

CHAPTER VI

CONCLUSION

This study investigated whether incorporation of antioxidants into liposome formulations would be beneficial in modulation of LPS-stimulated activity in J774A.1 macrophage cells. α -Tocopherol (TOC) and *N*-acetylcysteine (NAC) were used as models for lipophilic and hydrophilic antioxidants, respectively. Effects of liposome composition and negative surface charge on liposome membrane were also examined.

The results of this study indicated that blank liposomes could inhibit NO production in LPS-stimulated J774A.1 cells. The incorporation of antioxidants into liposome formulations, either as encapsulated molecules in the liposomes or as free molecules co-existing with blank liposomes, seemed to be ineffective in increasing modulation of LPS-stimulated J774A.1 macrophage cells by blank liposomes. On the contrary, presence of antioxidants seemed to antagonize the inhibitory effect of blank liposomes. Neutral and both negatively charged liposomes gave comparable results. Moreover, NAC-loaded negatively charged liposomes in the presence of free NAC displayed severe cytotoxic effect on J774A.1 cells. Further investigation with liposomes containing DCP and calcein solution indicated that NAC-encapsulated negatively charged liposomes might cause cytotoxicity by increasing free NAC uptake into the cells. However, a more refined experiment would be necessary to establish the exact mechanism. Due to the intrinsic inhibitory effect of liposomes on NO production, the overall results of this study indicated that an antagonistic effect might occur if liposomes were used concomitantly with antioxidants. Thus, liposomes might not be a good candidate for antioxidant delivery into the macrophage cells.

Although liposomes might not be a good candidate as delivery systems for antioxidants, the present study supported the regulatory link between liposomes and antioxidants in macrophages. Further study on the mechanism by which liposomes regulate NO production in LPS-stimulated macrophages may give useful information as to whether phospholipid liposomes would be of any therapeutic value in the treatment of pathologic conditions resulted from over-activity of macrophage cells.