CHAPTER I

INTRODUCTION

1.1 Statement of Problem

Nowadays a large number of synthetic polymeric materials with various different properties are available for medical applications. Most of the common materials have sufficient mechanical stability and elasticity as well as desired stability towards degradation, and are non-toxic. One important remaining problem is inadequate interaction between polymer and cells, leading to *in vivo* foreign body reactions, such as inflammation, infections, aseptic loosening, local tissue waste, and implant encapsulation as well as thrombosis and embolization. Approaches to improve biomaterials include reduction of unspecific protein adsorption, known as non-fouling properties, enhancement of adsorption of specific proteins, and material modification by immobilization of cell recognition motives to obtain controlled interaction between cells and synthetic substrates.

Polymeric biomaterials possessing specific cellular responses have become increasingly important in some biomedical applications of which biocompatibility is critically required, for example, prostheses, implants and tissue engineering matrices. Considerable success has been continuously reported on the material modification by immobilization of cell recognition motives to obtain desirable cellular responses. The RGD (R: arginine; G: glycine; D: aspartic acid) sequence is by far the most effective and most often employed cell recognition motives for stimulating cell adhesion on synthetic surfaces. Since its discovery in 1984 by Pierschbacher and Ruoslahti, RGD peptides have gained their reputation of being able not only to trigger cell adhesion effectively, but also to address selectively certain cell lines and elicit specific cellular responses. This tripeptide sequence is uniquely specific to integrin, a cell adhesion receptor at the cell membrane which is responsible for mediating cell adhesion and proliferation.

Tyrosine-derived polycarbonates having carboxyl pendant groups, poly (desaminotyrosyl-tyrosine ethyl ester-co-desaminotyrosyl-tyrosine carbonate) (poly(DTE-*co*-DT carbonate)), have been recently introduced as a new series of biodegradable polymer that can be potentially used for biomedical applications. The carboxyl groups can serve as versatile precursors for a wide range of chemical modification including an attachment with bioactive molecules including proteins and peptides.

This research aims to improve cellular responses of poly(DTE-*co*-DT carbonate by RGD attachment. An amide linkage is formed by reacting an activated carboxyl group with the nucleophilic *N*-terminus of the RGD peptides. Carboxyl groups can be activated by *N*-hydroxysuccinimide/1-ethyl-3-(3-dimethylaminopropyl) -carbodiimide (NHS/EDCI). *In vitro* adhesion and proliferation of fibroblasts are conducted in order to determine cellular responses of RGD-modified polycarbonates.

1.2 Objectives

1. To immobilize RGD-containing peptides on poly(DTE-*co*-DT carbonate) surfaces
2. To determine *in vitro* cell adhesion and proliferation of poly(DTE-*co*-20%DT carbonate) surfaces after immobilized with RGD-containing peptides

1.3 Scope of Investigation

The stepwise investigation was carried out as follows.

1. Literature survey for related research work.
2. To activate carboxyl groups of poly(DTE-*co*-DT carbonate) with *N*-hydroxysuccinimide under homogeneous condition
3. To activate carboxyl groups of poly(DTE-*co*-DT carbonate) with *N*-hydroxysuccinimide under heterogeneous condition
4. To immobilize RGD-containing peptides on poly(DTE-*co*-DT carbonate) surface
5. To determine *in vitro* cell adhesion and proliferation