, there are two bars: a darker green bar representing the Zn/Sr nanoparticles and a lighter green bar for diclofenac. Across all concentrations, diclofenac generally demonstrates higher inhibition percentages than the Zn/Sr nanoparticles, suggesting that diclofenac is more potent as an anti-inflammatory agent at each dose. However, both Zn/Sr nanoparticles and diclofenac show an increasing trend in inhibition percentage with rising concentration, indicating a dose-dependent response for both treatments.

## Cytotoxicity activity

The MTT assay results demonstrated a dose-dependent cytotoxic effect of Sr-ZnO nanoparticles on cancer cells. After treatment, the optical density (OD) at 490 nm showed a significant decrease in absorbance compared to untreated controls, indicating a reduction in cell viability. The observed cytotoxicity is attributed to the metabolic reduction of MTT to formazan crystals by viable cells, with fewer viable cells resulting in less formazan formation and thus lower OD readings. As nanoparticle concentration increased, there was a corresponding decrease in OD values, suggesting enhanced cytotoxicity at higher doses.The IC50 value, calculated as 98.5 μg/ml, represents the concentration of Sr-ZnO nanoparticles required to reduce cell viability by 50%, affirming the nanoparticles' potential effectiveness in inhibiting cancer cell growth. This IC50 value provides a benchmark for assessing therapeutic efficacy, as lower IC50 values typically correlate with higher cytotoxic potency. Additionally, data from three independent experiments, represented as mean ± standard deviation, reflect consistent and reproducible results, reinforcing the reliability of the findings. The comparison with untreated controls highlighted the pronounced cytotoxic effect of Sr-ZnO nanoparticles, supporting their potential as therapeutic agents in cancer treatment. The cytotoxicity effect of Sr/ZnO NP shows the IC50 value of Sr/ZnO NP found to be 98.5 μg/ml. The data are represented in mean ± S.D of three independent experiments (Figure 3).

