CHAPTER I
INTRODUCTION

The term dental prosthesis or denture denominated an artificial replacement or prosthesis of one or more teeth and associated dental or alveolar structures (Prosthodontics, 2005). There have been a lot of progresses nowadays for the use of dental prosthesis as a treatment approach in patients who lose their natural dentition. For an expected successful treatment with long-term prognosis, dental prostheses need to be supported by sufficient volume of healthy bone for being their steady foundation (Sennerby *et al.*, 1988; Taylor and Agar, 2002; Lee *et al.*, 2005). However, this requirement depends on the nature of post-dental extraction healing and rehabilitation of the alveolar process which generally end up with bone loss due to the remodeling resorption.

The complete healing of alveolar bone and related soft tissue leaves behind clinically the corresponding residual ridge (Bodic *et al.*, 2005). Factually, form and configuration of residual ridge are unstable due to the continuous remodeling resorption. Resorption of the residual ridge is a chronically irreversible and cumulative mechanism (Jahangiri *et al.*, 1998). It can be described as resorptive atrophy which is a fundamental and physiologic reaction to the loss of function and inactivity (Sennerby *et al.*, 1988). Statistically, residual ridge resorption occurs continuously within the first year, with a particularly fast rate during the first 3 to 6 months (Jahangiri *et al.*, 1998; Bodic *et al.*, 2005). Resorption continues at a slower pace throughout a life-span, resulting in removal of a large amount of jaw bone. It was estimated that bone loss occurred at ~21, ~36, and ~44% after a tooth had been extracted for 3, 6, and 12 months, respectively, and the alveolar bone may lose up to 10 mm of the lower jaw height after 25 years (Bodic *et al.*, 2005). Prevention of the alveolar bone resorption, therefore, has been of great concern and study particularly through the principle of tissue engineering.

Tissue engineering is an approach to regenerate living tissue with an aim at establishing healthy tissue or organ for being a substitute of the damaged or the diseased tissue (Hoffman, 2002). Progression in tissue engineering research since 1990 has been encouraging a reappraisal of the surgical approach for the treatment of

trauma and degeneration of an individual (Hollander and Hatton, 2004). Concerning alveolar bone resorption, concept of self regeneration has been carried out in many methods in order to preserve bone mass. Various materials have been immediately administered into dental root socket on purpose of enhancing process of novel cell or tissue development e.g., autogenous or allogenic bone grafts (Wiesen and Krrzis, 1998), hydroxyapatite-collagen implant materials (Hanne *et al.*, 1998), chemical agents like bisphosphonates (Yaffe *et al.*, 1999; Altundal and Guvener, 2004), and bone growth factors (Lalani *et al.*, 2003), for instance.

The fundamental of tissue engineering basically coalesces cell, supportive material termed "scaffold" and growth-inducing substance to encourage three-dimensional tissue growth (Langer and Vacanti, 1993). Scaffold, which is a three-dimensional construct, serves as a temporary territory for cells ingrowths. Ideal scaffold should perfectly imitate the extracellular matrix and provide necessary support for cells to proliferate and maintain their differentiated function (Hutmacher, 2000; Mikos *et al.*, 2004). Therefore, design and fabrication of a porous scaffold, which is an early stage of the procedures in tissue engineering particularly for bony tissue, should be done with concern of numerous scaffolding properties like biocompatibility, degradation, mechanical integrity and physical characteristics (Hutmacher, 2000).

The early design of scaffold has been focused on their physical and mechanical characteristics which relate to capabilities of scaffold in supporting cell growth. But recently, according to the rapid advancement of research in molecular biology, most scaffolds have been designed to serve an extra function of being a cellular guidance. This deliberation is compliant with the concept of cellular guidance which has been extensively discussed and progressively revised as a new knowledge of the cell-material interaction in tissue regeneration (Causa *et al.*, 2007; Tessmar and Gopferich, 2007). Scaffolds nowadays have been purposed as a route to transport therapeutic agents for cells like biological factors. They are capable of guiding and inducing cells adhesion, proliferation and differentiation or even recruiting the desired cells. All of these functionalities can be achievable by tailoring scaffold's physical properties, integrating certain bioactive agents into a scaffold, or both (Causa *et al.*, 2007).

