CHAPTER V

CONCLUSIONS

This study explored the effects of formulation factors on the role of liposomes as drug delivery system for U-937 human monocyte/macrophage cells. The factors studied were the type of charge-imposing lipids and inclusion of cholesterol. Preliminary investigation of mechanism by which liposomes interacted with the U-937 cells was also carried out. Based on biological responses of the cells, conclusions can be drawn from the study as follows:

Blank liposomes exhibited antiproliferative activity at concentrations devoid of cytotoxicity. The ability to inhibit cell growth depended on the composition of liposomes. Liposomes composed of PC/PS and PC/PG exhibited relatively strong antiproliferative action compared to liposomes composed of PC or PC/DCP. Thus, surface charge was not the sole determinant of liposome uptake into the macrophage U-937 cells.

Inclusion of CH into the blank liposomes did not affect the antiproliferative effect of those liposomes. An exception was PC/PS liposomes where inclusion of CH significantly reduced the antiproliferation seen with blank liposomes.

Increase in lipid concentration did not affect the antiproliferative effect of blank liposomes in most cases. Only liposomes composed of PC/PG exhibited significantly stronger antiproliferation at high lipid concentration compared to at lower lipid concentration.

Entrapment of PTU in liposomes did not enhance antiproliferation from that seen with blank liposomes. However, synergism was observed when blank liposomes were co-administered with PTU solution.

Preliminary study shows no evidence that PC liposomes underwent fusion with U-937 cells. On the contrary, fusion was seen with BALB/c 3T3 fibroblast cells.

Thus, formulation factors were significant in modifying the biological effects introduced by liposomes, which was an indirect indicator of liposome uptake. Blank liposomes also demonstrated synergism with the model drug used in this study. It might be possible that phospholipid liposomes modified permeability of the cell membrane as well as susceptibility of the cell to the drug. However, other mechanisms might also be involved. Further study would be necessary to elucidate the mechanisms by which liposomes interacted with the U-937 cells. Such mechanisms would, in turn, give insights into how liposomes enhanced drug effects.