ROLE OF SINGLET OXYGEN AND FREE RADICALS IN PHOTODYNAMIC CELL KILLING MEDIATED BY NOVEL NANOPARTICLE PHOTOSENSITIZERS

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Photodynamic therapy employs the combination of non-toxic photosensitizers and harmless visible light to generate free radicals and singlet oxygen and kill target cells. Fullerenes are nanoparticles composed of 60 or 70 carbon atoms with powerful photosensitizing capabilities. However, fullerenes are biologically inert unless derivatized with functional groups. We compared the photodynamic activity of six functionalized C_{60} with one, two, or three polar diserinol groups (BF1-BF3) and with cationic quarternary pyrrolidinium groups (BF4-BF6). The relative contributions of Type I (free radical) photochemistry and Type II (singlet oxygen) photochemistry were studied by ESR-oximetry, ESR-spin trapping and time-resolved luminescence at 1270 nm. The phototoxic effect of fullerenes was analyzed *in vitro* on three mouse cancer cell lines (J774, LLC and CT26) by incubating the cells for 24 h with fullerenes and illuminating with white light. Our data showed that BF4 was the most efficient sensitizer for photo-killing cancer cells by rapid induction of apoptosis. Although in organic solvents, BF4 and BF6 photogenerated singlet oxygen with comparable yields, in aqueous media the ability of BF4 to sensitize the Type II photoprocess was reduced to zero. Both photosensitizers generated superoxide anion in aqueous media in the presence of NADH. We conclude that certain functionalized fullerenes exhibit phototoxicity that may be mediated both by superoxide anion and singlet oxygen.