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Investigations into the in-vitro/in-vivo behaviour of polyhedral niosomes

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Niosomes are vesicles formed mainly by self-assembly of synthetic non-ionic surfactants with the optional combination of cholesterol and charged surfactants. They are made of the bilayer membranes and have therefore been used as model cells e.g. studying their response to osmotic gradients, membranes phase behaviour, and membrane permeability. Their capability to entrap solutes allows them to be used as drug carriers (Florence, 1993; Arunothayanun et al., 1997).

Apart from conventional spherical vesicles, various vesicle shapes, e.g. tubular, discomes, polyhedral, can be formed by varying their membrane composition (Uchegbu & Florence, 1996). We have found that certain non-ionic surfactants including $C_{16}G_2$ (a hexadecyl diglycerol ether), $C_{16}EO_2$ (a polyoxyethylene 2 cetyl ether, Brij 52), $C_{16}EO_5$ (a polyoxyethylene 5 cetyl ether), $C_{18}EO_2$ (a polyoxyethylene 2 stearyl ether, Brij 72), and $C_{18}EO_5$ (a polyoxyethylene 5 stearyl ether) form polyhedral niosomes with very low levels of cholesterol or none. They can entrap hydrophilic solutes (e.g. carboxyfluorescein, luteinizing hormone releasing hormone) and have been found to be more permeable when compared to their spherical counterparts formed with an equimolar amount of cholesterol. When subjected to a range of osmotic gradients, polyhedral niosomes were found to change in size to a lesser degree compared to their spherical counterparts. This is due to the highly rigid, non-elastic properties of their membranes and their higher permeability to some solutes.

Combination of hot-stage microscopy and high-sensitivity differential scanning calorimetry revealed that polyhedral niosomes undergo a reversible shape transformation into spherical structures when heated above their phase transition temperature. Change in vesicle shape was also found to affect their rheological properties. The viscosity of polyhedral niosomes at room temperature is higher than spherical niosomes due to their faceted shape, and is affected by temperature primarily due to their shape transformation to spherical vesicles.

Luteinizing hormone releasing hormone (LHRH) was chosen as a model peptide drug to study *in vivo* behaviour. LHRH was prepared as aqueous solution in phosphate buffered saline (PBS, pH 7.4), entrapped in polyhedral niosomes, or in spherical niosomes following an intramuscular injection into rat muscles. The clearance study of ^{125}I-LHRH from the intramuscular injection site showed that polyhedral niosomes can slow the release of drug from the site of injection when compared to drug prepared in solution following intramuscular injection in rats (Figure 1). The spherical niosomes loaded with LHRH act as a more efficient sustained release vehicles due to their cholesterol-bearing membranes which are less permeable.

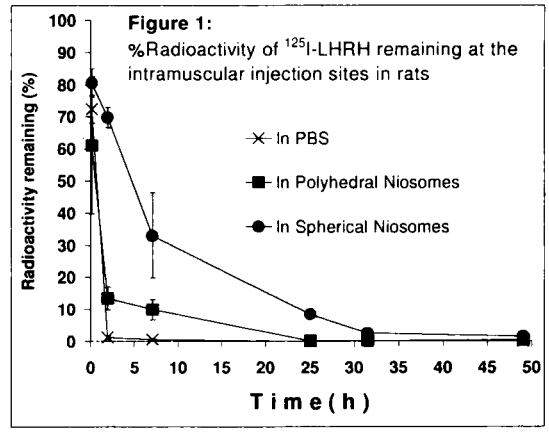

Figure 1: %Radioactivity of ^{125}I-LHRH remaining at the intramuscular injection sites in rats

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References:

1. Florence, A.T. (1993) In: Liposome Technology, Gregoriadis, G. (ed.), CRC Press, p. 157-176
2. Arunothayanun, P., Turton, J.A., Uchegbu, I.F., Florence, A.T. (1997) Pharm. Res. 14(suppl.):s-286
3. Uchegbu, I.F., McCarthy, D., Schätzlein, A., Florence, A.T. (1996) S.T.P. Pharma Sci. 6:33-4