Cyclodextrins as natural co-stabilising agents in submicron emulsions

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Introduction

Cyclodextrins have been used as pharmaceutical excipients for a long time. In a new approach, their potential as co-stabilising agents in eudermic topical drug delivery systems was evaluated. The aim of this study was the development of negatively as well as positively charged submicron emulsions (SME) with outstanding long-term stability, confirmed by measurements of both particle size and zeta potential. In addition, satisfying skin permeation of the model drug progesterone was achieved and the influence of the natural surfactant sucrose stearate (SS) on drug diffusion was evaluated.

Experimental Methods

Development of the formulations

Submicron emulsions were created by high pressure homogenisation. The surfactants used were lecithin and sucrose stearate while ß - Cyclodextrin was used as co-stabilising agent. Positively charged formulations were achieved by addition of the cationic phytosphingosine. Drug-loaded formulations were created by dissolving progesterone (1% w/w) in the oil phase.

Stability assessment

Physicochemical stability of the formulations was monitored over 6 months. Mean particle size and polydispersity index were measured by photon correlation spectroscopy. Zeta potential was analysed by laser Doppler electrophoresis.

Skin diffusion studies

Standard diffusion experiments were performed using dermatomised porcine skin. The drug content in the receptor medium was analysed by HPLC.

Results

The investigated formulations showed excellent long-term stability. The cationic phytosphingosine led to destabilisation of blank submicron emulsions after 6 months, whereas the negatively charged formulations remained stable.

Skin diffusion experiments showed that these formulations are suitable for the delivery of the lipophilic drug progesterone on skin. The release rate was about twofold higher from formulations with sucrose stearate, indicating that the sucrose ester might act as permeation enhancer. Positively charged SME did not provide for better skin permeation although literature suggests otherwise [1].

References

[1] M.P.Y. Piemi, D. Korner, S. Benita, J.-P. Martya. Positively and negatively charged submicron emulsions for enhanced topical delivery of antifungal drugs. J. Control. Rel. 58, 177–187 (1999)

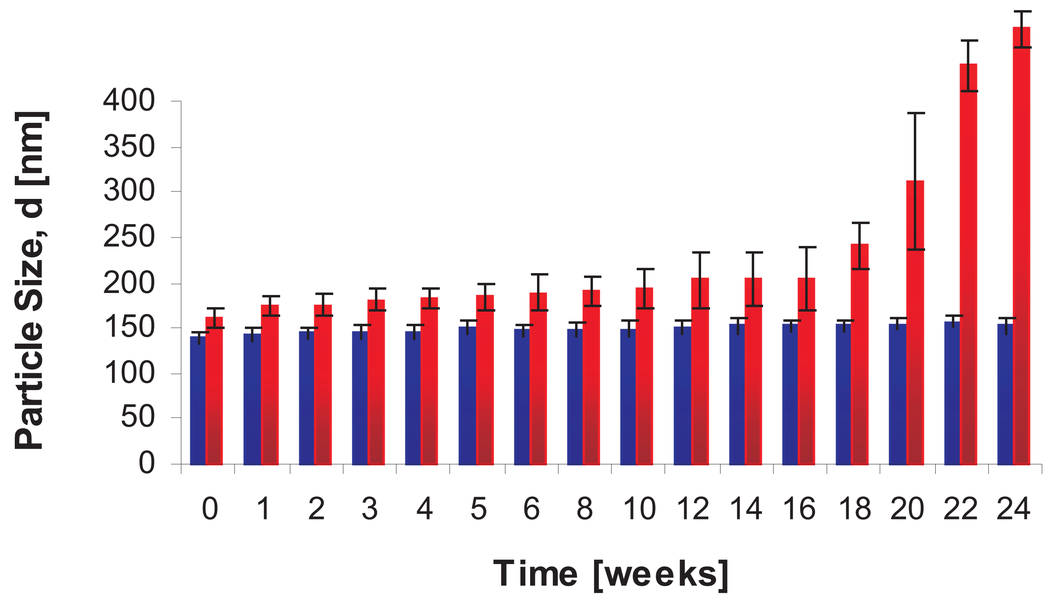

Fig. 1 Particle Size of blank SME: blue bars for negatively charged (-); red bars for positively charged (+).

