# Development of Human Mast Cell-Targeting Fullerenes

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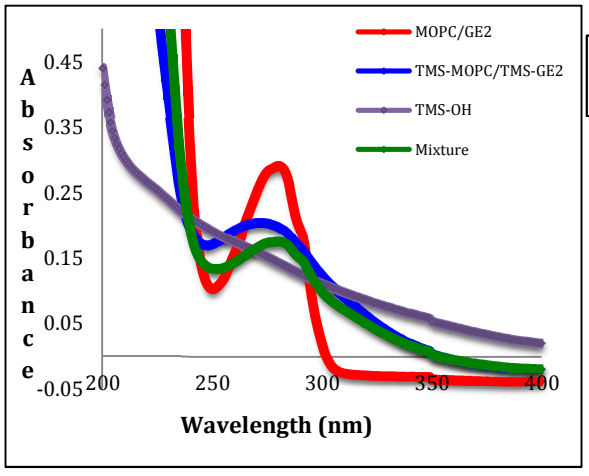
**Abstract:**
Fullerene-based therapies are being investigated as one approach for treating mast cell-driven disease. However, those fullerenes identified as potent mast cell stabilizers do not home directly to these cells. The goal of this study was to develop mast cell/basophil-targeting fullerenes and test them for their ability to inhibit FcεRI-mediated responses. To do this hydroxyl (–OH) derivatized gadolinium-containing fullerenes (TMS-OH) were used to covalently attach the FcεRI-targeting protein GE2 and non-specific antibody control (MOPC). While several methods were attempted using variously derivatized fullerenes the protocol chosen utilized protein thiolation with N-Succinimidyl S-acetylthiopropionate (SATP) at the terminal e-amine group of lysine amino acid residues. Next, the hydroxyl groups of TMS-OH were reacted with the isocyanate moiety of N-[p-maleimidophenyl] isocyanate (PMPI) crosslinker to form a carbamate linkage. The maleimide moiety of the TMS-OH-PMPI intermediate exclusively reacts with reduced sulfhydryl groups of thiolated protein to form stable thioether bonds. The conjugation was verified using Fourier transform infrared spectroscopy, UV spectroscopy and gel electrophoresis. Nanoparticle size distribution and zeta potential were determined by using Nanosight and Dynamic light scattering. The GE2-fullerene conjugates actively targeted mast cells, were endocytosed, and inhibited mast cell mediator release while the MOPC-fullerene conjugate controls did not. The fullerene-endocytosis into mast cells was verified ex-vivo using SEM/Helium ion microscope. These studies suggest that anti-inflammatory fullerenes can be targeted to specific cellular receptor targets in-vitro where they are able to inhibit immunologically-mediated inflammatory responses.




**UV absorption spectra of mast cell targeting fullerenes and unreacted components**

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