Development of Eudermic W/O/W Nanoemulsions for Delivery of Hydrophilic Drugs

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Introduction

Low-energy emulsification techniques such as the phase inversion temperature (PIT) method serve to conveniently and rapidly produce nano-sized O/W-emulsion systems without the need for high pressure devices. Recently, the PIT technique was employed to create novel W/O/W-nanoemulsions for incorporation of hydrophilic model compounds [1]. As opposed to conventional O/W-nanoemulsions, these systems contain an additional surfactant to solubilise the hydrophilic drugs in reverse micelles distributed within the oil phase. So far, the potential of these vehicles as drug delivery systems on skin has not been investigated. Therefore, the present study focuses on the development of novel Aciclovir-loaded W/O/W-nanoemulsions with a minimum amount of surfactant and their comparison to conventional O/W-nanoemulsions.

Experimental Methods

Fomulations

Reverse micelles were formed by addition of the lipophilic surfactant to the oil phase above the CMC. Subsequently, Aciclovir was added. This phase was then added dropwise to a mixture of the hydrophilic surfactant and water at about 85°C. As a last step, a sudden dilution with distilled water was performed. The amount of hydrophilic surfactant was varied, while the water-oil-ratio was kept constant at 70%. For reasons of comparison the same formulations were prepared without incorporating the drug into reverse micelles.

Physicochemical characterisation and stability

Physicochemical parameters such as particle size and polydispersity index were determined with a Zeta Sizer Nano ZS (Malvern, UK).

Skin permeation

The skin permeation of Aciclovir from the formulations was examined using Franz-typed diffusion cells with phosphate buffer pH 7,4 as acceptor medium. Dermatomed porcine skin was used as a model membrane. The permeated amount of Aciclovir was determined by HPLC.

Skin penetration

The skin penetration of Aciclovir from the W/O/W-nanoemulsions in comparison to the skin penetration of the drug from an aqueous solution was determined by Tape Stripping experiments. The formulations were applied on pig ear skin for one hour. Subsequently, the uppermost layers of the stratum corneum were removed with 20 tape strips. Corneocytes and Aciclovir were quantified by NIR and HPLC, respectively.

Results

The ideal concentration of the hydrophilic surfactant was found to be 5%. The W/O/W-nanoemulsions with Aciclovir showed mean particle sizes below 110 nm and PDI values below 0.19 over an observation period of six weeks. The nanoemulsions without reverse micelles exhibited significantly larger particle sizes and higher PDI values.

Satisfying skin permeation and penetration of Aciclovir from the W/O/W-nanoemulsions was achieved, which was clearly superior to the skin diffusion of an aqueous Aciclovir solution. The performance of the O/W-nanoemulsions was comparable to the W/O/W-nanoemulsion.

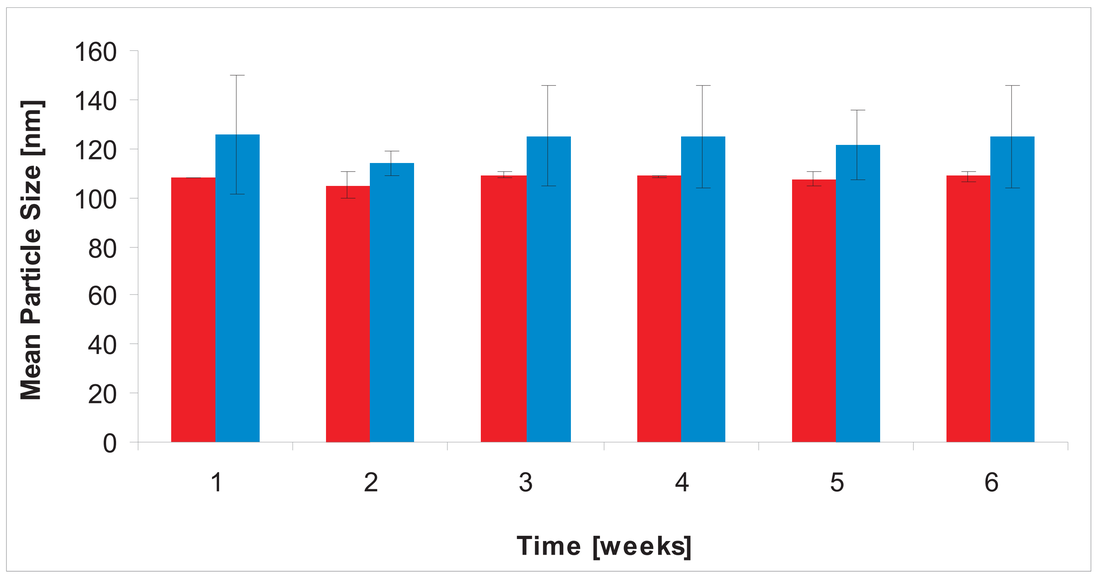

Figure 1: Mean particle sizes of W/O/W-nanoemulsions (red) and O/W-nanoemulsions (blue) with Aciclovir

