# CHAPTER V

# CONCLUSIONS

Dacarbazine has short stability in aqueous solution which makes it problematic to administer as continuous infusion. For this reason, nanotechnology was used to improve the dacarbazine stability in this study. The promising carriers that have been considered in drug delivery applications are chitosan-coated alginate nanoparticles.

In this study, dacarbazine was entrapped into chitosan-coated alginate nanoparticles in order to improve its stability. Six formulations using three concentrations of dacarbazine and two different molecular weight and percent deacetylation of chitosans were prepared by ionotropic gelation method. When compared to the polymer used, the product yield of dacarbazine chitosan-coated alginate nanoparticles was low in the range of 9.80 % – 17.93 %. This may because the nanoparticles were not completely separated from the suspensions with the 50,000 rpm of ultracentrifugation for 60 min. Thus, the increased revolution of ultracentrifugation or the increased time may be studied for better separation. The others method of preparation may be studied for higher yield. TEM micrograph showed the morphology in spherical shape. The mean particle sizes of dacarbazine chitosan-coated alginate nanoparticles were in range of 489 - 584 nm. The mean particle size of dacarbazine chitosan-coated alginate nanoparticles increased when the amount of drug increased. The mean particle size of particles measured from TEM and that from nanosizer was different. The dehydration of the hydrogel particles during sample preparation for TEM imaging leads to an under-estimation of their actual size. The measurement by nanosizer is based on the equivalent sphere principle, in which each particle is viewed as a sphere. Thus, the presence of a few aggregates will tremendously increase the mean size. The results should be interpreted cautiously because several parameters such as viscosity or pH of the suspension medium, temperature, concentration and particle sedimentation may influence the

data. The polydispersity index of particles were in the range of 0.30 - 0.57. The higher polydispersity index indicated a wider particle size distribution. The zeta potential of obtained dacarbazine chitosan-coated alginate nanoparticles were in the range of -28.97 to -28.03 mV. Dacarbazine increased the negative value of zeta potential independently on the amount of drug, whereas the molecular weight of chitosan did not influence to the zeta potential. The percentage of entrapment efficiency of dacarbazine chitosan-coated alginate nanoparticles was in range of 31.36% - 41.55 %. The further studies in the conditions of preparation and the drug-polymer interaction should improve the entrapment efficiency. The percentage of encapsulation efficiency was significantly affected by the amounts of dacarbazine. The obtained nanoparticles which contained 2 mg of dacarbazine either coated with chitosan 15000 dalton or 100000 dalton showed the highest percentage of entrapment efficiency. At the same amount of dacarbazine, the percentage of entrapment efficiency of dacarbazine alginate nanoparticle coated with the higher molecular weight chitosan was not different from that coated with the lower molecular weight chitosan. Thus, the molecular weight did not influence to the entrapment efficiency of dacarbazine chitosan-coated alginate nanoparticles. The percentage of recovery of dacarbazine in chitosan alginate nanoparticles were in range of 37.60 % to 44.59 %. The low percentage of recovery may due to the incompletely extraction of the drug from nanoparticles. Thus, the entrapped drug extraction must be developed for higher recovery. At the same amount of dacarbazine, the percentage of recovery of dacarbazine alginate nanoparticle coated with the higher molecular weight chitosan was not different from that coated with the lower molecular weight chitosan.

The stability in pH 3-4 citric acid solution and normal saline solution (NSS), either at room temperature or at 2-8°C of dacarbazine in chitosan-coated alginate nanoparticles was better than that of free dacarbazine up to 72 hours and showed no difference from that of free dacarbazine after 10 days of storage. In the further study, the stability of dacarbazine in nanoparticles should be compared with that in commercial products. The obtained dacarbazine nanoparticles must be formulated using the same amount of dacarbazine and the excipients as the commercial products.