Abstract

Recently, biodegradable implants attracted significant attention for a variety of clinical applications, including bone regeneration, replacement, and repair. Such perspective implants minimize the possibilities of revision surgery for their replacement and other related concerns. Additionally, the transfer of load from the implant to host tissue occurs successfully if the pace of degradation of the implant coincides well with the rate of neo-bone growth. This prevents the effect of stress shielding and thereby, maintains the mechanical strength at the interface.

Bone contains Mg^{2+}, Ca^{2+}, Zr^{4+} and Si^{4+} ions, which are essential for the regulation of several metabolic processes, including promotion of osteogenesis and prevention of osteoporosis. Living bone is mostly composed approximately 65 wt.% apatite (ceramic phase) and 23 wt.% collagen (polymeric phase). of ceramics, as seen from the standpoint of materials. Therefore, bioceramics have been successfully developed for orthopedic implant applications. Additionally, piezoelectric properties in natural bone regulate its metabolism. Because of its piezoelectric characteristic, natural bone undergoes polarization when exposed to mechanical stimulation, contributing to the facilitation of bone growth. The compressive load generates negative charge which promotes the osteoblastic activities. On the other hand, tensile load generates positive charge where osteoclastic activities dominate. Recently, polarization induced improved biocompatibility of piezoelectric bioceramics has been recognized as an interesting strategy for the development of prospective electroactive prosthetic orthopaedic implants.

The present study developed Ca and Zr co-doped $Mg_{1-x}Ca_xSi_{1-x}Zr_xO_3$ [(x = 0, 0.1, 0.2, 0.3 and 0.4), MCSZO – X, (X = 0 - 4)] bioceramics. After optimizing the processing parameters and microstructural analyses, the influence of electrical treatment on the osteogenic response (viability and differentiation) of prepared biocermics samples were analyzed using osteoblast-

like MG-63 cells, by considering HA as control. Also, the antibacterial response of MCSZO-X electret was analyzed. Further, the *in vivo* toxicity of MCSZO-X (X = 0 - 4) nanoparticles in a rat model was also performed.

For this purpose, the MCSZO – X and HA samples were prepared by solid-state and co-precipitation routes, respectively. The Cold isostatic pressing was used to achieve higher densification. After that, the prepared samples were corona (25 kV) poled at the temperature of 500 ºC to form electrets. The influence of electrets formation of prepared MCSZO-X (X = 0 - 4) ceramics on their surface chemistry, hydrophilicity and leaching behavior was assessed by X-ray photoelectron spectroscopy (XPS), contact angle measurement and inductive coupled plasma (ICP), respectively. Also, the surface charge that induces antibacterial activity of MCSZO-X ceramics was measured using reactive oxygen species (ROS), the levels of superoxide dismutase, catalase, and level of protein and lipid peroxide.

The thesis contains seven chapters. Chapter 1 provides a concise overview of the significance of the current study on silicate-based bioceramics. It also introduces the importance of silicate-based bioceramics for the application of bone tissue engineering along with the role of various ions such as, Mg, Ca, and Si in bone metabolism. Further, surface charge and electrodynamical stimulation have also been proposed as potential solutions to enhance the osteogenic response. Additionally, surface charge-induced antibacterial responses have been discussed, which is a major problem in prosthetic orthopedic implants.

Chapter 2, reviewed to evaluate the potentiality of Mg-Ca silicate-based crystalline bioceramics such as, $MgSiO_3$, Mg_2SiO_4, $CaSiO_3$, Ca_2SiO_4, Ca_3SiO_5, $CaMgSi_2O_6$, $Ca_2MgSi_2O_7$, $Ca_7MgSi_4O_{16}$, $CaMgSiO_4$ and $Ca_3MgSi_2O_8$ as new generation orthopaedic prosthetic implants. The chapter thoroughly reviewed and analyzed the influence of crystal structure, processing parameters/routes, and compositional alteration on in *vitro/in vivo* biocompatibility and degradation behavior of the above ceramics. Further, a correlation

between structure, processing and properties has been established. In addition, various stimuli, used to promote the cellular response and inhibit bacterial infection, including surface charge and external electrical stimulation have been critically reviewed.