Through this conception, scaffold does not only physically mimic the extracellular matrix but also biologically. Design and fabrication of scaffold today combines together the matter of being a cell carrier and the discipline of controlled drug delivery. The novel tissue engineering scaffold, therefore, can be considered as a special type of drug delivery apparatus (Tessmar and Gopferich, 2007) which is nominated as drug delivery scaffold in this dissertation.

With an aim to preserve alveolar bone form the remodeling resorption by means of tissue self-regeneration. This thesis endeavors to develop a drug delivery scaffold used for filling dental root sockets or bone lesions. The as-prepared scaffold is anticipated to be multi-functional which is mutually responsible for being a supportive matrix for cell growth and a controlled drug delivery device. The study was separated into four sections according to the types of prepared scaffold as describes below

Section 1 - ***Chapter IV: Mechanical Physical and Biological Properties of Scaffolds of α-Chitin Whiskers Reinforced Hyaluronan-Gelatin Nanocomposites*** – presents the fabrication of porous scaffolds from natural biodegradable polymers. Scaffolds were fabricated with α-chitin whiskers reinforced hyaluronan-gelatin nanocomposites by the freeze-drying technique. The study focused on the correlation between the content of chitin whisker and the ensuing properties of scaffold for bone tissue regeneration in term of physical, mechanical and biological features.

Section 2 - ***Chapter V: Delivery of Crude Bone Protein form Gelatin Microspheres and Microspheres Integrated Hyaluronan-Gelatin Blended Scaffold for Bone Tissue Regeneration*** – is devoted to the fabrication of a protein delivery scaffold on the basis of integrating a separate delivery device. The concept of the polyion complexation (Brown *et al.*, 1998) was applied to achieve a degree of ionic-molecular interaction between the carrier and model protein; gelatin microspheres and crude bone protein. The encapsulated gelatin microspheres were anticipated to be securely bound in the scaffold and provide the controlled release of crude bone protein in order to facilitate bone tissue regeneration.

Section 3 - ***Chapter VI: Effectual Drug-Releasing Porous Scaffolds from 1,6-Diisocynatohexane-extended Poly(1,4-Butylene Succinate) for Bone Tissue Regeneration*** – presents the fabrication of porous scaffolds from a synthetic biodegradable polymer, Poly(1,4-butylene succinate) extended with 1,6-diisocyanatohexane (PBSu-DCH), by solvent casting and particulate leaching technique and the characterization of their properties pertinent to bone tissue regeneration. Investigation was focused on the effect of porogen/polymer weight ratio on architecture and characteristics of the as-prepared scaffolds. The potential for use of these scaffolds as carriers for delivery of an active substance suitable for enhancing bone tissue regeneration was additionally investigated using ipriflavone, a synthetic derivative of isoflavone which has been known to accelerate osteoblast cell activity and, at the same time, inhibits bone resorption (Civitelli, 1997) as the model compound.

Section 4 - ***Chapter VII: Gelatin Microspheres Impregnated Porous Scaffolds of 1,6-Diisocynatohexane-extended Poly(1,4-Butylene Succinate) for Controlled Release of Protein*** – contains the development of another protein delivery scaffold on the basis of integrating a separate delivery device into a scaffold. Gelatin microspheres containing Tetramethylrhodamine conjugated albumin from bovine serum (BSA-Rhod) as a model protein, were impregnated into the PBSu-DCH porous scaffold and steadily attached with matrix of HA-Gelatin blend. The investigation was focused on the effect of the two factors; scaffold's pores sizes and proportion between HA and gelatin of the matrix on the release characteristics of BSA-Rhod.