CHAPTER 5
CONCLUSIONS

In this study, N-phthaloyl chitosan (N-PhCS) as an enteric polymer was successfully prepared by acylation at amino groups of chitosan via ring-opening reactions of phthalic anhydride (PA). The effects of various conditions by varying temperature at 25 and 40°C, stirring time for 4 and 24 h, mole ratio of chitosan:phthalic anhydride at 1:1, 1:3 and 1:5 mole ratio, neutralization pH (step 3 of preparation process) at pH 4, 5 and 6 and different molecular weights of chitosan 20 and 200 kDa could be summarized as follows:

1. The suitable condition for preparing N-PhCS was at 25°C under stirring time for 4 h. The preparation under high temperature resulted in the cyclization of phthalimido moieties.

2. The adjusted pH in the neutralization pH at pH 5 provided the structure of chitosan-N-phthalamidate sodium (sodium 2-(chitosan-N-carbonyl) benzoate) while the less sodium salts formation and the excess NaOH residue was observed at pH 4 and 6, respectively.

3. The degree of N-phthaloyl substitution increased as the mole ratio of chitosan: phthalic anhydride increased resulting in the increase of solubility of enteric polymer property of chitosan-N-phthalamidate sodium.

4. N-PhCS prepared from different molecular weights exhibited similar physicochemical properties except for the higher viscosity of the solution of the higher molecular weight salt.

5. The % degree of substitution of N-PhCS with 1:1, 1:3 and 1:5 mole ratio of chitosan: phthalic anhydride (46.0%, 64.3% and 73.2%, respectively), was calculated by ^{1}H-NMR assay whereas the FTIR assay was restricted according to the change of the hydroxyl band at 3450 cm^{-1} which was used as the reference band in

the calculation of % degree of substitution, during the substitution of N-phthaloyl groups.

6. The stability study suggested that N-PhCS was unstable when exposed to high temperature. Therefore, the applications of N-PhCS should be aware of dealing with high temperatures.

7. N-PhCS was non-toxic and compatible to Caco-2 cells when used at concentration of 0.01-1 mg/mL.

8. N-PhCS films exhibited a good enteric property and the solubility in simulated gastric fluid was 12.43% with complete dissolution in simulated intestinal fluid. The moisture barrier property and tensile strength of the films were closed to chitosan acetate film but they were more brittle as characterized by less elongation and higher gradient stress-strain value.

In conclusion, the suitable conditions to prepare N-PhCS was at 25°C under stirring for 4 h, CS:PA at 1:5 mole ratio and neutralization pH at pH 5. The obtained N-PhCS from CS 20 kDa was chitosan-N-phthalamidate sodium with the highest degree of substitution and the solubility best fitted to enteric polymer property. It was non-toxic with good film forming properties. Thus, chitosan-N-phthalamidate sodium can be applied in pharmaceutical dosage forms, especially in enteric and colonic drug delivery system.