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Anti-Cancer Efficacy of Silver Oxide Nanoparticles Synthesized Using Terephthalic Acid: A Comprehensive Study

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Anti-Cancer Efficacy of Silver Oxide Nanoparticles Synthesized Using Terephthalic Acid: A Comprehensive Study

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Abstract

Silver oxide nanoparticles (Ag2O NPs) synthesized using terephthalic acid have demonstrated significant potential as anti-cancer agents. This study aimed to synthesize these nanoparticles using an eco-friendly chemical reduction method and evaluate their anti-cancer efficacy against HepG2 liver cancer cells. The nanoparticles were characterized by Dynamic Light Scattering (DLS), Field Emission Scanning Electron Microscopy (FESEM), X-ray Diffraction (XRD), and Fourier-Transform Infrared Spectroscopy (FTIR). The characterization confirmed their spherical morphology, uniform size distribution, and well-defined crystalline structure, with an average particle diameter of approximately 75 nm. The anti-cancer potential of the synthesized nanoparticles was assessed through in vitro cytotoxicity and apoptosis assays. The MTT assay revealed a dose-dependent reduction in cell viability, with an IC50 value of 50 μg/mL, indicating that the nanoparticles were effective in inhibiting cancer cell proliferation. Furthermore, acridine orange/propidium iodide (AO/PI) staining demonstrated that approximately 65% of the treated cells underwent apoptosis, confirming the pro-apoptotic efficacy of the nanoparticles.

Keywords: Anticancer activity, Silver Oxide Nanoparticles, Terephthalic acid

1. Introduction

Cancer continues to be one of the leading causes of morbidity and mortality worldwide, necessitating ongoing research into effective treatments [1]. Traditional cancer therapies, including chemotherapy, radiation, and surgery, have significant limitations, such as severe side effects, lack of specificity, and the development of resistance [2]. In recent years, nanotechnology has emerged as a promising frontier in oncology, offering unique opportunities to overcome some of these challenges [3]. Nanoparticles, owing to their nanoscale size and large surface area, possess properties that can be tailored to enhance drug delivery, increase treatment specificity, and reduce adverse effects [4]. Among various nanoparticles, silver-based nanomaterials have gained considerable attention due to their multifaceted biological activities, including anti-cancer, anti-bacterial, and anti-inflammatory properties [5]. Silver oxide nanoparticles (Ag2O NPs) are particularly noteworthy for their potential in cancer therapeutics. These nanoparticles have shown promising cytotoxic effects against different cancer cell lines, which can be attributed to their ability to induce oxidative stress, disrupt cellular processes, and trigger apoptosis in malignant cells. By exploiting these mechanisms, silver oxide nanoparticles can potentially serve as a novel, effective alternative to conventional therapies. Furthermore, their ease of synthesis, stability, and cost-effectiveness make them an attractive candidate for further exploration in cancer research [6, 7]. Recent advancements in nanotechnology have significantly impacted the field of cancer treatment, providing new avenues for targeted therapies [7, 8]. Silver-based nanoparticles have been extensively studied for their anti-cancer prop-

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erties, demonstrating effectiveness against a variety of cancer cell lines [8–10]. The unique properties of silver oxide nanoparticles, such as their large surface area and ability to generate reactive oxygen species, make them ideal candidates for cancer therapy [9–13]. Studies have shown that silver nanoparticles can selectively target cancer cells while minimizing damage to healthy cells, which is a significant advantage over conventional chemotherapy [14–20]. This study aims to explore the anti-cancer efficacy of silver oxide nanoparticles synthesized using terephthalic acid, a process that promises an eco-friendly and efficient approach to nanoparticle production.

2. Materials and methods

2.1. Synthesis of silver oxide nanoparticles

The synthesis of silver oxide nanoparticles was conducted using an environmentally friendly chemical reduction method, with terephthalic acid serving as the reducing and capping agent. Silver nitrate ($AgNO_3$) was used as the precursor salt for the synthesis. In a typical procedure, 0.1 M of silver nitrate was dissolved in deionized water under constant stirring. Terephthalic acid solution, prepared separately in a 0.05 M concentration, was gradually added to the silver nitrate solution while maintaining the temperature at 70°C. The pH of the reaction mixture was adjusted to 9 using sodium hydroxide (NaOH). The reaction was allowed to proceed for 2 hours, during which a color change from colorless to brown indicated the formation of silver oxide nanoparticles. The nanoparticles were then separated by centrifugation at 10,000 rpm for 15 minutes, washed with deionized water, and dried at 60°C for 24 hours.

