Humectants: Their influence on the Structure and Thermotropic Behaviour of Phospholipids found in Dermatological Formulations

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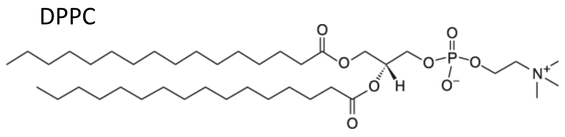
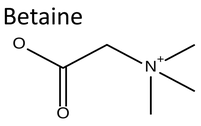
1. Introduction

Saturated phospholipids can be important components in clinically efficacious topical dermatological formulations. The **aim of this investigation** is to understand the influences of humectants on the thermal properties and structure of a lipid bilayer. The lipid studied in excess of water was 1,2-dipalmatoylphosphatidycholine (DPPC) and three humectants were focused on: betaine, sarcosine and acetamide monoethanolamine (AMEA). The primary method of investigation used was X-ray Scattering which allows to determine changes in the thermal behaviour as well as any nanostructural changes. Differential Scanning Calorimetry (DSC) was also applied as a complimentary technique.

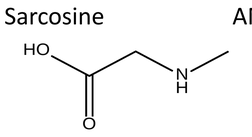
DPPC



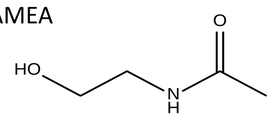
Betaine



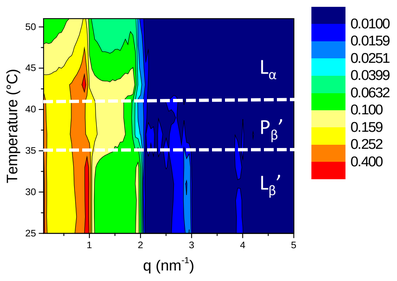
Sarcosine



AMEA

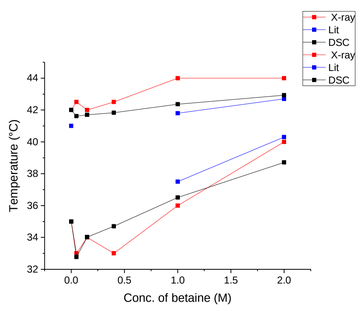


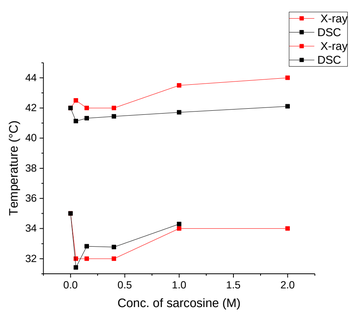
2. Thermotropic Changes

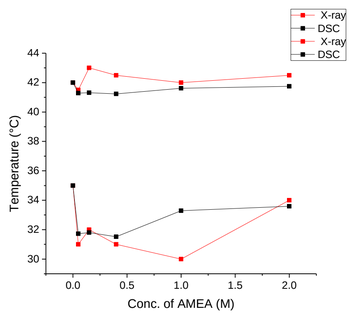


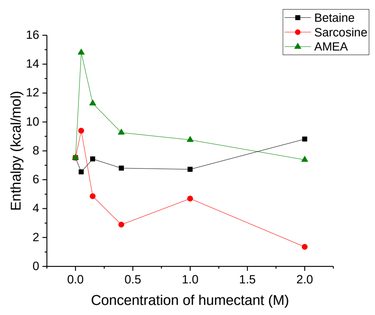
Pure DPPC forms different lamellar structures in excess of water [1]; the lamellar gel phase (L_β'), ripple phase (P_β') and lamellar fluid phase (L_α). This can be seen by small-angle X-ray scattering (SAXS).

Rudolph and Goins [2] showed that increasing the concentration of betaine increases both the pre-transition temperature (L_β' to P_β') and the main transition temperature (P_β' to L_α). In this study, much lower concentrations of betaine were studied in addition to higher concentrations (1 and 2 M). DSC and X-ray results show that the addition of any humectant at low concentrations will in fact **lower** the pre-transition temperature of DPPC.



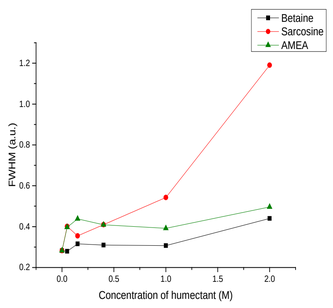




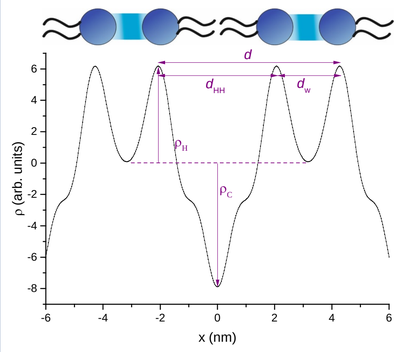


The enthalpy values for the main transition have been deduced from the DSC scans. The enthalpies for each humectant seem to follow an opposite trend to the observed main transition temperatures.

