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Optimization of deformable vesicles for epidermal delivery of oestradiol

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A special type of highly deformable lipid vesicles (named Transfersomes) was reported to penetrate intact skin (Cevc & Blume, 1992). To prepare these vesicles, edge-activators were incorporated in the vesicles. Surfactants were suggested as example of edge-activators (Cevc et al, 1993).

The aims of this study were to optimise deformable vesicles for epidermal delivery of oestradiol and to evaluate Span 80 and Tween 80 as edge-activators in comparison with the reported sodium cholate (Cevc et al, 1995). Lipid vesicles containing phosphatidylcholine mixed with different concentrations of the surfactants (0, 10, 16, 20 and 30 %w/w) and containing 1 mg/ml radiolabelled oestradiol were prepared by the bath sonication method. The vesicles were homogenised by manual extrusion through polycarbonate membranes 200 and 100 nm, respectively. The final preparations contained 7% v/v ethanol.

Vesicles size was measured using photon correlation spectroscopy (Z average=150.6 nm). The entrapment efficiency was determined after separation of the free drug by the minicolumn centrifugation method (58-99 %).

The permeation of oestradiol through human epidermal cadaver membrane was studied using an automatic diffusion apparatus (Akhter et al, 1984). Saturated aqueous solution of oestradiol was used as control. The studies involved a finite dose design and were performed in two stages. The first stage used aqueous receptor for 12 hours at the end of which the donor compartment was washed; the second stage used 50% ethanol as receptor for further 12 hours. Permeation parameters and skin deposition were calculated. The flux data were fitted by a 6 order polynomial. The maximum flux (F_{max}) and the time of F_{max} (T_{max}) were calculated from the equations. When comparing different runs, the relative F_{max} was used to minimise skin variability. The optimum formulas were predicted from the fitted relative F_{max} versus surfactant concentration curves. The predicted optimum formulations were then prepared and tested against the control. The optimum concentrations were 14.0, 13.3 and 15.5 %w/w for sodium cholate, Span 80 and Tween 80 respectively. At optimum concentration they increased F_{max} by 18, 16 and 15-fold (illustrated in Figure 1) and skin deposition by 8, 7 and 8-fold compared with the control.

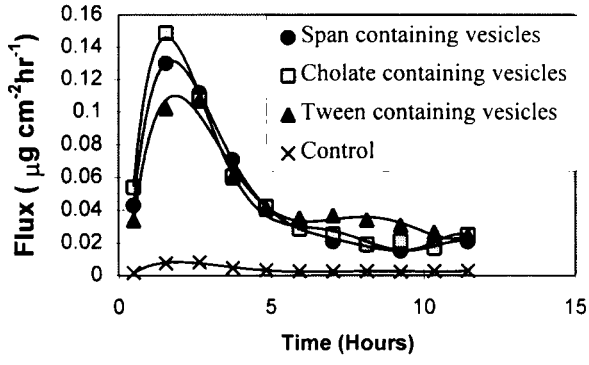

Fig 1. Fitted flux plots of oestradiol from different vesicles and control.

In conclusion, Span and Tween were as effective as cholate in lipid vesicles. Deformable vesicles improved the epidermal delivery of oestradiol.

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