CHAPTER VI
CONCLUSIONS AND RECOMMENDATIONS

Chitosan is an important bio-based material to apply for a variety of applications. It posses a wide range of useful properties, such as biodegradability, biocompatibility, non-toxicity, antibacterial and antiviral properties. Due to the fact that chitosan is inert and stabilized by inter- and intra-molecular hydrogen bonding, most reactions of chitosan have to be done in heterogeneous system or in some specific acid solutions, and this limits the variety of the reactions and brings the difficulty in developing chitosan to practical products. From this point, the development of chitosan to the 'organo-soluble chitosan' and 'water-soluble chitosan' including the uses of homogeneous systems to achieve the effective system for functionalization and materialization were studied and reported in this dissertation.

Chapter III deals with the development of chitosan to organo-soluble derivative and further materialization to obtain a novel hybrid chitosan-hydroxyapatite (HAp) composite gel for potential used as paste or glue in bone tissue engineering. It is important to note that various derivatization to achieve organo-soluble chitosan have been proposed as an effective way for functionalization for the past decades. However, only few researches extended the work to the materialization. In this study, *N*-phthaloylchitosan was applied as an organo-soluble derivative for further materialization to obtain a novel chitosan-epoxy gel with HAp. The epoxy group was successfully introduced onto the hydroxyl group by reacting epichlorohydrin with *N*-phthaloylchitosan in homogeneous system. The phthaloyl group was subsequently removed while the oxirane ring was open to obtain the crosslinked structure as soon as the addition of hydrazine. An alternate soaking process was applied to establish HAp formation in the epoxy-chitosan gel. The work should be extended to the control of gelation, including the physical and mechanical properties. The improvement of cell adhesion, the reduction of toxicity which might come from the trace amount of hydrazine should be studies.

Chapter IV and V demonstrate the water-soluble chitosan-hydroxybenzotriazole (HOBt) complex is an effective system in preparing chitosan

derivatives in water without the use of acids or organic solvents. Although the uses of conjugating agent; e.g. 1-ethyl-3-(3-dimethylaminopropyl-carbodiimide) (EDC), 1,3-dicyclohexylcarbodiimide (DCC); and conjugating additive; e.g. HOBt, 1-hydroxy-7-azabenzotriazole (HOAt), *N*-hydroxysuccinimide (HOSu); with chitosan have been reported for many years, most reactions were carried out in organic solvents or faced the problems of multi-step reaction, harsh condition, complicate purification. In this study, the chitosan aqueous solution achieved from mixing chitosan and HOBt in water is a key factor to provide the mild conditions for conjugation by using the carbodiimide conjugating agent. Chapter IV showed the functionalization of chitosan with poly(ethylene glycol) methyl ether (mPEG) via a single step reaction in water at room temperature. The reaction gives mPEG content as high as 42%. The compound obtained showed the good solubility in water in various pHs, and swelling in methanol and chloroform. Chapter V declared the chitosan-HOBt in water as an organic salt complex and originally proposed a series of model reactions via water based system such as the conjugation with boc-L-phenylalanine, mPEG, and PEG-crosslinked chitosan. The reactions were successful at room temperature by using EDC as a conjugating agent. Furthermore, the work also declared that the organo complexation of chitosan with other conjugating additives, i.e. HOAt, HOSu, can be simply formed in water to result the chitosan water solution. The product obtained will be a good model to develop chitosan for various purposes especially in biomedical and pharmaceutical applications. The further works to be done are such as (i) the confirmation of chitosan-HOBt by UV technique, (ii) the lipogel formation for chitosan crosslinked with dicarboxylated PEG, and (iii) the cell adhesion and toxicity of the chitosan material obtained.