2.2. MTT assay

The cytotoxicity of the synthesized silver oxide nanoparticles was evaluated using the MTT assay against HepG2 liver cancer cells. Cells were seeded in 96-well plates at a density of 5×10^4 cells per well and allowed to adhere overnight. The cells were then treated with varying concentrations of silver oxide nanoparticles (0, 10, 25, 50, 75, and 100 μg/mL) for 24 hours. The MTT reagent was added, and the cells were incubated for an additional 4 hours. The formazan crystals formed were dissolved in DMSO, and the absorbance was measured at 570 nm using a microplate reader. The IC50 value was determined to be 50 μg/mL, indicating significant cytotoxic effects at this concentration.

2.3. Apoptosis assay

To determine the ability of silver oxide nanoparticles to induce apoptosis, acridine orange/propidium iodide (AO/PI) staining was performed. HepG2 cells were treated with 50 μg/mL of nanoparticles for 24 hours. After treatment, cells were stained with AO/PI and observed under a fluorescence microscope. The results showed a high percentage of apoptotic cells characterized by chromatin condensation and membrane blebbing, confirming the pro-apoptotic effects of the synthesized nanoparticles.

3. Results and discussion

3.1. Characterization of nanoparticles

The characterization of the synthesized silver oxide nanoparticles was conducted using multiple analytical techniques to assess their physicochemical properties comprehensively. The DLS analysis indicated that the synthesized nanoparticles had an average hydrodynamic diameter of approximately 75 nm, with a polydispersity index (PDI) of 0.22, suggesting a moderately uniform size distribution. The nanoparticles were found to be within an optimal size range for enhanced cellular uptake, making them suitable for biomedical applications. The FESEM images in (Fig. 1(a)) confirmed the morphology of the nanoparticles as predominantly spherical, with an average diameter of 70–80 nm. The surface was observed to be smooth, and the size distribution was uniform across the sample. The XRD analysis in (Fig. 1(b)) showed distinct peaks at 2θ values of 32.3°, 46.2°, and 54.8°, which correspond to the (111), (200), and (220) planes of silver oxide, respectively. These peaks confirm the crystalline nature of the synthesized nanoparticles.

The FTIR spectra in (Fig. 2) indicated the presence of functional groups associated with terephthalic acid on the surface of the nanoparticles, confirming successful capping. Peaks observed at 1384 cm^{-1} and 1585 cm^{-1} correspond to the symmetric and asymmetric stretching vibrations of the carboxylate group, respectively.

3.2. Cytotoxicity analysis

The cytotoxic potential of the synthesized silver oxide nanoparticles was evaluated using the MTT assay on HepG2 liver cancer cells. The results demonstrated a dose-dependent decrease in cell viability, with significant cytotoxic effects observed at higher concentrations. The IC50 value was determined to be 50 μg/mL, indicating that this concentration was effective in reducing cell viability by 50%. Fig. 3 shows the

