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Water-Soluble Fullerenes for Anti-Cancer Treatment

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Abstract

Fullerenes, spherical carbon molecules often referred to as "buckyballs," have garnered significant attention in cancer research due to their unique structural and chemical properties. These nanomaterials offer promising applications in drug delivery, imaging, and cancer therapy. Their ability to be functionalized and carry therapeutic agents makes them versatile tools for targeting difficult-to-treat cancers. In particular, fullerene-based nanomaterials have emerged as potential solutions in addressing the challenges of pancreatic ductal adenocarcinoma (PDAC), one of the most lethal cancers, largely due to its dense, fibrous tissue and complex tumor microenvironment. In our research, we developed water-soluble aminofullerenes conjugated with the EGFR inhibitor erlotinib to target PDAC cells. These nanomaterials showed the ability to induce cell cycle arrest and modulate cell death processes, such as autophagy and apoptosis, in PDAC models. Toxicological evaluations also suggest their potential as theranostic agents, which combine therapeutic and diagnostic functions. Moreover, we addressed gemcitabine's limitations—one of the main drugs used to treat PDAC—by creating a fullerene-glycine gemcitabine nanoconjugate (nanoC60GEM). This nanomaterial demonstrated enhanced cytotoxicity against PDAC cells, inducing cell cycle arrest in the S phase and apoptosis. Notably, its effects were amplified by the generation of reactive oxygen species when exposed to light, presenting a novel approach to overcome drug resistance in PDAC treatment. Finally, we discovered that glycofullerenes (GF1, GF2) can act as non-receptor Src kinase inhibitors, specifically targeting Fyn A and BTK proteins, critical in cancer progression. These glycofullerenes showed no cytotoxic effects but altered cellular behavior by interacting with proteins in their environment, making them promising candidates for modulating kinase activity in cancer treatment. Together, our studies highlight the potential of fullerene-based nanomaterials as multifunctional agents in both treating pancreatic cancer and inhibiting key cancer-related pathways.