Abstract

Advancements in the field of nanobiotechnology have motivated the pursuit of identifying nanostructured materials that are not impeded by associated toxicity and are compatible to biological systems. The present thesis attempts to contribute in this pursuit by routing for the biocompatible, thermally stable, and chemically as well as biologically inert, zirconium phosphate (ZrP) system as a promising contender in the field. Although the layered morphology of ZrP (*viz.* α-ZrP and θ-ZrP) have been previously reported for their biomedical application, but their relatively larger sizes (ranging between 175-275 nm) have often overridden their relevance in *in vivo* intracellular applications. Deliberating on this, the present study focuses on the design and synthesis of ZrP in the nanoparticulate form and attempts to explore their efficacy as nanocarriers for drug delivery and as bioactive fillers in nanocomposite scaffolds for tissue engineering application, by virtue of their small size and high surface to volume ratio.

The present research endeavors to establish a facile aqueous-based sonochemical method for the synthesis of ZrP and a solution based template method for the preparation of Fe_3O_4@ZrP core-shell nanoparticles. Their suitability and efficiency as potential nanocarriers in drug delivery application have been assessed through cytotoxicity studies, carried out *via* conventional MTT [3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide] assay using human breast cancer cell lines MDA-MB-231, while *curcumin* has been used as a model anti-tumor drug molecule. The ZrP nanoparticles were further expended as bioactive fillers in the fabrication of nanocomposite films of poly (vinyl alcohol) (PVA)/ZrP (undoped and doped with Ca, Mg, and Ti) and PVA/montmorillonite (MMT)/ZrP *via* solvent casting method. Biocompatibility, bioactivity, biodegradability and mechanical properties of the nanocomposite films were examined for recognizing their potency as tissue engineering scaffolds.

Investigates (i.e., *in vitro* experiments) revealed that the synthesized spherical ZrP (average size 48 nm; surface area ~206.51 m^2/g) and Fe_3O_4@ZrP core-shell nanoparticles exhibit good biocompatibility and cellular internalization behavior. Their drug (*curcumin*) loading capacity was observed to be ~11.5% and ~11.15% respectively, while the release of the drug molecule was found to be triggered by acidic pH conditions. This validated the potency of these nanoparticles as nanocarriers for drug delivery application, where the drug-release could be triggered by the acidic pH of the tumor *micromilieu*. In addition, reasonable magnetization depicted by the Fe_3O_4@ZrP core-shell nanoparticles (superparamagnetism at

room temperature) enable them to be magnetically chauffeured to the tumor site. Further, it was observed that the cytotoxicity and the bioavailability of *curcumin* molecule were enhanced in the nanoformulations compared to its native form.

The nanocomposite films of PVA/ZrP (undoped and doped with Ca, Mg, and Ti) and PVA/MMT/ZrP were successfully fabricated. The nanocomposite films with doped ZrP (doped with Ca, Mg, and Ti) were found to exhibit improved nanomechanical properties, biocompatibility and bioactivity in contrast to the PVA/ZrP (undoped) and neat PVA films. The PVA/Ca-doped ZrP nanocomposite film exhibited the highest bioactivity, while PVA/Ti-doped ZrP demonstrated the highest hardness and elastic modulus values. This recognizes the ZrP (doped with Ca, Mg, and Ti) nanoparticles as promising bioactive fillers for scaffolds in tissue engineering application. Further, the PVA/MMT/ZrP nanocomposite film showed good bioactivity, biocompatibility and mechanical properties, which validated their efficacy as matrix materials in tissue engineering application compared to PVA/MMT, PVA/ZrP or the neat PVA films.

***Keywords*:** Zirconium phosphate; Nanocarriers; Drug delivery; Bioactive fillers; Scaffold; Tissue engineering.