Cytocompatibility of Hafnium Oxide (HfO_2) Nanoparticles for Diagnostic Imaging and Sensing

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Statement of Purpose: Hafnium oxide (HfO_2) nanoparticles (NPs) possess unique functional properties for use as an X-ray contrast agent [1,2] and mid-infrared biosensor [1,3]. In X-ray imaging, HfO_2 NPs exhibit superior or comparable X-ray contrast compared to Au NPs, while both NPs exhibit greater contrast compared to iodine at clinical CT tube potentials [1]. Therefore, HfO_2 NPs could provide a lower cost alternative to Au NPs and higher performance attenuator to iodinated contrast agents, the most prominent contrast agents used in research and in clinical imaging, respectively. However, investigation of the cytotoxicity of HfO_2 NPs has been limited to fibroblasts and epidermal cells exposed to industrial nanomaterials [4,5]. Therefore, the objective of this study was to investigate the cytocompatibility and cellular uptake of HfO_2 NPs *in vitro*.

Methods: HfO_2 NPs were synthesized using a hydrothermal reaction adapted from established methods [6]. The crystalline phase and crystallite size were characterized using X-ray diffraction (XRD) with Rietveld refinement, while the NP size and morphology were characterized using scanning electron microscopy (SEM). The hydrodynamic diameter and count rate of HfO_2 NPs in water, DMEM, and RPMI media was measured over ten days using dynamic light scattering (DLS) to assess colloidal stability. In order to assess cytocompatibility, human monocyte (THP-1, ATCC) and epithelial (HeLa, ATCC) cell lines, were incubated with 0.098, 0.45, and 0.833 mg/mL HfO_2 NPs. Mitochondrial activity and cell viability were measured at 4 and 24 h for each concentration of HfO_2 NPs using MTT (n = 6/group) and Live/Dead (n = 3/group) assays, respectively, and normalized to controls which contained no NPs.

Results: As-synthesized HfO_2 NPs were monoclinic with an average crystallite size of 14 nm, and a slightly ellipsoidal morphology with major and minor axes ~90 and ~60 nm, respectively (Fig. 1). The hydrodynamic diameter was ~250 nm and remained stable in various culture media over 10 days. Mitochondrial activity was decreased with increased NP concentration, and from 4 to 24 h, for both HeLa and THP-1 cells, but was never less than 80% of the control group ($p < 0.05$, ANOVA). Cell viability was maintained at ~100% for up to 24 h at all concentrations for both HeLa and THP-1 cells (Fig. 2).

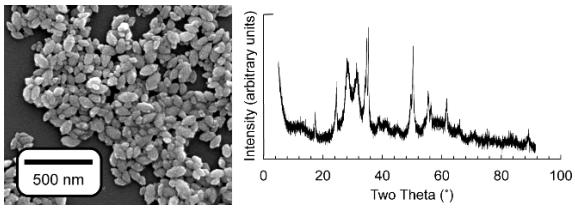

Figure 1. SEM micrograph and XRD pattern for as-prepared, hydrothermally derived HfO_2 NPs. All peaks correspond to monoclinic HfO_2.

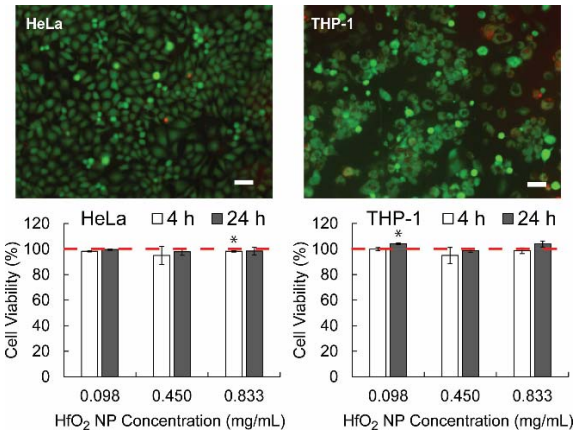

Figure 2. Live/Dead staining for HeLa and THP-1 cells after 24 h incubation with 0.833 mg/mL HfO_2 NPs. Scale bars = 20 μm. A measured cell viability of ~100% was maintained for up to 24 h exposure to up to 0.833 mg/mL HfO_2 NPs. *$p < 0.05$ vs. 100, Mann-Whitney *U*-test.

Conclusions: HfO_2 NPs exhibited no cytotoxicity at concentrations up to 0.833 mg/mL in both HeLa and THP-1 cells. Therefore, the results of this study suggest that HfO_2 NPs are suitable as an *in vivo* imaging probe and *in vitro* diagnostic biosensor.

References:

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