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## ACCEPTED MANUSCRIPT

#### Antioxidant and Antibacterial Hydroxyapatite-based Biocomposite for Orthopedic Applications

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#### Abstract

Post-implantation, vicinity acquired oxidative stress and bacterial infections lead to apoptosis with eventual bone-resorption and implant failure, respectively. Thus, in order to combat aforementioned complications, present research aims in utilizing antioxidant ceria (CeO<sub>2</sub>) and antibacterial silver (Ag) reinforced hydroxyapatite (HA) composite with enhanced mechanical and cytocompatible properties. Highly dense (>90%) spark plasma sintered HA-based composites elicits enhanced elastic modulus (121-133 GPa) in comparison to that of HA. The antioxidant activity is quantified using ceria alone, wherein HA-ceria and HA-ceria-Ag pellets exhibits ~36 and 30 % antioxidant activity, respectively, accrediting ceria as a scavenger of reactive oxygen species, which was corroborated with the % Ce<sup>3+</sup> change quantified by X-ray photoelectron spectroscopy. The HA-Ag pellet shows antibacterial efficacy of ~61 % for E. coli and ~53 % for S. aureus, while a reduction of ~59% for E. coli and ~50 % for S. aureus is observed for HA-ceria-2.5Ag pellet, affirming Ag reinforcement as an established bactericidal agent. The enhanced hydrophobicity on all the HA-based composites affords a high protein adsorption (24 h incubation). Further, elevated hFOB cell count (~6.7 times for HA-ceria-Ag on day 7) with filopodial extensions (60-150 µm) and matrix-like deposition reflect cell-substrate intimacy. Thus, synergistic antioxidant ceria and antibacterial Ag reinforcement with enhanced mechanical integrity can potentially serve as cytocompatible porous bone scaffolds or bioactive coatings on femoral stems.

Keywords: Hydroxyapatite; Osteoblasts; Antibacterial; Antioxidant; Cytocompatible.

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