CHAPTER I
INTRODUCTION

Chitosan, an amino polysaccharide, is available from a renewable resources derived from deacacetylated chitin. Chitin, a naturally occurring material, commercially extracted from the exoskeleton of marine shells of crustaceans such as shrimps and crabs. Chitosan has been paid more attention over chitin due to two main advantages. Firstly, due to its lower crystallinity, chitosan can be readily dissolved under milder conditions than chitin. Secondly, a unique active site of its free amino groups renders chitosan more reactive for chemical reactions and reveals its specific biological properties (i.e., antimicrobial, mucoadhesive and antioxidant properties).

Solubility is an important factor for applying chitosan in versatile applications. Due to its inter-and intra-hydrogen bonding, chitosan can only be soluble in diluted acid solutions (i.e., hydrochloric, formic, acetic, and citric acid). Therefore, chemical modification of chitosan is needed for improving its solubility. Because of reactive functional groups of chitosan including primary amino, primary and secondary hydroxyl groups, a variety of functional groups can be desired into chitosan structure. To produce water soluble chitosan derivatives, several chemical reactions have been reported such as reductive alkylation, sulfonation, quaternization and carboxyacylation.

Among these chemical modifications, *N*-carboxyacylation is one of the effective methods to produce water soluble chitosan derivatives by the introduction of cyclic anhydride groups at the amino group of chitosan structure. Various types of cyclic anhydrides, for example, maleic, succinic, phthalic and citraconic anhydride have been used for synthesis of such *N*-carboxyacyl chitosan derivatives. Maleic and succinic anhydrides, the small molecular structures of anhydrides, were introduced into amino group of chitosan in order to produce *N*-maleoyl chitosan and *N*-succinyl chitosan, respectively. It was reported that the solubility of *N*-maleoyl chitosan decreased within 2 weeks after preparation due to the reformation of their meleic anhydride substitution groups (Sashiwa and Shigemasa, 1999). In comparison with *N*-maleoyl chitosan, *N*-succinyl chitosan derivative exhibited a good solubility

(Sashiwa and Shigemasa, 1999) in a wide range of pH; therefore, they have been extensively studied for various applications, especially in the medical applications. *N*-succinyl chitosan has been proved for its biocompatibility and *in vivo* low toxicity (Song, Onishi and Nagai, 1993). The commercial wound dressing product of *N*-succinyl chitosan (Moistfine liquid®) has been produced (Izume, 1998) and furthering developed for a suitable wound healing conditions (Tajima, *et al.,* 2000). Due to its unique anionic characteristic, *N*-succinyl chitosan can sustain its life time in blood circulation system (Kato, Onishi and Machida, 2004) which can be applied for long term chemotherapeutic drug delivery. Furthermore, *N*-succinyl chitosan can be adsorbed with various types of heavy metal ions and were selectively adsorbed with lead ion and cupper ion when used them(Sun and Wang, 2006; Sun, Wang and Wang, 2007) as a template ions.

Several biomaterials, especially, chitosan as well as its water soluble derivatives has been exposed to the gamma radiation for several proposes such as for low molecular weight production by degradation (Choi, *et al.*, 2002; Hai, *et al.*, 2003; Huang, *et al.*, 2007), hydrogel production by crosslinking (Yoshii, *et al.*, 2003) and sterilizations in such medical materials (Siekman, 2006; Huang, *et al.,* 2007) before use.

In these present works, both of *N*-maleoyl chitosan and *N*-succinyl chitosan were synthesized and prepared into various such as film, hydrogel and solution.

At first, according to its self crosslinking property, *N*-maleoyl chitosan was fabricated into films and further characterized its physicochemical properties for furthering use in medical applications.

Various degrees of *N*-succinyl chitosan were synthesized into hydrogel for the second work by incorporation of citric acid and characterized for their physicochemical properties, absorption-release characteristics, and biodegradability, respectively. For the last work, the effect of gamma radiation on the structure of *N*-succinyl chitosan was also elucidated.