CHAPTER 7

SUMMARY AND SUGGESTIONS FOR FUTURE WORK

7.1 SUMMARY

Biomaterials are materials of natural or artificial origin that are used to direct, supplement, or replace the functions of living tissues of the human body. Artificial biomaterials are classified as metal, ceramic, polymer and composites. Biomaterials in the form of implants (bone plates, joint replacements, ligaments, vascular graft, heart valves, intraocular lenses, dental implants, etc.) and medical devices (pacemakers, biosensors, artificial hearts, blood tubes, etc.) are widely used to replace and/or restore the function of degenerated tissues or organs to assist in healing, improve function, correct abnormalities and improve the quality of life of the patients.

Widely ceramics are widely used in medical field due to their good bioactivity and biocompatiability. Bioceramics consists of calcium phosphates, alumina, zirconia, carbon, etc. HAp is one of the major phase in calcium phosphates which is the main constituent of hard tissues such as bones and teeth. The powder, solid block and thin films of synthetic HAp is used for hard tissues replacement which is implanted into our body based on affected area of the bone. In addition, it is used for local drug delivery system for the treatment of bone diseases such as cancer and osteomyelitis (infection). But, stoichiometric HAp has poor bioactivity due to poor resorbability. Owing to this reason, researchers are developing new types of bone filler and drug delivery carrier of resorbable and non-resorbable

materials such as mixed phases of calcium phosphates, polymer scaffolds and organic/inorganic composites to enhance its biological performances.

HAp thin films are used as implants in load bearing application. HAp coated metal substrate have their disadvantages such as less adhesion strength, lattice mismatching between metal and HAp thin film, low bioactivity, bacterial infections and no clear chemical composition. The bioactivity of the calcium phosphate coated metal implants is improved through different processes like surface modification and preparation techniques.

Surface properties of biomaterials play an important role in initiating and sustaining new bone growth. For commercial purposes, biomaterial engineers modify the surface properties of biomedical implants by various techniques. The ion beam irradiation/implantation provides significant modification on the surface properties of HAp which improves the biointeraction for cell adhesion. In addition, swift heavy ion irradiation induces free lattice mismatch of HAp film and improves the bioactivity. To understand the interaction between biomaterial and tissues it is essential to aid in the design, fabrication and its surface modification of biocompatible and bioactive materials. In addition, study of the physico-chemical properties of custom designed new biomaterials is necessary for specific medical applications.

The present work deals to improve the bioactivity of nanosized HAp/polymer composites, HAp thin films, and their investigation on antibiotic drug loading/release behavior. The HAp thin films were prepared by various methods and their surface modification were performed by swift heavy ion irradiation.

Nanorods of HAp/agarose composite were synthesized by sol-gel technique at low temperature followed by microwave treatment and their pH was maintained using pH stat. HAp/agarose composite was confirmed by XRD and FTIR. Microwave treatment is a better route to synthesize high crystallinity sample than calcination process. HAp/agarose nanorods of length 10-100 nm and width 5-20 nm were observed on as-synthesized samples and decreased in length (5-70 nm) after microwave treatment. The calcined samples showed interconnected porous structure of bioceramic which is very much useful for osseointegration. There was no significant variation in chemical composition for different condition prepared samples. The specific surface areas of as-synthesized and microwave treated samples were higher (50 %) than that of calcined samples. In vitro bioactivity initially absorbable subsequently exhibited bioactive nature in the as-synthesized and microwave treated samples. Microwave treated samples showed controlled drug (antibiotic and anticancer) release profile than the other samples. The antibacterial activity results showed that the samples prepared by both techniques are strongly active against the most common bacterial strains, and it may be used as an implant material and for reconstructive surgery applications. All samples showed bioacitivity, more haemocompatability and no cytotoxicity.

CHAp/agarose composite was prepared by solvothermal method under different temperatures. The interaction between HAp and agarose was confirmed from FTIR and Raman analysis. SEM and TEM analysis showed the nanorods of HAp/agarose were of length 10-80 nm and width 40-190 nm for solvothermal synthesized samples at a temperature 120 and 150 °C. The calcinations process has converted rods into spherical (10-50 nm), rectangular (10-60 nm length and 20-45 nm width) along with small rod shaped particles (40-120 nm length and 20-30 nm width). The elemental analysis, showed all samples were in nearly stoichiometric composition of HAp (Ca/P = 1.67).

