

Hyaluronic Acid Enriched with Cerium Oxide Nanoparticles for Countering Oxidative Damage in Chondrocytes Affected by Hydrogen Peroxide-mediated Injury

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INTRODUCTION: Osteoarthritis (OA) stands as the prevailing form of joint ailment, often coupled with diverse levels of functional impediments. The utilization of hyaluronic acid (HA) joint injections and pain alleviators emerges as efficacious interventions for the initial phases of osteoarthritis. Nonetheless, the efficacy of HA injection therapy is restricted by its susceptibility to degradation via hyaluronidase and the detrimental impact of free radicals within the knee joint. Enter cerium oxide nanoparticles (CeO₂), renowned for their prolonged capacity to scavenge free radicals. By amalgamating CeO₂ with HA, the anticipation is to protract the degradation timeline of HA, consequently fostering a constructive influence on osteoarthritis treatment.

METHODS: In the current investigation, the hydrothermal technique was effectively employed to synthesize CeO₂ nanoparticles, exhibiting a particle size approximately measuring 120 nm. These nanoparticles demonstrated remarkable dispersibility within the culture medium. To emulate the in vitro osteoarthritis (OA) scenario, a cellular model was established wherein cells were subjected to a 30-minute treatment with H₂O₂.

RESULTS SECTION: Our research unveiled a notable trend wherein the inhibition of chondrocyte proliferation escalated proportionally with the concentration of H₂O₂. However, this inhibitory effect was conspicuously mitigated upon the introduction of cerium oxide nanoparticles in a dose-dependent manner.

DISCUSSION: Following exposure to H₂O₂, there was a significant reduction observed in the expression of COL2a1 and ACAN genes within chondrocytes. Nevertheless, this trend underwent alteration subsequent to the administration of cerium oxide nanoparticles. This alteration strongly implies a safeguarding effect against oxidative stress for the impaired chondrocytes.

SIGNIFICANCE/CLINICAL RELEVANCE: These discoveries indicate the potential utility of cerium oxide nanoparticles in therapeutic interventions during the initial phases of osteoarthritis (OA).

IMAGES AND TABLES:

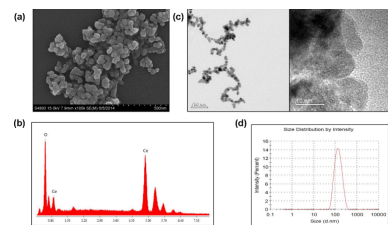


Figure 1. The structure and constitution of CeO₂ nanoparticles. The depiction covers: (a) the exterior topography of the cerium oxide nanoparticles; (b) the Energy Dispersive X-ray Analysis (EDXA) pattern for the cerium oxide nanoparticles; (c) the Transmission Electron Microscopy (TEM) depiction of the cerium oxide nanoparticles; and (d) the distribution of particle sizes.

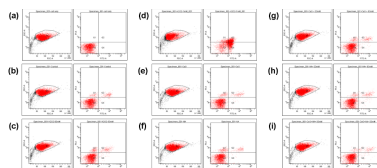


Figure 2. Flow cytometry-based apoptosis assessment. Panels: (a) unstained cell for gating; (b) control; (c) 0.3 mM H₂O₂; (d) 1 mM H₂O₂; (e) CeO₂ assay; (f) HA assay; (g) CeO₂ protection; (h) HA protection; (i) CeO₂/HA combined protection. Remarkably, 0.01 ug/ml CeO₂ nanoparticles with 1% HA safeguarded chondrocytes from 0.3 mM H₂O₂ harm.

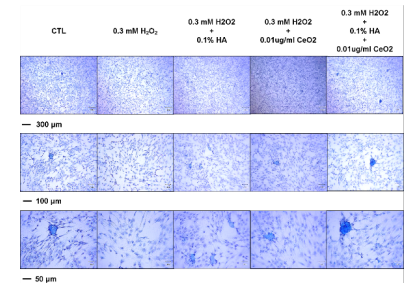


Figure 3. Impact of HA with CeO₂ Nanoparticles on GAG Synthesis: H₂O₂ exposure reduced sulfated proteoglycan synthesis, aligned with ACAN, COL1A1, and COL2A1 gene expression. H₂O₂-treated samples displayed reduced cell density and compromised membranes. Conversely, HA and CeO₂ countered H₂O₂ damage effectively. Co-applying HA and CeO₂ notably boosted sulfated proteoglycan accumulation.