

CALORIMETRIC INVESTIGATIONS OF LIPOSOME FORMATION

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Differential scanning calorimetric techniques have frequently been employed in the study of pre-formed liposomes, particularly for investigation of the phospholipid phase transition (Oldfield and Chapman 1972). In the present study solution calorimetry has been used to examine the enthalpy changes associated with the formation of dimyristoylphosphatidylcholine (DMPC) liposomes.

Thin films of DMPC with 0, 5, 10, 20 and 50 mole % cholesterol or 0, 5, 10 and 20 mole % beclomethasone dipropionate were prepared in 1 mL glass calorimeter vials by evaporation of organic solutions under nitrogen. All films had a total weight of 10 mg. Certain films were hydrated at 310 K for 30 minutes with 10 μ L of deionized water prior to loading into the calorimeter. Enthalpies were measured using a Tronac 450 Adiabatic Calorimeter. The glass vials were sealed and suspended in 50 mL deionized water, held at 310 K. The vials were automatically broken resulting in mixing of the film with the aqueous phase. The associated heat changes were measured using a thermocouple. In all cases transmission electron microscopy revealed the presence of liposomes.

An endothermic reaction was observed when water was introduced to calorimeter vials containing anhydrous DMPC films. When cholesterol was incorporated into the lipid films there was a progressive decrease in the total enthalpy associated with the process with no detectable response at 50 mol% cholesterol (Fig 1). The incorporation of beclomethasone dipropionate into DMPC films at 5 mol% also resulted in a decrease in the total enthalpy of the process. However, increasing the proportion of drug further had a much less pronounced effect on enthalpy.

It was noted that films to which 10 μ L water had been added prior to ampoule breakage produced no enthalpic response. Studies by Offringa et al (1987) have indicated that the maximum number of water molecules associated with each molecule of phospholipid is approximately 20. As 10 μ L of water is equivalent to a water to DMPC molecular ratio of 37.8 it may be assumed that full hydration occurred when this volume of water was used.

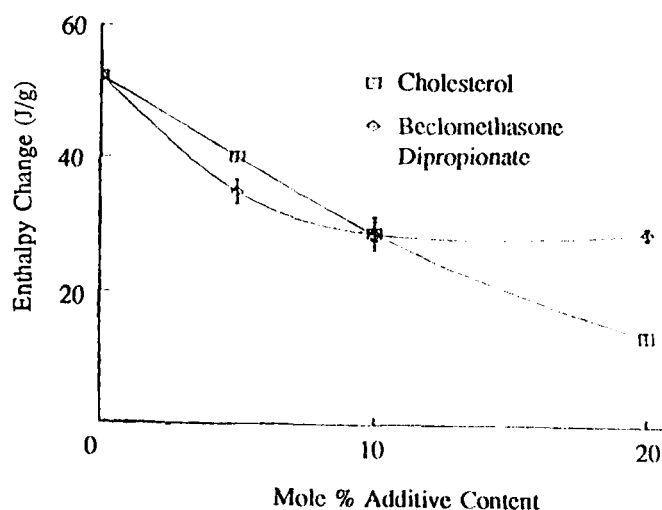


Fig.1. Effect of cholesterol and beclomethasone dipropionate content on enthalpy of liposome formation from DMPC films. (n = 3 \pm SE).