Chapter 3, deal with the synthesis method, and characterizations of $Mg_{1-x}Ca_xSi_{1-x}Zr_xO_3$, (x = 0, 0.1, 0.2, 0.3 and 0.4) MCSZO-X and hydroxyapatite ceramics are described. To analyse the phases, microstructure, surface chemistry and physical characterization of the developed bioceramics, various phase evolution techniques including X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), microstructural characterization (SEM and EDX), contact angle measurement and X-ray photelectric spectroscopy (XPS) were used. The effect of electrostatically and electrodynamically treatment in *in vitro* cellular response is also demonstrated. In addition, the electrostatically treated antibacterial response of prepared bioceramics have also presented. Further, *in -vivo* experiment is also performed to investigate the toxicity of MCSZO-X nanoparticles in the rat model.

Chapter 4 discusses the influence of formation of bioelectrets Ca and Zr co-doped $MgSiO_3$ [$Mg_{1-x}Ca_xSi_{1-x}Zr_xO_3$ (x = 0 - 0.1, 0.2, 0.3, 0.4); MCSZO-X, X=0 – 4] and electrodynamic stimulation towards improving their osteogenic response. The effect of surface charge on the wettability, surface chemistry and leaching of ions (Mg, Ca, Zr and Ca) was examined using contact angle measurement, X-ray photoelectron spectroscopy (XPS), and inductively coupled plasma (ICP) analyses, respectively. Further, the combined effect of electrostatic charge and electrodynamic stimulation along with compositional modification on cell proliferation, adhesion and differentiation were analyzed. Further, the mechanism of enhanced cellular functionality was revealed by the measurement of intracellular Ca^{2+}.

Chapter 5 discusses the effect of surface charge and co-substitution of Ca and Zr in $MgSiO_3$ [$Mg_{1-x}Ca_xSi_{1-x}Zr_xO_3$ (x = 0 - 0.1, 0.2, 0.3, 0.4); MCSZO-X, X=0 – 4] on their antibacterial response. The MCSZO-X bioceramics were synthesized using solid-state route. The influence

of Ca and Zr co-doping on crystallite size of MCSZO-X has been analysed using X-ray peak profile analyses. The surface charged were developed by corona poling (30 min) of sintered MCSZO-X samples as well as HA samples at temperature and voltage of 500°C and 20 kV, respectively. In addition, the antibacterial response of MCSZO-X ceramics was evaluated by measuring of reactive oxygen species (ROS), the levels of superoxide dismutase, catalase, and level of protein and lipid peroxide.

Chapter 6 explores the *in vivo* potentiality that aims to assess both local and systemic toxicity of co-substitution of Ca and Zr in $MgSiO_3$ [$Mg_{1-x}Ca_xSi_{1-x}Zr_xO_3$ (x = 0 - 0.1, 0.2, 0.3, 0.4); MCSZO-X, X=0 – 4] nanoparticles using rat model. The cytotoxicity of MCSZO-X (X=0 – 4) nanoparticles was preliminarily evaluated by exposing MG-63 cells to varying concentrations as 0.25, 2.5, 25 mg/ml. Consequently, the biocompatibility of MCSZO-X nanoparticles was tested by injecting the eluates of concentration of 25 mg/ml into the synovial joints of rats for 7 days. Histological analyses were conducted on the organs, to detect the signs of inflammation. Furthermore, the biochemical assays (Alkaline phosphatase and Creatinine activities) were conducted on the extracted serum from the rats, subjected to particulate treatment.

Chapter 7 provides a comprehensive overview of the notable discoveries made throughout the study and proposes recommendations for potential future research endeavours.