The surface area (~50-65 m^2/g) with mesoporous (~20-30 nm) structure was observed on solvothermally synthesized sample which is more useful for drug delivery systems. In addition, bioactivity, low dissolution rate and more haemocompatibility were found for all samples. Nanorods of CHAp/agarose composite showed extended drug (AMX and 5-FCil) release when compared to calcined (HAp) samples. The antimicrobial activity showed all samples are strongly active against E. coli, S. aureus and S. epidermidis. HAp composites prepared by this method showed excellent properties such as bioactivity, increased surface area with mesopores, extended drug release and high antimicrobial resistance. Hence, it could be used as hard tissue implants, local drug delivery system and for tissue engineering application.

Biphasic calcium phosphate (HAp and β-TCP) thin films were produced on Si (001) substrate using the e-beam deposition technique. The ASBCP and BCP500 were found to be amorphous. The post annealing (> 500 °C) produced crystalline BCP films. The ASBCP and BCP500 coating dissolved within a week when it was immersed in SBF. The surface roughness and dissolution of the calcium phosphate layer was decreased by thermal treatment. The crystalline BCP700 showed better bioactivity. BCP700 enhanced hydrophilicity which is very much helpful to the cell attachment during implantation. No toxicity was observed on BCP deposited on silicon substrate. AMX loaded BCP film showed very good bacterial resistant against S. aureus. The electron beam evaporation method is a suitable and cost effective technique for the preparation of BCP films. Biphasic calcium phosphate thin film having resorbable β-TCP and non-resorbable hydroxyapatite (HAp) phases revealed enhanced bioactivity. Therefore it could be used as a promising material for bone tissue regeneration and repair which is difficult to achieve as a single phase on the metal substrate.

Nanosized HAp was deposited on three different (Ti, SS316L and Si) substrates with different conditions by RF magnetron sputtering. HAp layer grown on Ti substrate was confirmed by XRD. The condition for the preparation of uniform layer of HAp on the substrate was optimized and it was adapted for the preparation of thin films. The surface was modified by swift heavy silicon ion irradiation (125 MeV) on HAp thin films. The irradiation caused variation of surface roughness and particle size on the surface without modifying its phase along with a decrease in its optical band gap energy. The HAp thin films irradiated with fluence of $1x10^{11}$ ions/cm^2 showed enhanced wettability and aided the deposition of a layer of bone like apatite when it was immersed in SBF. Irradiated samples showed no cytotoxicity. Therefore, SHI irradiation with Si^{9+} ion beams can be an ideal technique to enhance the wettability and bioactivity of HAp related biomaterials. The efficacy against S. aureus was high for $1x10^{10}$ and $1x10^{11}$ ions/cm^2 irradiated films and it could be used for osteomyelitis treatment.

The effect of 100 MeV Ag^{7+} ion irradiation on HAp thin film prepared by PLD technique was investigated. Reduction of particle size and variation in lattice parameters was obtained at low fluence irradiated samples. Films turned amorphous at $1x10^{13}$ ions/cm^2. From Raman study, the decrease in peak intensities with increase in FWHM indicated that, there was modification on the surface. In addition, peak shift of symmetric stretching peak indicated the stress developed in the unit cell of HAp on irradiation. SEM result showed reduction of particle size (0.1-3 μm) without clear morphology at higher fluence of irradiation compared with pristine. The optical band gap and roughness of the surface was decreased due to increase in SHI fluences. There was no significant variation in Ca/P ratio on irradiation. This result suggested that HAp is more stable after SHI irradiation. The adsorption of drug (~10 %) and hydrophilic property (~25 %) increased for ion beam irradiated samples. Drug release profile exhibited

initial burst release followed by slow release for pristine and low fluences irradiated samples. The irradiated samples showed fast release compared to pristine, due to the decrement of crystallinity of HAp film by irradiation. Antimicrobial properties of irradiated samples were highly active against S. aureus when compared to pristine. Therefore, SHI irradiation can be a best tool for surface modification, enhanced drug loading, bioactivity and wettability.

7.2 SUGGESTIONS FOR FUTURE WORK

Work can be extended to fabricate HAp polymer (gelatin, collagen, etc.) composites, thin films and their surface modification by swift heavy ion irradiation can be performed along with its study on mechanical properties. The in vivo investigation can be carried out to understand the biocompatibility, bioactivity, non-toxicity and chemical durability of the drug loaded bioceramics. Different drugs with various combinations can be studied for local drug delivery system.

The variation in physical, chemical and biological properties of the HAp composites and method of preparation can also be investigated. Surface modification of biomaterials like CaP could be carried out using various (O, Mg, Zn, Ni and Au) ions with different fluences, which would help us to fabricate biocompatible, hard tissue replacement materials.