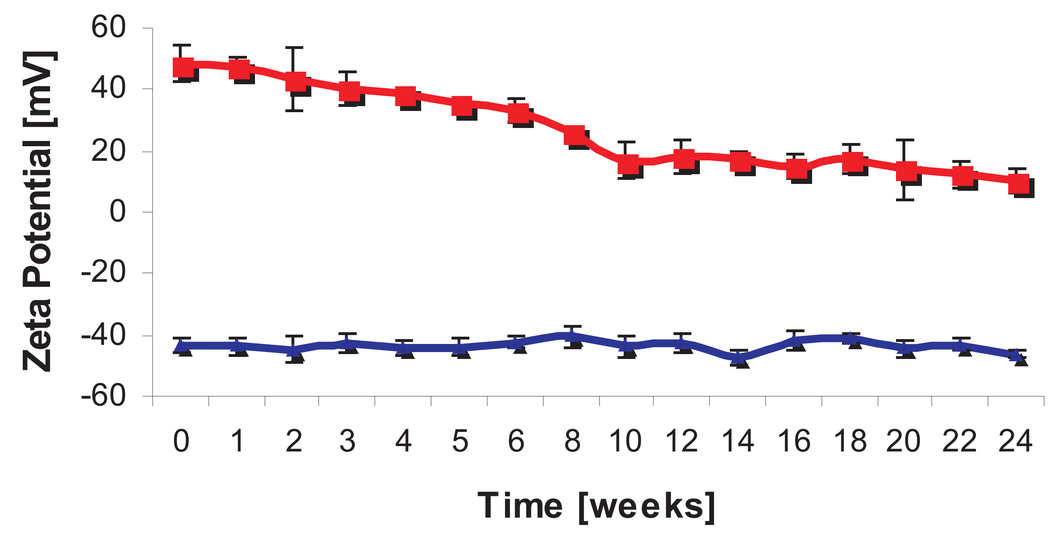

Fig. 2 Zeta Potential of blank SME: blue line for negatively charged (-); red line for positively charged (+).

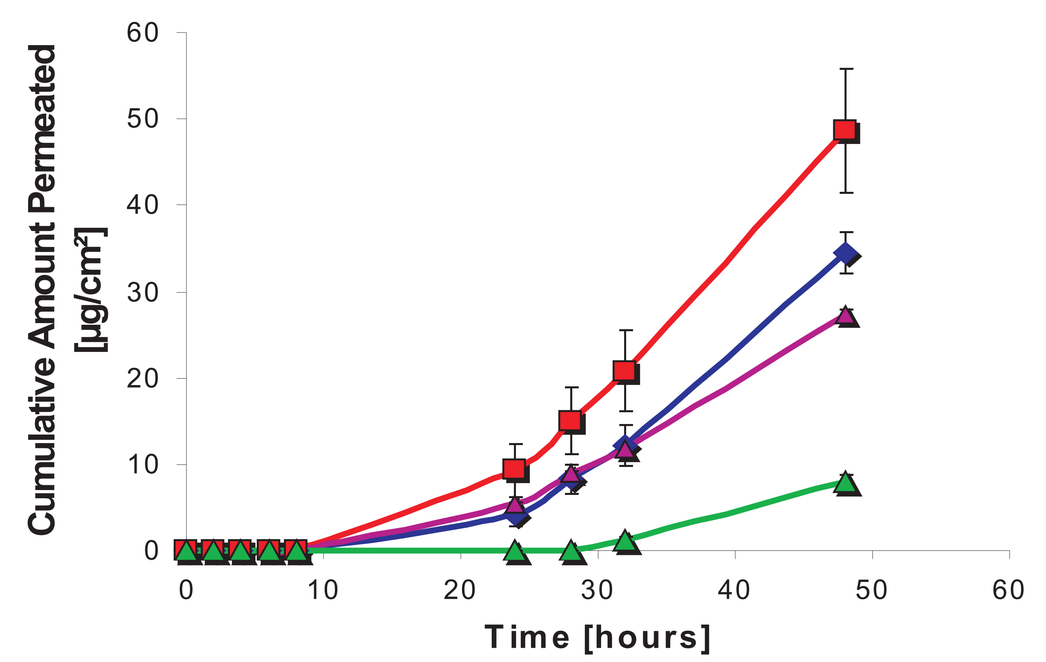

Fig. 3 Skin permeation of progesterone from negatively and positively charged SME. Red: (-) with SS; blue: (+) with SS; pink: (-); green: (+).

Conclusion

Cyclodextrins are able to form new surface active molecules with suitable fatty acid residues of the oil phase. Thus, they can be used as co-stabilising agents instead of synthetic surfactants. Natural surfactants like sucrose stearate provide further stability in terms of higher zeta potential values as well as permeation enhancement of drug diffusion through skin.