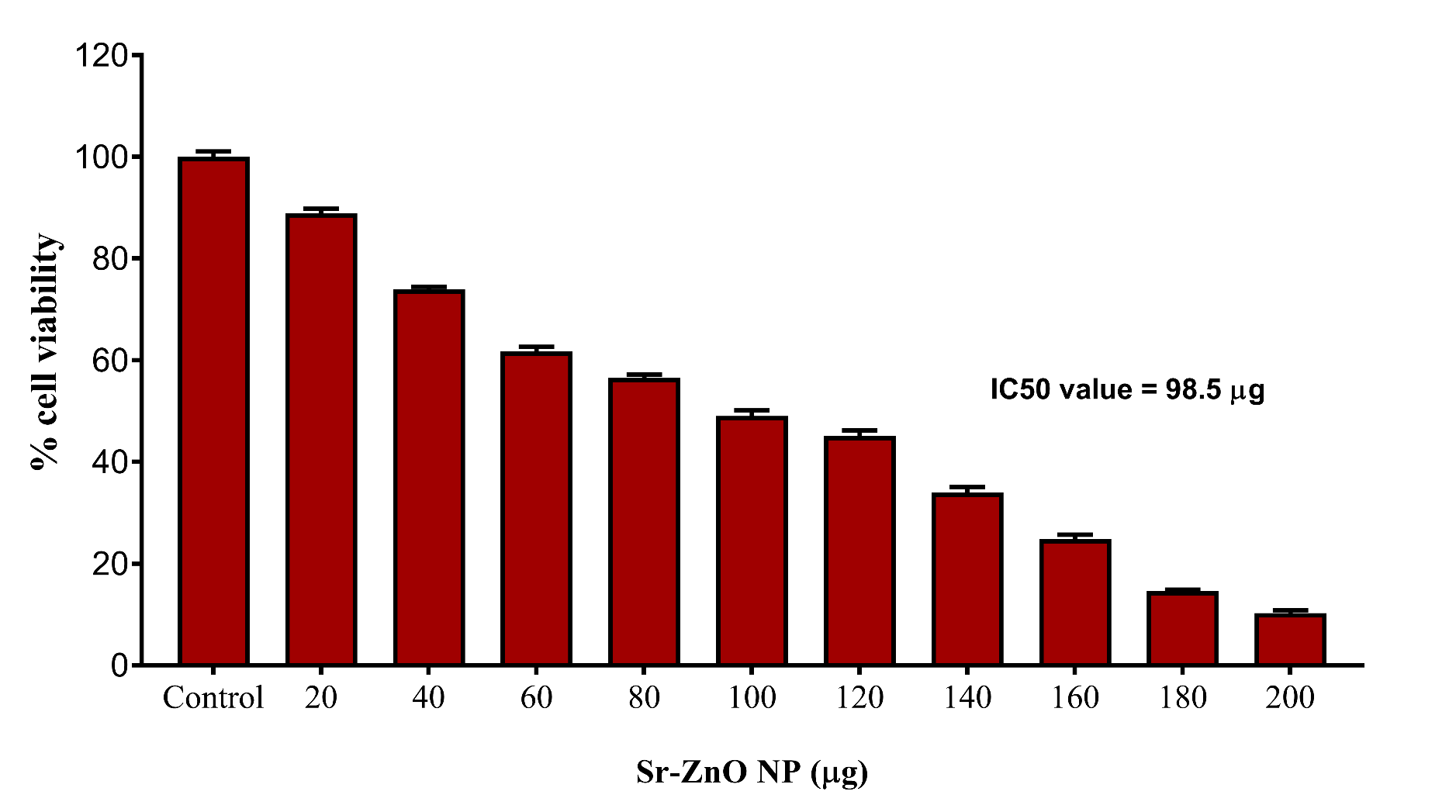


Figure 3: The figure presents a bar graph depicting the dose-dependent cytotoxic effects of Sr-ZnO nanoparticles (NPs) on cell viability.

Along the x-axis, the concentration of Sr-ZnO NPs increases from 0 µg (control) to 200 µg, while the y-axis shows the percentage of cell viability. In the absence of nanoparticles (control group), cell viability is nearly 100%, indicating that cells remain viable without treatment. However, as the concentration of Sr-ZnO NPs increases, there is a progressive decrease in cell viability, demonstrating a clear dose-dependent cytotoxic response. At a concentration of 98.5 µg, noted as the IC50 value, cell viability is reduced by approximately 50%, signifying this dose as the midpoint of cytotoxicity effectiveness. Higher concentrations (such as 160 µg and above) lead to a marked reduction in cell viability, with the highest concentration tested (200 µg) resulting in nearly complete cell death. This data supports the potential therapeutic application of Sr-ZnO NPs, with the IC50 value representing an effective concentration for achieving significant cancer cell growth