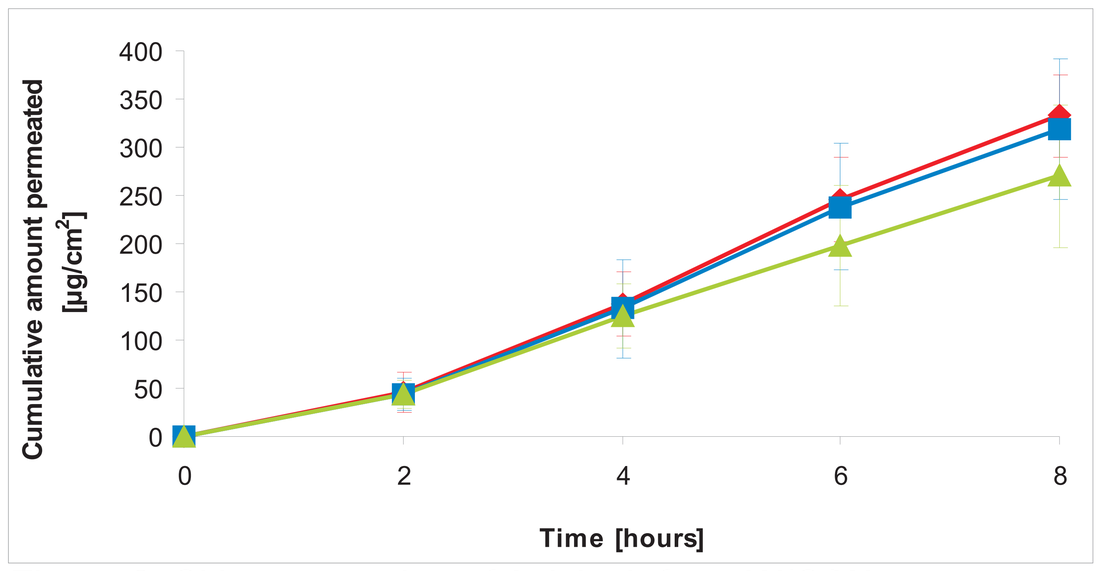

Figure 2: Skin permeation of Aciclovir from W/O/W-nanoemulsions (red), O/W-nanoemulsions (blue) and aqueous solutions (green), n = 8

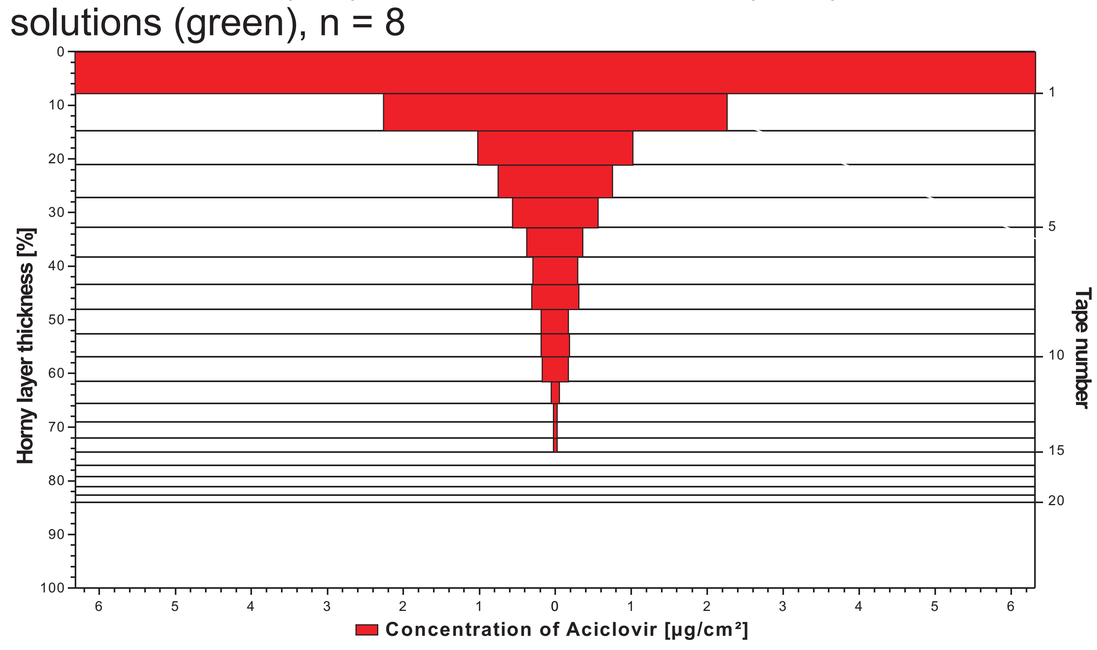

Figure 3: Skin penetration profile of Aciclovir from W/O/W-nanoemulsions, n = 6

Conclusion

The presented W/O/W-nanoemulsions are interesting candidates for dermal drug delivery due to their superior potential to incorporate hydrophilic drugs. To this end, other hydrophilic compounds are being investigated in further studies.

Acknowledgements

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References

[1] Anton N, Mojzisova H, Porcher E, Benoit JP, Saulnier P, Reverse micelle-loaded lipid nano-emulsions: New technology for nano-encapsulation of hydrophilic materials, Int J Pharm 398 (2010) 204-209.