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COMBINATION PHOTODYNAMIC THERAPY AND CHEMOTHERAPY FOR TEMOZOLOMIDE-RESISTANT GLIOBLASTOMA

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Polymer based nanoparticles (NPs) are useful vehicles for drug therapy in treating glioblastoma because of their ideal characteristics such as small size, to cross the blood-brain barrier, and bind to overexpressed transferrin receptors via peptide conjugation and surface modification of NPs. The use of a photosensitizer drug such as verteporfin, or BPD, in combination with a repurposed drug, Cediranib (CED), prepared as a nanoparticle therapy will provide the medical field with new research on the possible ways to treat glioblastoma. BPD-CED-loaded NPs have the potential to induce cytotoxicity in glioblastoma cells by 1) remotely triggering BPD through photodynamic therapy by irradiating laser at 690 nm and subsequent production of reactive oxygen species and 2) anti-angiogenesis mechanisms which may allow for longer progression free survival in patients and fewer systemic side effects due to the nanoparticle drug delivery. The specific aims of this research were to synthesize, using nanoprecipitation, and characterize pegylated and transferrin-peptide conjugated PLGA-CED NPs, PLGA-BPD NPs, and PLGA-BPD-CED NPs which were less than 100 nm in size for enhanced permeation and retention effects. NPs were characterized using dynamic light scatter (DLS) to determine particle size, PDI, and zeta potential, while absorbance spectroscopy was used to find encapsulation efficiency of loaded drugs. Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) were used to obtain topographical and 3-D structural imaging of NPs. The cytotoxicity of the free drugs, targeted and non-targeted single and dual-drug-loaded NPs was evaluated using MTT assay in the U87-MG cell line. MTT assay results showed increased cell death by combination nanoparticles. The size, PDI, zeta potential and encapsulation efficiency of synthesized nanoparticles were acceptable. The major goal of this research was to investigate a new combination of photodynamic-chemotherapy drugs in NP formulation to provide for a more effective targeted cell therapy in glioblastoma patients.

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