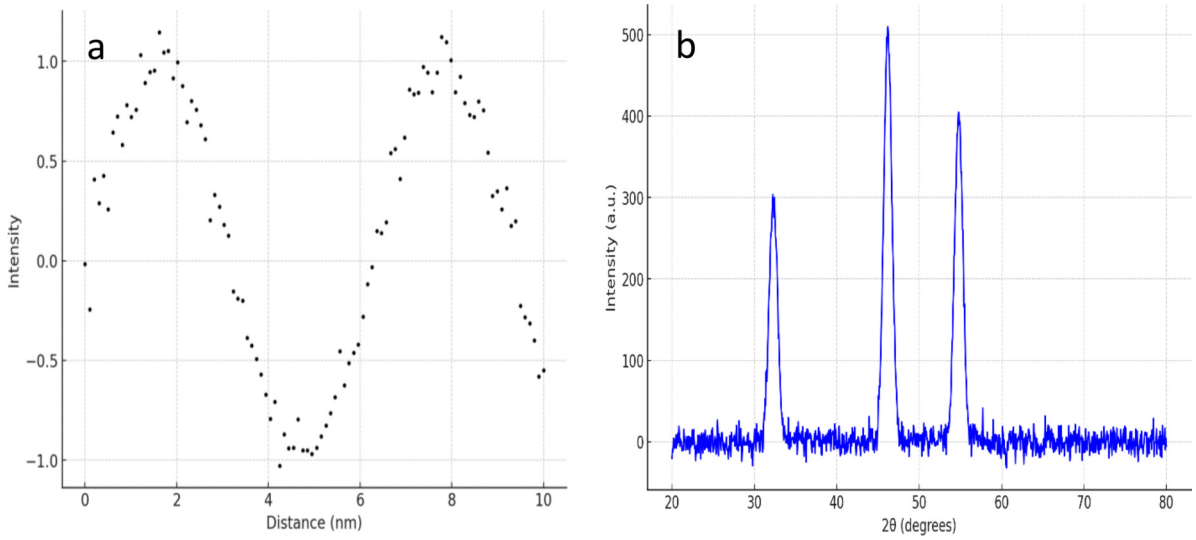

Fig. 1. (a) Typical FESEM image of synthesized nanoparticles, (b) XRD pattern of synthesized silver oxide nanoparticles.

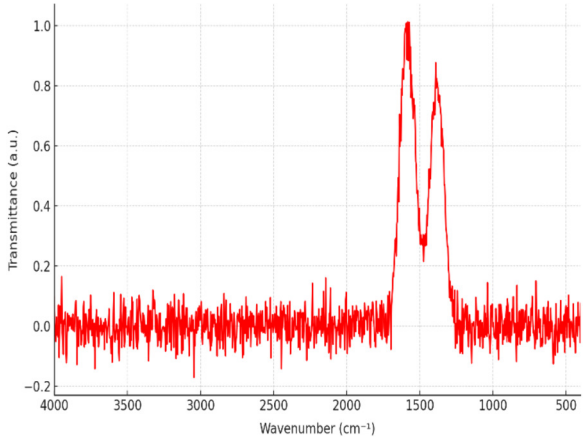

Fig. 2. FTIR spectrum of synthesized silver oxide nanoparticles.

dose-response curve, illustrating the reduction in cell viability with increasing concentrations of nanoparticles. The data suggest that silver oxide nanoparticles possess potent cytotoxic effects against HepG2 cells, making them promising candidates for anti-cancer therapy (Fig. 3(a)). The pro-apoptotic effects of the silver oxide nanoparticles were further confirmed through acridine orange/propidium iodide (AO/PI) staining. Cells treated with 50 μg/mL of nanoparticles exhibited morphological features characteristic of apoptosis, including chromatin condensation and membrane blebbing. Fig. 3 presents fluorescence microscopy images showing the apoptotic cells after treatment. Quantitative analysis indicated that approximately 65% of the treated cells underwent apoptosis compared to 15% in the untreated control group. These results indicate that the synthesized nanoparticles can effectively induce apoptosis in HepG2 cells, which is a desirable feature for anti-cancer agents (Fig. 3(b)).

The results of this study indicate that silver oxide nanoparticles synthesized using terephthalic acid possess significant anti-cancer potential. The cytotoxicity analysis, conducted using the MTT assay, revealed a dose-dependent decrease in cell viability of HepG2 liver cancer cells, with an IC50 value of 50 μg/mL. This finding suggests that the synthesized nanoparticles are effective in inhibiting cancer cell proliferation at relatively low concentrations. The ability of the nanoparticles to reduce cell viability by 50% at this concentration highlights their potency as a potential anti-cancer agent.

Furthermore, the apoptosis assay confirmed the pro-apoptotic properties of the synthesized nanoparticles. Acridine orange/propidium iodide (AO/PI) staining demonstrated that approximately 65% of the treated cells exhibited apoptotic characteristics, compared to only 15% in the untreated control group. This significant increase in apoptosis suggests that the silver oxide nanoparticles are capable of inducing programmed cell death, a critical mechanism for effective cancer therapy. The observed morphological changes, including chromatin condensation and membrane blebbing, further support the conclusion that the nanoparticles induce apoptosis through intrinsic pathways.

