CHAPTER VII
CONCLUSIONS AND RECOMMENDATIONS

7.1 Conclusions

In present works, the water soluble *N*-maleoyl chitosan and *N*-succinyl chitosan derivatives were successfully synthesized under mild condition. The success of fabricated and radiated of these products was obtained. To avoid the use of any crosslink agents, the self-crosslinkable *N*-maleoyl chitosan films and *N*-succinyl chitosan hydrogel were directly crosslinked by themselves. For the *N*-maleoyl chitosan derivative, the self crosslinking of the fabricated films confirmed by the reduction of their swelling and weight loss behaviors toward the aging time of films showed consistency to the increase of the crosslinking density. Moreover, the swelling behavior of *N*-maleoyl chitosan films was also depended on both the pH due to the presences of both amino and carboxylic groups of their structure and ionic strength of solution due to the screening effect of sodium and chloride ions. For the *N*-succinyl chitosan derivative, the formation of covalently crosslinked hydrogel was enhanced by the initial present structure of chitosan-citric acid complexation. The high degree of substitution of *N*-succinyl chitosan can enhance the succinyl linkage, cationic interaction and susceptibility to the lysozyme degradation. In addition, indirect cytotoxicity evaluation of the *N*-succinyl chitosan hydrogel films was confirmed by the non-toxicity of these hydrogel films toward the culture of mouse fibroblast cells (L929) with extraction media from these materials. Effectively, the low molecular weight of *N*-succinyl chitosan induced by γ-ray radiation at low dose (5-30kGy) is more susceptible in dilute aqueous solution system than in solid state due to the promotion of waterlysis. The maintained structure of radiated *N*-succinyl chitosan characterized by FT-IR, ^{1}H-NMR, UV-vis and EA suggested that the main chain scission occurs at the β-(1,4) glycosidic linkages and some of succinyl substitution groups are eliminated. According to the characterizations of these water soluble chitosan derivatives, *N*-maleoyl chitosan films and *N*-succinyl chitosan hydrogels exhibited the proper physicochemical and biological properties for

furthering developed as biomaterials for medical applications such as for pH-sensitive drug carrier, wound dressing, implant scaffold, respectively. Moreover, the low molecular weight of *N*-succinyl chitosan produced by gamma radiation in dilute solution can be further used as antimicrobial agent for low degree of substitution and antioxidant agents for high degree of substitution conditions.

7.2 Recommendations

7.2.1 The Improvements of Their Physicochemical and Biological Properties of *N*-Carboxyacyl Chitosan Derivatives

To improve the mechanical properties and retard their biodegradability, the fabricated *N*-maleoyl chitosan and *N*-succinyl chitosan should be blended with other water soluble polysaccharides (i.e., alginate, PVA or hyaluronic acid) or coated with biosynthetic polymer (i.e., polylactic acids (PLA), polycaprolactone (PCL) and polyhydroxybutyrate-valerate (PHBV)) which showed the slow or long term biodegradability rate. Therefore, the desirable strength and biodegradability rate of these blend polymers can be obtained.

It was known that both of the degree of substitution and molecular weight of chitosan derivatives are directly affected not only on physicochemical properties but also on biological properties. The antimicrobial properties of these *N*-maleoyl chitosan and *N*-succinyl chitosan derivatives should be achieved at the suitable degree of substitution or minimal degree of substitution that showed both efficient carboxylic groups for water solubility and available of free amino groups for their antimicrobial activity. In addition, the antimicrobial, antioxidant as well as mucoadhesive properties of the different molecular weight, especially for the obtained low molecular weight of *N*-succinyl chitosan, could be evaluated.

7.2.2 Fabrications of *N*-Carboxyacyl Chitosan Derivatives

Besides fabricated as film form, these derivatives can be fabricated in forms of scaffold by using freeze-dying technique because of their water as solvent which can be further developed as an implant biomaterial. To fabricate hydrogel, *N*-succinyl chitosan at high concentration (>10%, paste-like state) can be also produced by using γ-ray radiation technique in the same manner as previously studies of others

water soluble polysaccharides (i.e., carboxyl methyl cellulose and carboxyl methyl chitosan).

7.2.3 Application of *N*-Carboxyacyl Chitosan Derivatives

These fabricated *N*-maleoyl chitosan and *N*-succinyl chitosan derivatives can be deeply studied and developed in these applications : (1) Film coating or packaging for retardation the shelf life of fruits, vegetables or meats, (2) Wound dressing with anti-adhesion and antimicrobial properties, (3) Bioabsorbents for various types of heavy metals such as Cu^{2+}, Hg^{2+},Zn^{2+}, Pb^{2+},Cd^{2+} and Co^{2+} ions, (4) Drug carriers by incorporating with water soluble bioagents such as DNA, proteins and drug and (5) Controlled degradation implant materials by selection of suitable degree of substitution and blended or coated with long term biodegradable materials.