

## **DF-1, A Nontoxic Carbon Fullerene Based Antioxidant, is Effective as a Biomedical Countermeasure Against Radiation**

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A long-term goal of radiation research is the mitigation of inherent risks of radiation exposure. Thus the study and development of safe agents, whether biomedical or dietary, that act as effective radioprotectors is an important step in accomplishing this long-term goal. Some of the most effective agents to date have been aminothiols and their derivatives. Unfortunately, most of these agents have side effects such as nausea, vomiting, hypotension, weakness, and fatigability. For example, nausea and emesis occur in most patients treated with WR-2721 (Amifostine), requiring the use of effective antiemetics, with hypotension being the dose-limiting side effect in patients treated. Clearly, the need for a radioprotector that is both effective and safe still exists. Development of biocompatible nanomaterials for radioprotection is a promising emerging technology that could be exploited to address the need to minimize biological effects when exposure is unavoidable. Testing free radical scavenging nanoparticles for potential use in radioprotection is exciting and highly relevant. Initial investigations presented here demonstrate the ability of a particular functionalized carbon fullerene nanoparticle, (DF-1), to act as an effective radioprotector. DF-1 was first identified as the most promising candidate in a screen of several functionalized carbon fullerenes based on lack of toxicity and antioxidant therapeutic potential against oxidative injuries (i.e. organ reperfusion and ionizing radiation). Subsequently, DF-1 has been shown to reduce chromosome aberration yield and cell death, as well as overall ROS levels in human lymphocytes and fibroblasts after exposure to gamma radiation and energetic protons while demonstrating no associated toxicity. The dose-reducing factor of DF-1 at LD50 is nearly 2.0 for gamma radiation. In addition, DF-1 treatment also significantly prevented cell cycle arrest after exposure. Finally, DF-1 markedly attenuated COX2 upregulation in cell culture after irradiation thus preventing an inflammatory response to irradiation. Taken together, these results suggest that DF-1 provides potent protection against several deleterious cellular consequences of irradiation in mammalian systems including oxidative stress, DNA damage, inflammation and cell death.