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The microstructure of creams revealed by confocal laser scanning microscopy

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Confocal laser scanning microscopy (CLSM) is widely used in biological sciences for its ability to provide high resolution, thin, optical sections, free from the out of focus flare associated with conventional fluorescence microscopy (Pawley, 1995). In pharmaceutical research, the potential of CLSM is only now being exploited for imaging inside dosage forms and investigating drug release mechanisms, (Cutts et al, 1996, Melia et al, 1997). This study examines the potential of CLSM to image the complex ultrastructure of an oil-in-water cream, and describes the microstructural changes that occur during evaporation at skin temperature.

CLSM images of aqueous cream BP, stained with Nile Red crystals 30 minutes prior to imaging, were obtained at Ex488nm/Em>515nm. They revealed a complex internal structure, with the size distribution of the dispersed phase being clearly highlighted by the lipophilic fluorophore. Long needle-like regions were also apparent, corresponding in size to the liquid crystalline lamellar regions. Some batches also showed solid crystalline surfactant (Eccleston, 1986, 1997). Features of 1μm were clearly resolvable, in contrast with the poor resolution of transmitted light or fluorescence microscope images obtained under the same conditions. A hydrophilic fluorophore, fluorescein selectively highlighted the aqueous phase of the cream, producing a negative contrast image, but less structural detail was revealed in comparison with Nile Red.

The progress of structural and phase changes within the cream were followed at 32±0.2°C to mimic evaporation at skin temperature. CLSM and reflected light images were acquired at intervals, and were related to cream weight loss. Assuming that weight loss was purely due to the evaporation of the aqueous phase, 50% and 97% of the water content was lost after 3 hr and 18 hr respectively.

At 9% water loss, the well-defined and separated phases, particularly the liquid crystalline regions, started to disappear. The oil phase coalesced, first to a distorted, patchy structure and later into a homogenous structure, composed principally of the oil phase, which appeared when 92% water was lost. The confocal image of the cream at this stage was comparable to that obtained from white soft paraffin.

This study shows how internal structure and component distribution changes as aqueous cream undergoes evaporation, and demonstrates the ability of CLSM to follow, in detail, the changes in microstructure related to this behaviour.

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