Abstract

The significant progress of nanotechnology has been evident over the last few years in many scientific areas, including oncology and medicine. The heterogeneity and complexity of cancer often render current treatment options insufficient. The diversity of genetic mutations requires a simultaneous multi-faceted approach; thus, nanoparticles have become promising alternatives to conventional therapies. By the 2023, the FDA has approved at least 15 nanotherapeutics for cancer treatment.

The exceptionality of fullerenes among other nanotherapeutic lies in their multifunctionality and unique optical properties. The fullerene cage serves as excellent nanoplatform for further modifications while also exhibiting intrinsic therapeutic potential. The possibility to encapsulate metal ion inside fullerene cage makes them available for diagnosis systems.

In this work, several fullerene derivatives were engineered and synthesised to perform therapeutic functions. This includes photodynamic therapy, siRNA delivery, visualisation *in vitro*, BTK and EGFR kinase inhibition and MRI screening potential. The suitable malonic acid derivatives were synthesised and attached to the fullerene core by an optimised Bingel-Hirsch reaction to ensure the solubility of final nanomaterials in physiological solvents. All the product structures were confirmed and characterised by the following techniques: ^{1}H NMR, ^{13}C NMR, FT-IR, UV-VIS, XPS and mass spectrometry analyses. DLS, zeta potential, TEM and SEM were also performed for final fullerenes. The EPR spin trapping and lipid peroxidation assays confirmed the ability for ROS generation upon laser irradiation. The activity of fullerene-siRNA conjugate was validated *in vitro* in the GFP silencing test. A new method of pro-diagnostic activation of fullerenes *in vitro* (using click reaction) was developed. The inhibition of selected protein was determined using western blot analysis and tyrosine kinase assay. Anticancer activity was assesed on human cancer cell lines. The cytotoxicity tests were also conducted in vivo on the *Drosophila melanogaster* model for theranostic fullerene nanomaterial containing Gd ions.

I believe that my work expanded the knowledge about fullerenes as multifunctional nanotherapeutics. The described research indicates the significance of designing new biocompatible nanotherapeutic systems for improving existing therapies and reducing off-side effects. Moreover, through exploration of the fullerene inhibition potential of several proteins, I believe my work opens a new path for developing alternative therapeutic strategies that operate on a molecular level.