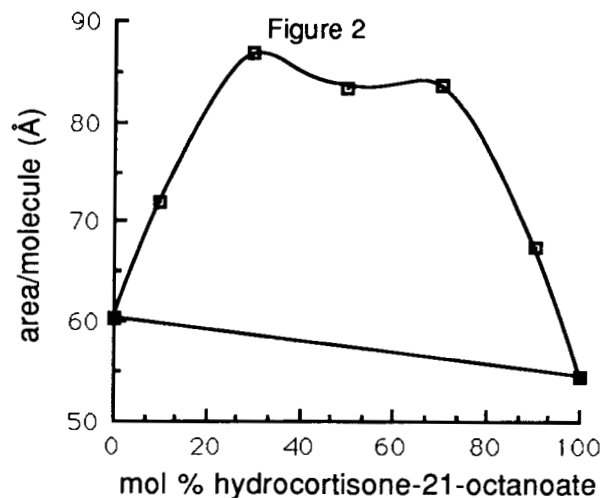
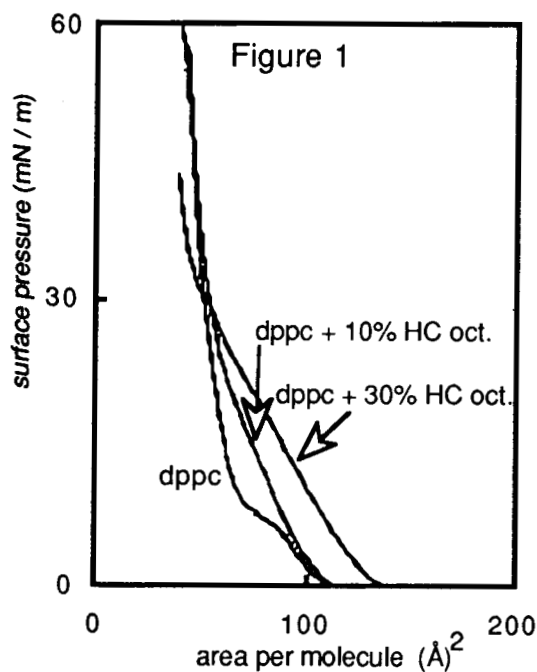


INTERACTION OF HYDROCORTISONE AND HYDROCORTISONE ESTERS WITH DIPALMITOYLPHOSPHATIDYLCHOLINE MONOLAYERS

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The main permeability barrier to percutaneous absorption is thought to be the structured intercellular lipid bilayers of the stratum corneum (Elias 1983). Hydrocortisone (HC) and its esters penetrate human skin slowly with evidence of some accumulation (Vickers 1963). The nature of this interaction has been investigated by incorporating these compounds into a dipalmitoyl phosphatidyl choline (DPPC) monolayer. This technique involves delivering the lipids in a volatile solvent to a water surface and measuring the change in surface pressure whilst laterally compressing the lipid film. Comparison of the surface pressure (π) vs. molecular area (A) compression isotherms of the lipid alone with isotherms from mixed films gives information about the nature of incorporation of the compound into the lipid monolayer. π vs. A compression isotherms were recorded at 25°C using an automated Langmuir film balance. Monolayers were spread as premixed solutions in hexane/ethanol (9:1, 100 μ l) from an Agla microsyringe onto a water subphase.

A set of compression isotherms for HC-21-octanoate is shown in Fig.1. Incorporation of the ester generally causes a shift to a larger molecular area (when examined at a particular pressure). There is a marked effect on the liquid expanded/liquid condensed transition, the incorporation of only 10% of ester causing abolition of the transition. A plot of mean molecular area (at a specific π) against film composition can indicate the nature of mixing. A plot for HC-21-octanoate (Fig 2) shows a large expansion over ideal mixing. These results indicate that HC-21-octanoate appears to disrupt a DPPC monolayer quite considerably. Confirmation of the disordering is obtained by examining the effect of incorporating this compound into DPPC liposomes. Using a light scattering technique a decrease in phase transition temperature is seen indicating a more fluid environment. Similar but smaller effects are seen with shorter chain esters and HC itself using these two techniques.



Elias, P.M. (1983) *J. Invest. Dermatol.* 80: 445-495.
Vickers, C.F.H. (1963) *Arch. Derm.* 88: 20-29.