STUDIES OF SYNOVIAL FLUID INTERACTION WITH LIPOSOMES

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Synovial fluid may be considered a tissue fluid that changes with disease, characterised by alterations in synovial tissues (synovial fluid and synovium) and intra-articular metabolism (Van Pelt 1962). The complex components of synovial fluid which are charged proteins often associated with hyaluronic acid, may be adsorbed onto particles such as liposomes when administered intra-articularly. This may alter the particles surface charge, drug efflux rate and the rheological properties of the fluid.

Synovial fluids from healthy bovine knee joints have been examined by a rotational cone and plate rheometer. The investigation also attempted to evaluate the influence of synovial fluid upon the release kinetics of chloroquine from liposomes above and below their phase transition temperature (T_c), and any resulting changes in liposomal electrophoretic mobilities (EPM).

All synovial fluid samples exhibited Newtonian behaviour even at low shear rates. The viscosities, η, obtained for pure synovial fluid decreased with increasing temperature and were in agreement with those reported by Davies and Palfrey (1966). Addition of pure dipalmitoylphosphatidylcholine (DPPC) vesicles to 50% synovial fluid in buffer reduced η, with a maximal reduction observed in the vicinity of the T_c of DPPC (41°C). A similar rheological profile was observed upon the addition of liposomes containing ionic lipids, to the synovial fluid. The formation of liposomes in 50% synovial fluid, when synovial components are distributed throughout the particles, exhibited little or no change in η compared with liposomes formed in buffer. The effect of surface charge on the liposomes could influence the cellular uptake and release characteristics of the drug. Liposomal EPMs were therefore measured by microelectrophoresis. Pure DPPC vesicles in synovial fluid exhibited a negative EPM, which was reduced upon the incorporation of the cationic chloroquine. However, the EPM values for liposomes in synovial fluid were lower than those observed for DPPC in buffer (Chawla et al 1979). Liposomes containing stearylamine and chloroquine exhibited positive EPMs which were lower than those obtained for the same liposome formulations dispersed in buffer.

Chloroquine efflux from various liposomes formulations into 50% synovial fluid was measured. It was observed that the efflux rate (k) was dependent upon the temperature and surface charge of the vesicles. Higher k values were obtained compared with measurements in buffer, although the incorporation of cholesterol into the liposomes reduced k. A maximum in k was observed in the vicinity of the T_c of DPPC, for neutral, positive and negatively charged vesicles. The formation of vesicles in 50% synovial fluid resulted in a higher efflux rate compared with vesicles added to 50% synovial fluid. This increase may be attributed to the surface adsorption and bilayer penetration of the component proteins; similar effects have been observed in serum (Zborowski et al 1977).

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