Abstract (English)

This thesis provides a series of fundamental physico-chemical parameters associated with the formation of limit size nanoparticles of hydrophobic test material glyceryl Trioleate (Triolein) and anticancer drug Niclosamide stearate using rapid solvent shifting technique.

Chapter 1 provides the overall background and the motivation for this thesis including an introduction to the design of the LDL nanoparticle (20-25 nm) and how it motivated the design of the nanoparticles presented in this thesis. **Chapter 2** tests eight key parameters that govern the size of Triolein (TO) nanoparticles by rapid solvent shifting. It shows the fabrication of limit size uncoated TO nanoparticles of hydrodynamic diameter ~25 nm by rapid ethanolic injection at 833 µL/s in water under stirring (500 RPM). This limit size is then shown to be comparable with its critical nucleation diameter 24.2 nm (at 25 µM) calculated from the classical nucleation theory. The growth of uncoated TO nanoparticles at the higher concentrations is due to the increased collision frequency of the nuclei (1.24×10^{18} mL^{-1} s^{-1} for 1 mM) that lead to the aggregation and coalescence. It is shown to be prevented by kinetically trapping the nuclei in phospholipid (POPC) monolayer. At 10 mM TO, with POPC:TO mol ratio of 1:0.95, the avg. diameter is shown to be 24.0 ± 5.6 nm from cryo-TEM image analysis. Replacing the POPC with a tighter, sterically stable monolayer of DSPC:Cholesterol:DSPE PEG^{2000} at 45:50:05 mol ratio, formation of stable TO nanoparticles of size ~25 nm is shown. **Chapter 3** uses this same design and the listed eight parameters to formulate the lipid coated stealth nanoparticles of Niclosamide stearate (NSNPs) and then tests the effect of pH, temperature and enzymes on their stability. The limit size for 1 mM uncoated NS nanoparticles is shown to be 17.5 ± 6.8 nm from single particle analysis of cryo-TEM images which overlaps with the range of predicted critical diameter for 1 mM NS of 9.5-13.3 nm. The aggregate size from cryo-TEM image analysis at 10 mM NSNPs in water of 20.5 ± 9.2 nm thus confirmed the strategy of kinetically trapping the nuclei to obtain limit size nanoparticles of hydrophobic anticancer drug in the size range of LDL nanoparticles.