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Biosynthesis of a Nanoparticle-Antibody Phthalocyanine Photosensitizer for Use in Targeted Photodynamic Therapy of Cervical Cancer

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Abstract : Cancer cell resistance to therapy is the main cause of treatment failures and the poor prognosis of cancer convalescence. The progression of cervical cancer to other parts of the genitourinary system and the reported recurrence rates are overwhelming. Current treatments, including surgery, chemo and radiation have been inefficient in eradicating the tumor cells. These treatments are also associated with poor prognosis and reduced quality of life, including fertility loss. This has inspired the need for the development of new treatment modalities to eradicate cervical cancer successfully. Photodynamic Therapy (PDT) is a modern treatment modality that induces cell death by photochemical interactions of light and a photosensitizer, which in the presence of molecular oxygen, yields a set of chemical reactions that generate Reactive Oxygen Species (ROS) and other free radical species causing cell damage. Enhancing PDT using modified drug delivery can increase the concentration of the photosensitizer in the tumor cells, and this has the potential to maximize its therapeutic efficacy. In cervical cancer, all infected cells constitutively express genes of the E6 and E7 HPV viral oncoproteins, resulting in high concentrations of E6 and E7 in the cytoplasm. This provides an opportunity for active targeting of cervical cancer cells using immune-mediated drug delivery to maximize therapeutic efficacy. The use of nanoparticles in PDT has also proven effective in enhancing therapeutic efficacy. Gold nanoparticles (AuNps) in particular, are explored for their use in biomedicine due to their biocompatibility, low toxicity, and enhancement of drug uptake by tumor cells. In this present study, a biomolecule comprising of AuNPs, anti-E6 monoclonal antibodies, and Aluminium Phthalocyanine photosensitizer was synthesized for use in targeted PDT of cervical cancer. The AuNp-Anti-E6-Sulfonated Aluminium Phthalocyanine mix (AlPcSmix) photosensitizing biomolecule was synthesized by coupling AuNps and anti-E6 monoclonal antibodies to the AlPcSmix via Polyethylene Glycol (PEG) chemical links. The final product was characterized using Transmission Electron Microscope (TEM), Zeta Potential, Uv-Vis Spectrophotometry, Fourier Transform Infrared Spectroscopy (FTIR), and X-ray diffraction (XRD), to confirm its chemical structure and functionality. To observe its therapeutic role in treating cervical cancer, cervical cancer cells, HeLa cells were seeded in 3.4 cm^2 diameter culture dishes at a concentration of $5x10^5$ cells/ml, in vitro. The cells were treated with varying concentrations of the photosensitizing biomolecule and irradiated using a 673.2 nm wavelength of laser light. Post irradiation cellular responses were performed to observe changes in morphology, viability, proliferation, cytotoxicity, and cell death pathways induced. Dose-Dependent response of the cells to treatment was demonstrated as significant morphologic changes, increased cytotoxicity, and decreased cell viability and proliferation This study presented a synthetic biomolecule for targeted PDT of cervical cancer. The study suggested that PDT using this AuNp- Anti-E6- AlPcSmix photosensitizing biomolecule is a very effective treatment method for the eradication of cervical cancer cells, in vitro. Further studies in vivo need to be conducted to support the use of this biomolecule in treating cervical cancer in clinical settings.

Keywords : anti-E6 monoclonal antibody, cervical cancer, gold nanoparticles, photodynamic therapy
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