Title *

FREE RADICAL GENERATION AND ATHEROSCLEROTIC EFFECTS OF REDOX MODIFIED COBALT OXIDE NANOPARTICLES

Abstract *

Given the prominent cardiorespiratory effects of nanoparticles in air pollution, the potential for manufactured nanomaterials (MNMs) to have cardiovascular actions requires urgent attention. Here, we investigate if redox-modified cobalt oxide nanoparticles promote the vascular disease atherosclerosis *in vivo*.

Cobalt oxide (Co_3O_4) nanoparticles were redox modified by incorporation of Fe_2O_3 into the crystal structure. Free radical generation from MNMs (acellular) was determined using electron paramagnetic resonance following reaction with the superoxide-selective spin-trap, Tempone-H. 100%Fe MNMs produced significantly greater levels of superoxide than 100%Co, with Fe-doped-Co_3O_4 producing intermediate levels.

Three forms of Co/Fe (100%Co, 100%Fe & 50:50%Co:Fe) were investigated in atherosclerosis-prone apolipoprotein-E knockout ($ApoE^{-/-}$) mice. Mice were repeatedly instilled with MNMs (35 μg twice weekly) by aspiration. All three forms of Co/Fe induced pulmonary inflammation, however, there was no significance difference in response between the different forms of Co/Fe, or evidence of systemic inflammation in the blood (IL-6, TNF-alpha, SAA-3). There was a small, but statistically insignificant, increase in the extent of atherosclerosis in animals exposed to 100% Co_3O_4 nanoparticles. Analysis of plaque composition showed a trend of decreased lipid content and increased foam cell content with increasing Fe-doping.

We found that cobalt oxide MNMs had minimal atherosclerotic effects following subacute inhalation and that redox-modification of MNMs had limited effects on these responses. Further studies with alternative MNMs of greater inherent toxicity or wider redox band gap are required to fully assess the influence of redox-modification on the vascular toxicity of MNMs.

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