CHAPTER 1
INTRODUCTION

1.1 MOTIVATION AND BACKGROUND

Treatment of Bone defects due to severe trauma and several pathological conditions like bone tumours and infections represent a major challenge for orthopedic surgeons worldwide and are a global health problem. Suitable techniques to regenerate bone in oral, maxillofacial and orthopedic surgery have become the prominent clinical issue in the field of regenerative medicine. Major dent is created in the quality of life of persons dealing with such enormous physiological handicaps making it an imperative social problem. Osteoporosis and osteopenia related to advanced age in people add to the need of suitable bone regeneration therapy (Arvidson et al. 2011). Although considerable progress have been made in medical sciences and technologies, organ failure and tissue loss are still treated with transplantation.

At present bone grafts and metallic/ceramic implants are two major treatments to bone loss in the world. The materials used in bone grafting can be divided into autografts, allografts, xenografts, and synthetic materials. In clinical medicine, autologous bone grafting is the best choice for enhancing bone repair and reconstructive bone defects. However, the use of autografts is hampered by the limited supply of bone grafts, the necessity of an additional incision site, donor site morbidity, nerve damage, and injury of the donor site (Heo et al. 2011). Allografts are frequently used in orthopaedic surgery for the treatment of bone nonunion, enhancing the repair of spine fracture, and reconstruction of bone defects (Sinibaldi 1989). The advantages of allografts include the absence or minimization of donor site morbidity and the unlimited choice of graft shape and size (Finkemeier 2002). Allografts and xenografts lack the osteoinduction and osteogenesis properties of autogenous bone, and they introduce the potential for both transferring disease and
triggering a host immune response (Erbe et al. 2001). Metallic/ceramic implants differ from native bone in terms of structure and mechanical properties, often leading to additional bone damage. Three specific properties define the characteristics of natural bone and autografts: osteoconductivity; osteogenicity; and osteoinductivity. The search for suitable biomaterial to act as bone implant is the need of hour for scientist across the world.

Tissue engineering is the science of design and fabrication of new tissues for functional restoration of impaired organs and replacement of lost parts due to cancer, disease and trauma (Reddi 1998, Reddi 2000). Among many tissues present in the body, bone has the highest tendency to self heal and regenerate and therefore is an archetype for the elocution of principles of tissue engineering. With the help of tissue engineering techniques we can design bones with predetermined shapes for orthopedic surgery applications (Langer and Vacanti 1993). Biologic tissues consist of the cells, and the signaling systems, which are brought into play through differential activation of genes whose transcriptional products are responsible for cueing tissue building and differentiation (Glowacki 2001). Orthopedic surgeons have been utilizing bone grafts for more than a century. Bone induction is a sequential multistep process that includes chemotaxis and attachment of mesenchymal stem cells, proliferation of progenitor cells and differentiation into cartilage and bone. Bone induction can be functionally divided into the following phases: initiation, promotion and maintenance. Osteogenin and bone morphogenetic proteins primarily initiate bone induction. According to basic tissue engineering approach, cells are isolated from appropriate donor site and cultured in desired cell culture medium, further they are seeded on a scaffold and then implanted into the defect site to form new tissue (Bonassar and Vacanti 1998). Primarily, the seeded cells provide the main source for new tissue regeneration and in turn the scaffolds act as a supporting three-dimensional template for cell growth which degrades in due course of time as the tissues are regenerated.
The important requirement of three-dimensional biocompatible scaffolds for tissue engineering includes providing suitable surface features for cell attachment with appropriate mechanical strength to bear the initial load of seeded cells and also to enable cell infiltration. Nanoscale surface topographical cues can control cell morphology and motility; also they can guide cell attachment and alignment – and consequently the alignment of the ECM (Bashur et al. 2006, Frank et al. 1983). The scaffold should be designed with high degree of porosity with greater control over pore size and their interconnectivity to allow for cell infiltration (Wang et al. 2003). Truly the choice of appropriate scaffold material with these desired characteristics is the need of hour. The focus relies on nanocomposites comprising of polymer ceramic matrix which has already gained incredible popularity in the field of bone tissue engineering (Chung et al. 2007, Boudriot et al. 2006).

1.2 AIM AND OBJECTIVE OF RESEARCH

The main hypotheses of this thesis are: (1) To assess the biocompatibility of seeded MG-63 osteoblast cell lines on electrospun nanocomposite systems to facilitate the scaffold as precursor material leading to high quality bone regeneration; (2) The fabrication of constitutional intricacy in scaffolds to mimic the compositional properties of natural extracellular matrices in terms of porosity, pore morphology, fiber size and orientation which will facilitate complex tissue regeneration. The specific aims of this thesis are listed below:

1. To develop 3D nanofibrous scaffolds from PVA-PVP blend system and characterize the polymer composites for their structural, chemical and morphological behavior and to evaluate the biocompatibility of these scaffolds on seeded NIH 3T3 cell lines in vitro, Specifically, we focus on finding the cell viability percentage of fibroblast cell lines on generated scaffolds to use it as suitable matrix for tissue engineering.
2. Development, characterization and evaluation of electrospun PVA-PCL bilayer system as suitable scaffold for tissue regeneration. The *in vitro* biocompatibility was assessed using NIH 3T3 fibroblast cell lines. Specifically the adherence and growth of cell lines on bilayer composite system was morphologically analyzed.

3. To synthesize nanocomposites of various calcium phosphate ceramic incorporated PVA-PVP and PVA-PCL blend and bilayer systems. The fabricated nanofibrous polymer-ceramic nanocomposites were evaluated for their chemical, structural complexity, crystalline behaviour and morphological variation including fiber diameter, porosity and pore diameter to act as suitable scaffold for bone tissue regeneration. Specifically, the *in vitro* biocompatibilities of prepared matrices were evaluated using MG-63 osteoblast cell lines.