

Semiconductor Nanoparticles as Potential Radiosensitizing Agents for Cancer Treatment

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Introduction: Cancer is a leading cause of death worldwide. This deadly disease is established when the immune system fails to recognize the threat of intrusion due to a variety of shortcomings [1]. Radiation therapy is one of the most common treatments for cancer. It uses high-energy particles or waves, such as x-rays to destroy or damage cancer cells. X-ray radiation produces ionizing photons that are adsorbed by human body, causing radiolysis of water, and generating free radicals that can damage various cellular components including DNA, therefore preventing cancer cell growth [2]. One of the critical challenges in current radiotherapy for cancer treatment is to provide a fatal dose only to a tumor within the tolerance of normal tissues [3]. To this end, different types of nanoparticles (metallic, oxide, and semiconductor nanoparticles) are being investigated in order to provide a lethal dose to cancer cells without impacting surrounding healthy tissues [4]. The objective of the present study is to evaluate and investigate the performance of semiconductor nanoparticles as radiosensitizing agents during X-ray irradiation of cancers cells.

Materials and methods: Three types of spherical nanoparticles were investigated in this study. Commercially-available gold and titanium dioxide nanoparticles ranging from 20 to 30 nm were examined. In addition, bismuth ferrite nanoparticles were synthesized through a wet chemical route from bismuth nitrate and iron nitrate at low temperature [5] and characterized using X-ray diffraction and TEM techniques. In order to evaluate the performance of these nanoparticles towards cancer radiotherapy, hydroxyl radicals generated during X-ray radiation of 0.5 mM coumarin solutions containing nanoparticles were quantified by fluorescent measurements. Due to the short lifetime of radicals ($\sim 10^{-9}$ s), coumarin was used as a fluorescent probe as it forms, when exposed to hydroxyl radicals, a fluorescent molecule known as 7-hydroxycoumarin [6]. Cell viability of Hela cells (derived from cervical cancer cells) incubated with 10 $\mu\text{g/ml}$ gold, titanium dioxide, and bismuth ferrite nanoparticles were measured through absorbance measurements after being subjected to MTT assay.

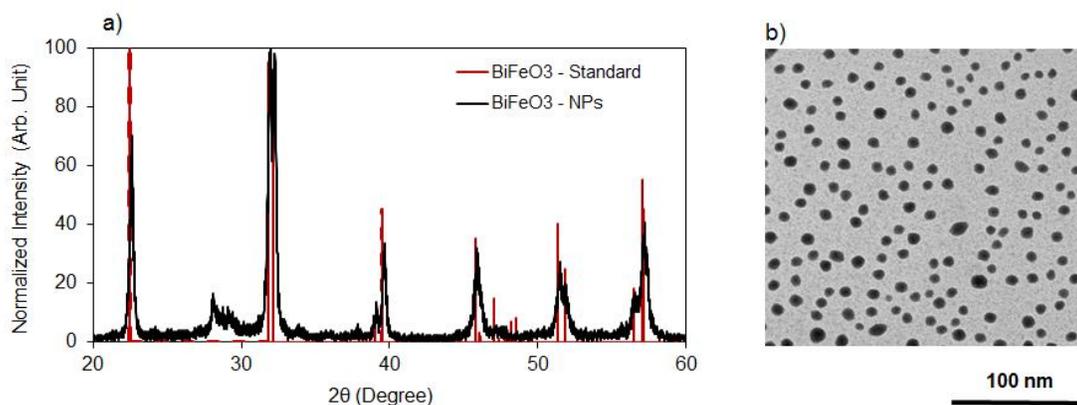


Figure 1: a) XRD pattern of the synthesized BiFeO_3 nanoparticles compared to standard XRD pattern for BiFeO_3 nanoparticles reported by Hu [7], b) TEM image of synthesized BiFeO_3 nanoparticles.