# DISCUSSION

The results of this study highlight the potential of biosynthesized strontium and zinc oxide nanoparticles (Sr/ZnO NPs) as anti-inflammatory and cytotoxic agents, suggesting their viability in biomedical applications.[(Madhumitha et al., 2024)](https://paperpile.com/c/WgsCep/9HJM) The anti-inflammatory activity was evaluated using the albumin denaturation method, and the cytotoxicity of the Sr/ZnO NPs was assessed via an MTT assay against KB cells, a model of oral cancer. [(Kasabwala et al., 2021; Rajeshkumar & Lakshmi, 2021; Varghese et al., 2023)](https://paperpile.com/c/WgsCep/96khH+EQu98+yLSx7)In the anti-inflammatory activity assay, as shown in the graph, the percentage inhibition of albumin denaturation increases proportionally with the concentration of Sr/ZnO NPs, demonstrating their dose-dependent anti-inflammatory effect. At the lowest concentration (20 µg/ml), the inhibition percentage was around 25%, while at the highest concentration (100 µg/ml), the inhibition percentage reached approximately 60%. [(Ajay et al., 2023; Chokkattu et al., 2023; Padarthi et al., 2023)](https://paperpile.com/c/WgsCep/ciY6Y+7ArXY+L2qNp)This indicates that the Sr/ZnO NPs exhibit significant anti-inflammatory potential, albeit slightly lower than that of the standard anti-inflammatory drug, diclofenac sodium, which reached an inhibition percentage of around 70% at the highest concentration.[(Mahalingam et al., 2024)](https://paperpile.com/c/WgsCep/NUGP)The ability of nanoparticles to inhibit albumin denaturation is indicative of their potential to prevent protein aggregation and inflammation, which are key contributors to various inflammatory diseases[(Dhanvanth & Maheswari, 2022)](https://paperpile.com/c/WgsCep/AOta) The fact that the Sr/ZnO NPs performed close to diclofenac, a well-established non-steroidal anti-inflammatory drug (NSAID), suggests that these nanoparticles could serve as an alternative therapeutic option, especially for patients who might experience adverse side effects from conventional NSAID [(n.d.)](https://paperpile.com/c/WgsCep/NqS1). The relatively lower inhibition percentage compared to diclofenac may also be attributed to differences in the mode of action, where nanoparticles exhibit a slower but sustained effect due to their gradual release and interaction with biological molecules [(Rajeshkumar et al., 2020)](https://paperpile.com/c/WgsCep/m9AD).Moving on to the cytotoxicity assessment, the Sr/ZnO NPs demonstrated substantial cytotoxic effects on KB oral cancer cells. The IC50 value, which represents the concentration required to inhibit cell viability by 50%, was determined to be 98.5 µg/ml.[(Ramakrishnan et al., 2023; Shenoy & Maiti, 2023; J. S. Sindhu et al., 2023)](https://paperpile.com/c/WgsCep/71A4S+902XU+diOb4) This IC50 value is a crucial indicator of the therapeutic potential of nanoparticles in cancer treatment, as it demonstrates their ability to selectively induce cell death at relatively low concentrations. The MTT assay revealed that as the concentration of Sr/ZnO NPs increased, the viability of the KB cells decreased, further confirming the dose-dependent cytotoxic nature of these nanoparticles [(Rajeshkumar et al., 2021)](https://paperpile.com/c/WgsCep/UbmS).The cytotoxicity mechanism of Sr/ZnO NPs could be attributed to several factors, including the generation of reactive oxygen species (ROS), disruption of cellular membranes, and interference with intracellular pathways. Zinc oxide nanoparticles are well-known for their ability to induce oxidative stress in cancer cells, leading to apoptosis [(Shakthi et al., 2024)](https://paperpile.com/c/WgsCep/sXmf) Strontium, on the other hand, plays a dual role in enhancing bone regeneration and potentially disrupting cancer cell metabolism. The combination of these two elements in nanoparticle form provides a synergistic effect that enhances their cytotoxic potential against cancer cells.Despite the promising results, further studies are necessary to fully understand the biocompatibility and safety of Sr/ZnO NPs, especially in non-cancerous cells. It is crucial to ensure that these nanoparticles selectively target cancer cells without causing significant harm to normal tissues.[(Dharman et al., 2023; S. Sindhu et al., 2023; Sreenivasagan et al., 2023)](https://paperpile.com/c/WgsCep/0nAlg+9orxU+X5gE4) In addition, in vivo studies are required to assess the therapeutic efficacy and biodistribution of Sr/ZnO NPs in animal models before they can be considered for clinical applications[(Parmar & Kar, 2008)](https://paperpile.com/c/WgsCep/6ctr).In summary, the Sr/ZnO nanoparticles synthesized in this study exhibit strong anti-inflammatory and cytotoxic properties, making them promising candidates for the treatment of inflammatory diseases and cancer. Their ability to inhibit albumin denaturation suggests potential use as anti-inflammatory agents, while their cytotoxicity against oral cancer cells highlights their potential as novel therapeutic agents in cancer treatment. However, additional research is needed to further optimize their biomedical efficacy and ensure their safety in clinical settings.

# LIMITATIONS

Despite the promising results, the current study has several limitations. Firstly, the one-pot biosynthesis method, although green and sustainable, may result in nanoparticles with varying size distributions and morphologies, which could affect their biomedical efficacy. More precise control over nanoparticle synthesis is needed to ensure consistency in size and surface properties. Additionally, the anti-inflammatory and cytotoxicity studies were conducted in vitro, limiting the direct applicability of these findings to real-world clinical scenarios. The cytotoxic effects of Sr/ZnO nanoparticles were tested only on KB oral cancer cells; broader cytotoxicity studies on other cancer types and non-cancerous cells are necessary to fully understand the nanoparticles' selectivity and safety profile. Moreover, long-term in vivo studies assessing biocompatibility, biodistribution, and potential side effects were not conducted, which limits the ability to translate these findings into therapeutic applications.

# CONCLUSION

In conclusion, the one-pot biosynthesis of strontium and zinc oxide nanoparticles using a green method demonstrated significant anti-inflammatory and cytotoxic properties. The nanoparticles effectively inhibited protein denaturation and displayed substantial cytotoxicity against KB oral cancer cells. These findings suggest that Sr/ZnO nanoparticles hold potential as therapeutic agents for inflammation-related diseases and cancer. However, further research is necessary to optimize their synthesis, ensure biocompatibility, and validate their efficacy through extensive in vivo studies before clinical applications can be considered.

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