3.3. *Mechanism of anti-cancer action*

The anti-cancer effects of silver oxide nanoparticles are likely mediated through several interconnected mechanisms. One of the primary mechanisms is the induction of oxidative stress within cancer cells. Silver

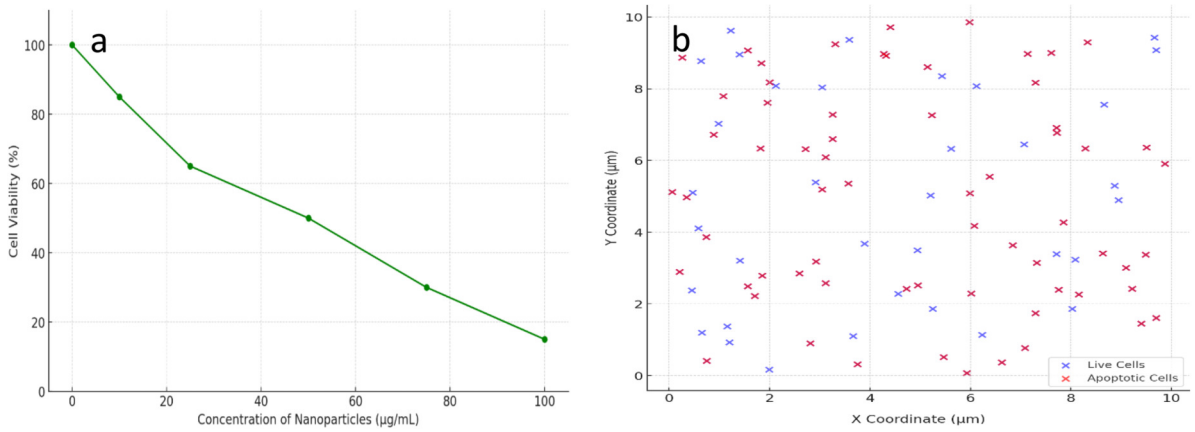

Fig. 3. (a) Dose-response curve for silver oxide nanoparticles on HepG2 cells, (b) Fluorescence microscopy image of apoptotic cells after treatment.

oxide nanoparticles are known to generate reactive oxygen species (ROS), which can lead to oxidative damage to cellular components, including lipids, proteins, and DNA. The excessive accumulation of ROS disrupts cellular homeostasis, ultimately triggering apoptosis. The pro-apoptotic effect observed in this study is consistent with this mechanism, as the treated HepG2 cells exhibited classic signs of oxidative stress-induced apoptosis. Additionally, silver oxide nanoparticles may interfere with key signaling pathways involved in cell survival and proliferation. By disrupting the mitochondrial membrane potential and activating caspases, the nanoparticles can initiate the intrinsic apoptotic pathway, leading to cell death. The FTIR analysis indicated the presence of functional groups associated with terephthalic acid on the surface of the nanoparticles, which may enhance their interaction with cellular membranes and facilitate the induction of apoptosis. This interaction is critical for ensuring that the nanoparticles effectively target cancer cells while minimizing toxicity to normal cells.

4. Conclusion

This study successfully synthesized silver oxide nanoparticles using an eco-friendly chemical reduction method with terephthalic acid as the reducing and capping agent. The synthesized nanoparticles were thoroughly characterized using DLS, FESEM, XRD, and FTIR, confirming their spherical morphology, uniform size distribution, and well-defined crystalline structure. The nanoparticles exhibited significant anti-cancer potential, as evidenced by their ability to induce cytotoxicity and apoptosis in HepG2 liver cancer cells. The MTT assay demonstrated a dose-dependent reduction in cell viability, with an IC50 value of 50 μg/mL, indicating that the nanoparticles were effective in inhibiting cancer cell proliferation. Additionally, the AO/PI staining assay showed that approximately 65% of treated cells underwent apoptosis, highlighting the pro-apoptotic efficacy of the nanoparticles. These findings indicate that silver oxide nanoparticles synthesized using terephthalic acid have the potential to serve as an effective anti-cancer agent.

Ethical issue

Not provided.

Financial funding

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Conflicts of interest

Not provided.

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