Results and discussions: Bismuth ferrite (BiFeO_3) nanoparticles were successfully synthesized as their X-ray powder diffraction (XRD) pattern overlaps perfectly with a standard reported pattern (Fig. 1(a)). Furthermore, the synthesized BiFeO_3 nanoparticles have a diameter size ranging from 10 to 20 nm, as

shown in Fig 1(b). Fluorescent measurements showed that X-ray irradiation across the 3 types of nanoparticles successfully produced therapeutic levels of hydroxyl radicals with concentrations proportional to the radiation dose provided. As shown in Fig. 2(a), higher levels of hydroxyl radical production (obtained from the graph slope) were detected for the gold nanoparticles in contrast to titanium dioxide and bismuth ferrite nanoparticles. The efficacy of nanoparticles in cancer radiation therapy was then tested. Preliminary *in vitro* measurements showed that up to 80% of Hela cells can be efficiently eradicated upon irradiation when exposed to our nanoparticles, Fig. 2(b). These results, which are consistent with those obtained through fluorescent measurements of coumarin solutions, indicate the importance of material composition as well as secondary X-rays generated during X-ray irradiation of gold nanoparticles in hydroxyl radical formation.

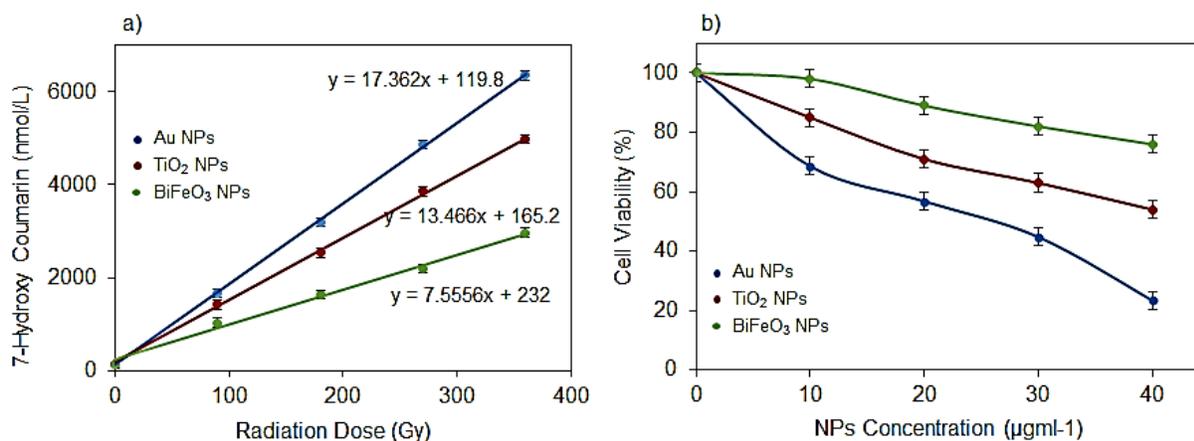


Figure 2: a) 7-OH coumarin formation as a function of the dose for 10 μgml^{-1} of Au, TiO₂, and BiFeO₃ nanoparticles at 8.8 Gymin⁻¹, b) Cell viability of Hela cells incubated with 10 μgml^{-1} of Au, TiO₂, and BiFeO₃ nanoparticles and irradiated at 1.2 Gymin⁻¹.

Conclusions: Our preliminary data suggest that across the 3 screened inorganic materials, the gold nanoparticles had the most potent nanoparticle-aided radiation therapy. Additionally, our results indicate the importance of material composition as well as secondary X-rays generated during X-ray irradiation of gold nanoparticles in hydroxyl radical formation. The next steps in this project will consist not only to increase cellular uptake of nanoparticles and evaluate their *in vitro* antitumor efficacy upon X-ray irradiation in 3D to properly recreate the native tumor microenvironment, but also to faithfully mimic modern clinical radiotherapy in small-animal cancer models. Looking into the near future, a combination of radiation with other emerging therapies such as immunotherapy could confer a synergistic antitumor therapy as the battle against cancer has to be fought on multiple fronts.

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