THE INCORPORATION AND IN-VITRO RELEASE OF SODIUM CROMOGLYCATE FROM MULTILAMELLAR AND REVERSE PHASE EVAPORATION LIPOSOMES

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Reverse-phase evaporation (REV) liposomes have been reported to entrap greater amounts of polar compounds than multilamellar (MLV) liposomes of equivalent composition, due to the higher efficiency of encapsulation of aqueous phase in the former vesicles (Szoka and Papahadjopoulos, 1978). However little information is available concerning the release of entrapped substances from REV preparations. In this work the effect of the method of liposome preparation on the entrapment and in vitro release of the drug sodium cromoglycate (SCG) is examined.

MLVs were prepared by producing films of egg phosphatidylcholine (EPC) or dipalmitoylphosphatidylcholine (DPPC) with 50 mole % cholesterol (Chol). These were hydrated with a solution of SCG in 0.9% saline to give final concentrations of 10 mg ml^{-1} lipid and 10 mg ml^{-1} SCG. REVs were produced by sonicating a mixture of aqueous SCG (10 mg ml^{-1}) and lipid in diethyl ether/chloroform (50:50). Removal of organic solvent resulted in a preparation having a volume slightly less than the original aqueous phase. Drug entrapment and release at 37°C (following 1 in 100 dilution of the suspension with 0.9% saline) were determined by centrifuging samples and assaying the supernatent at 326 nm.

Results indicate that encapsulation of SCG is greater for REV formulations than for corresponding MLV formulations. Entrapment for EPC/Chol liposomes was : MLV; 6.2 % (mg SCG per 100mg of lipid) and REV; 9.4 % and for DPPC/Chol liposomes: MLV; 5.4 % and REV; 10.5 %. However up to 40% of entrapped drug was lost when REV preparations were centrifuged and resuspended. Negative stain electron microscopy demonstrated the presence of large unilamellar and multilamellar vesicles in these preparations, and it seems likely that disruption of the unilamellar vesicles is responsible for the loss of drug on centrifugation, whilst efflux across the single bilayer of the same vesicles produced the initial rapid release of drug from REV formulations in vitro (Fig.). Post 8h half-lives of efflux for EPC/Chol formulations were: MLV; 84h, REV; 90h, and for DPPC/Chol formulations: MLV; 139h and REV; 151h, indicating that after the intitial phase of rapid release, drug efflux is dependent upon the composition of the liposome bilayer rather than the method of production.

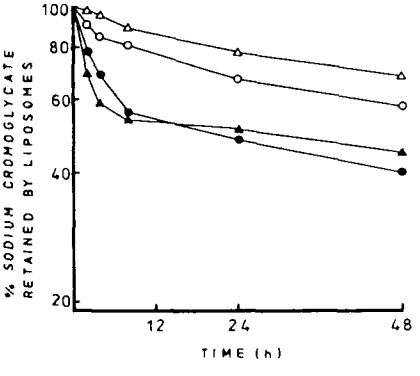

Fig. Efflux of SCG from MLV and REV liposomes.
MLV - DPPC/Chol, 1:1 (n=3)
MLV - EPC/Chol, 1:1 (n=3)
REV - DPPC/Chol, 1:1 (n=3)
REV - EPC/Chol, 1:1 (n=3)

Szoka, F. and Papahadjopoulos, D.(1978) Proc. Natl. Acad. Sci. USA. 75: 4194-4198.