NF-B-Dependent Prevention of Atherosclerotic Foam Cell Formation and Vessel Plaque Accumulation by Fullerene-Based Nanomedicines

Anthony L. Dellinger BS[1], Zhiguo Zhou PhD[1], Marinella Sandros PhD[2], Ashraf Sawafta, PhD[2], Patty Elkins, MS[2], and Christopher L. Kepley PhD, MBA[2]

1. Luna NanoWorks, 521 Bridge St, Danville, VA 24541
2. University of North Carolina Greensboro, Joint School of Nanoscience and Nanoengineering, Greensboro, NC

Abstract

Fullerenes are carbon spheres that have been shown to have anti-inflammatory properties. The transformation of monocytes into foam cells is an inflammatory process underlying atherosclerotic disease. We hypothesized that fullerene derivatives (FD) could inhibit the monocyte-to-foam cell transformation step involved in atherosclerosis. Fullerene derivatives inhibited the phorbol myristilic acid/oxidized low-density lipoprotein differentiation of monocytic U937 cells into foam cells as determined by lipid staining, cell adhesion, and scanning electron microscopy. Oxidized low density lipoprotein-induced generation of TNF-α, leukocyte integrin Mac-1-driven cell clumping, and CD36 receptor expression were significantly inhibited in FD treated cells compared to non-treated cells. For the first time it is shown that FD can dramatically reduce NF-κB expression in the oxidized low-density lipoprotein-dependent transformation of macrophages into foam cells. Apolipoprotein E knockout mice (ApoE -/-) fed a high fat diet (HFD) had dramatic inhibition of plaque formation in the blood vessels when treated with FD compared to non-treated controls. Lastly, no in vitro or in vivo toxicity was detected with FD; instead the FD helped reduced liver toxicity associated with the HFD. Thus, FD may be a heretofore unrecognized way to prevent atherosclerotic lesions through the inhibition of foam cell formation.

Key Words: Atherosclerosis, Foam Cells, Fullerenes, Low-Density Lipoprotein