The FWHM values for the main transition have also been calculated from the DSC thermograms. This gives an indication of the cooperativity of the transition – an increase in FWHM means a decrease in cooperativity. Apart from 2 M sarcosine, the cooperativity seems to only slightly decrease with increasing concentration of humectant.

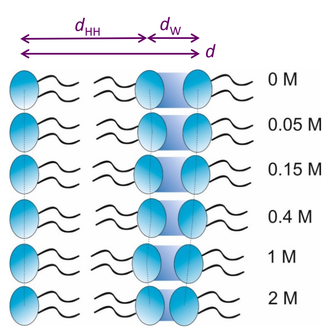


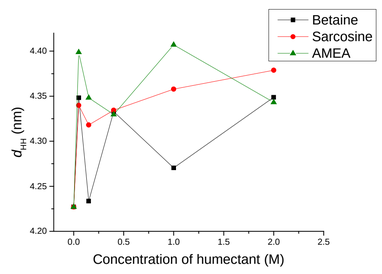
3. Structural Changes

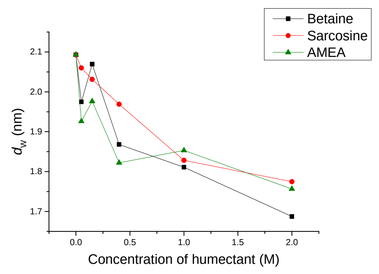


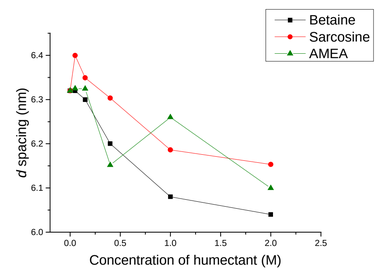
Electron density profiles (EDPs) are obtained from the SAXS data [3]. This exposes structural information such as the *d* spacing, d_{HH} and d_W. After the addition of humectant, any changes to the nanostructure of the DPPC bilayer can be observed by plotting the EDPs.

All three humectants affect the DPPC nanostructure in a similar manner; for the L_β' phase, the membrane thickness (d_{HH}) increases with increasing concentration of humectant. Consequently, the water layer (d_W) decreases with increasing concentration of humectant. An illustration of the overall change in the DPPC bilayer with addition of humectant is displayed.

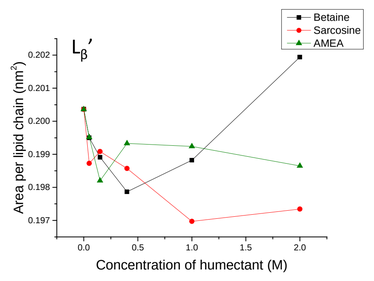


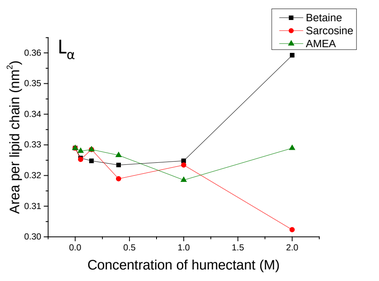


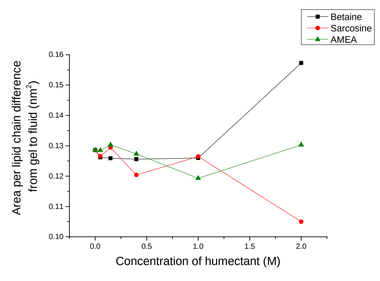




Despite the observed structural changes to the bilayer of DPPC, humectants do not appear to alter the area per lipid chain, at least at low concentrations. Also, the difference in the area per lipid chain from gel to fluid phase shows similar, unchanged behaviour.







4. References

1. Rappolt, M. *et al*. *Recent Research and Development in Biophysics*. 2004, **3**, pp.363-393.
2. Rudolph, A.S. and Goins, B. *Biochimica et Biophysica Acta (BBA) - Biomembranes*. 1991, **1066**(1), pp.90-94.
3. Li, N.Y.D. *et al*. *Electrotechnical Review.* 2017, **84,** pp. 69-75.

5. Acknowledgements

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