CHAPTER VI
GENERAL DISCUSSION

General Discussion

In recent years, liposomes have achieved considerable interest in their possible use as vesicles for the targetting of drugs and macromolecules to selective tissues. Among the various routes of administration, oral feeding is the easiest and most convenient for the patient. Enzymes, hormones or drugs which are not normally amenable to oral administration may also be capable of oral use, when encapsulated in liposomes. One report claimed hypoglycaemic effect in mice by the oral administration of insulin entrapped in phosphatidyl inositol liposomes (1). An identical reduction of blood glucose was obtained with glucose oxidase entrapped in liposomes of similar composition (2). However, little effect was observed when insulin entrapped in liposomes composed of egg lecithin, cholesterol and dicetyl phosphate was administered in diabetic rats (3). So appropriate changes in the composition of liposomes could improve their survival in the gut thus allowing a effective transport of liposomal component into the periphery. It was found that liposomes made of certain semisynthetic phospholipids e.g. DPPC, DSPC are quite resistant to pancreatic phospholipases, detergents and low pH at physiological temperature (4).

In Chapter II, ^{125}Iodine labelled human immunoglobulin G encapsulated liposomes made from natural and synthetic phospholipids have been utilized to check their efficacy in oral administrations. Gel filtration of plasma from the heart and portal vein of rats fed with liposomes showed the presence

be markedly dependent on its phospholipid composition and cholesterol concentration. Liposomes with different size and phospholipids composition have been tested in vitro to act as better carriers for oral presentation of factor VIII to hemophilic patient and reverse-phase-evaporation vesicles with high concentration of cholesterol have been shown more resistant to the hostile environment of the gastrointestinal tract (12).

In Chapter III, DPPC liposomes with different cholesterol concentration have been tested for the better efficacy in the use as vesicles for oral application. It is indicated from the observations that higher incorporation of cholesterol in liposomes imparts greater stability to liposomal encapsulated protein. Intact protein and liposomes were detected in portal blood of rats fed with cholesterol-rich DPPC liposomes for a longer period compared to cholesterol-poor preparations. It has been concluded that cholesterol-rich liposomes exhibit greater stability to encapsulated protein in the G.I. tract. There are conflicting reports regarding the mode of absorbtion of liposomes from gut. Rowland and Woodely (13) using rat everted intestinal sac technique showed that absorption of intact liposomes could occur across mucosal cells. However, Patel et. al. found no evidence for the transport of intact liposomes across the intestine (14) by using isolated perfused rabbit intestine.

Liposomes had been tested by several groups for selective delivery. Specific liver targetting of liposomes has been achieved by using sugar coated vesicles (15). Other

insulin orally to diabetic animals. In the Chapter V liposomes composed of high cholesterol concentration and phospholipid with Tc temperature above the physiological temperature has been utilized to check the efficacy of those vesicles as oral carriers of hormones. From the gel filtration study it was observed that 60% and 20% of the total radioactivity found in the portal blood of rats was associated with liposomes and insulin respectively after 1.5 hr of feeding cholesterol-rich DPPC liposomes. But neither the liposomes nor the hormone was detected in cardiac blood at the same time. It is interesting to note that no free ^{125}I-Insulin was detected in portal blood of rats at any time after feeding free labelled insulin. These results indicate that insulin in cholesterol-rich DPPC liposomes when administered orally, will be able to reduce the blood glucose level in rats.

References

1. Patel, H.M. and Ryman, B.E. (1976). FEBS Lett. 62, 60-63.
2. Dapergolas, G. and Gregoriadis, G. (1976). Lancet II, 824-827.
3. Nishida, Y., Kamatani, N. and Miyamoto, T. (1984) Jp Phaarmacol. 36, 354-355.
4. Rowland, R.N. and Woodley, J.F. (1980) Biochim. Biophys. Acta. 620, 400-409.
5. Morell, A.G., Vandenhamer, C.J.A. and Schienberg, I.H. (1970) J. Biol. Chem. 245, 759-766.
6. Morell, A.G., Irovine, R.A.; Sterhlieb, I., Schienberg, I. H. and Ashwell, G. (1968) J. Biol. Chem. 243, 155-159.
7. Gregoriadis, G., Morell, A.G., Sternlieb, I. and Schienberg, I.H. (1970) J. Biol. Chem. 245, 5833-5837.
8. Kirby, C.J., Clarke, J. and Gregoriadis, G. (1980) Biochem. J. 186, 591-598.
9. Shichiriw M., Okada, A., Kawamori, R., Etani, N., Shimizu, Y., Hoshi, M., Shigeta, Y. and Abe, H. (1973) Endrocrinology, 93, 1371-1377.
10. Deshmukh, D.S., Bear, W.D. and Brokerhoff, H. (1981) Life Sci. 28, 239-242.
11. Patel, H.M. and Ryman, B.E. (1977) Biochem. Soc. Trans. 5, 1054-1056.
12. Kirby, C.J., and Gregoriadis, G. (1985) in Liposome Technology (Gregoriadis, G. ed.), 3rd Ed. Vol-II, 69-81.
13. Rowland, R.N. and Woodley, J.F. (1981) Bioscience Report 1, 345-352.

14. Patel, H.M., Tuzel, N.S. and Stevenson, R.W. (1985) Biochim. Biophys. Acta. 839, 40-49.

15. Ghosh, P. and Bachhawat, B.K. (1980) Biochim. Biophys. Acta. 632, 562-572.

16. Abru, R.M., Bosworth, M.E. and Hunt, A.C. (1980) Res. Commun. Chem. Pathol. Pharmacol. 29, 344-360.

17. Tanaka, T., Taneda, K., Kobayashi, H.,Okumura, K., Maranushi, S., and Sezaki, H. (1975) Chem. Pharm. Bull. 12, 3069-3074.

18. Souhami, R.I., Patel, H.M. and Ryman, B.E. (1981) Biochim. Biophys. Acta. 674, 354-371.

19. Ryman, B.E. and Tyrgell, D.A. (1978) Annal. N.Y. Acad. Sci., 308, 281-306.

20. Patel, H.M., Stevenson, R.W., Parsons, J.A. and Ryman, B.E. (1982) Biochim. Biophys. Acta. 716, 188-193.