INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	VARUN SAXENA
Roll Number	:	156106030
Programme of Study	:	Ph.D.

Thesis Title: Metal-oxide integrated Calcium Hydroxyapatite as a Potential Nano-antibiotic for Biomedical Applications

Name of Thesis Supervisor(s)	:	Dr. Lalit M. Pandey
Thesis Submitted to the Department/ Center	:	Biosciences and Bioengineering
Date of completion of Thesis Viva-Voce Exam	:	03-September-2021
Key words for description of Thesis Work	:	Hydroxyapatite, ZnO, Nanomedicine, Antibacterial activity, Antibacterial mechanism, Bone Tissue engineering

SHORT ABSTRACT

Hydroxyapatite (HAp) is a widely studied material for bone tissue engineering applications, but it has no intrinsic antibacterial properties to prevent infection. Further, target deficiency is also an obstacle in its commercialization. Various nanoparticles (NPs) such as ZnO, Fe_3O_4, Ag, peptides, and peptoids, a new class of bio-organic nanomaterials, have been found to possess antibacterial activity. The objective of this thesis was to explore the effect of metal ion integration with the HAp lattice to incorporate the self-antibacterial activity as well as the target efficacy for biomedical applications. The entire thesis is divided into five sections explaining the step-wise extension of the thesis. The first section deals with the synthesis and characterization of the ZnO nanoparticles and the evaluation of their antibacterial activity. The antibacterial activity of ZnO remains dependent on its size and morphology. The size and morphology can be tuned by using various sophisticated techniques. Our idea was to obtain the required antibacterial activity by simple co-precipitation method via metal ion doping. In this section, we have scrutinized the effect of doping of trivalent Al^{3+} ions into the ZnO lattice to enhance its antibacterial action. The minimum inhibitory concentration (MIC) value was decreased by ~19 times at 15 % doping, and the major antibacterial activity was found due to the intracellular accumulation of the Zn^{2+} ions and reactive oxygen species (ROS) independent. However,

rupturing in the bacterial cell wall could not be achieved. Hence, in the second section, we doped another trivalent ion, Fe^{3+}, into the ZnO lattice and explored its antibacterial activity and mechanism. In the case of Fe doping, the release of the Zn^{2+} ions was linear as compared to Al doping (exponential), leading to the rupturing into the bacterial cell wall. These two sections explained the tuning of the Physico-chemical properties of ZnO based on the dopant type.

Following the rupturing of the bacterial cell wall and enhanced antibacterial activity, in the third section, Zn and Fe were co-integrated with the HAp lattice. A biphasic ferric-HAp-zincite nanoassembly was designed and was explored for its antibacterial, biocompatibility, and bone cell proliferation ability. The designed ferric-HAp-zincite nanoassembly possessed excellent antibacterial activity, which was ROS independent, and due to the linear release of the Zn and Fe ions, causing the rupturing of the bacterial cell wall. Additionally, the designed ferric-HAp-zincite nanoassembly possessed a cell viability ~300 times higher than that of control cells and reflected no inflammatory response studied via TNF-α activity. Furthermore, the designed ferric-HAp-zincite nanoassembly possessed excellent bone cell proliferation ability (alkaline phosphatase activity) based on the concentration of the Zn within the designed HAp based nanoassembly. Moreover, this ferric-HAp-zincite nanoassembly possessed paramagnetic behavior, which is ideal for the target efficiency. This section explained the role of metal ion doping into the HAp lattice and tuning of its biological responses via altering the lattice parameters and phases.

The fourth section of this thesis explains the bone tissue engineering application of the designed ferric-HAp-zincite nanoassembly. In this section, we fabricated the Chitosan-CMC-ferric-HAp-zincite scaffold and scrutinized its biochemical properties. The biochemical properties such as porosity, swelling behavior, and enzymatic degradation were found to be dependent on the concentration of the ferric-HAp-zincite nanoassembly. The designed scaffolds possessed excellent bone cell proliferation and bio-mineralization ability. Hence, the scaffolds are plausible for bone tissue engineering applications. This thesis's fifth and final section comprises the design, characterization, and antibacterial activity of the novel peptidomimetics "peptoid" (Ampetoids) micelles. These micelles may be suitable to fabricate the ferric-HAp-zincite-Ampetoids organic-inorganic hybrid nanomedicine systems.