Positivley charged nanoemulsions for enhanced topical delivery of fludrocortisone-acetate

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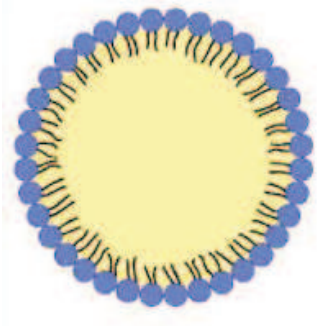
This study tested the hypothesis that the cationic compound Phytosphingosine (PS) increases skin permeabilty by interacting with negatively charged residues of proteins in the outer membran of epithelial cells and with selective active ion pumps of the membrane [1,2].Therefore the focus was to design and characterise positively charged nanoemulsions by measuring particle size and zeta potential (ZP). In addition the influence of the positively nanoemulsions on skin permeation of the model drug fludrocortisone-acetate was investigated.

Formulation

Nanoemulsions were prepared using high pressure homogenisation technique.



Particle Size and Zeta Potential

The mean particle size and the size distribution were determined by photon correlation spectroscopy and the zeta potential was analysed by laser Doppler electrophoresis at 25°C.

Diffusion cell preparation

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

Results

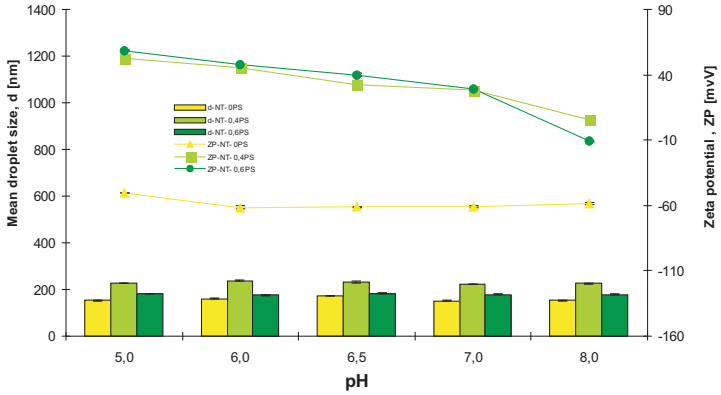


Fig. 1

The surface charge of the positive charged nanoemulsions was influenced by pH (Fig. 1). When the pH values were decreased below 6.5 the ZP values increased indicating physical stable nanoemulsions. The particle size is not influenced by the pH probably due to the steric stabilising effect of the hydrophilic surfactant polysorbate 80.

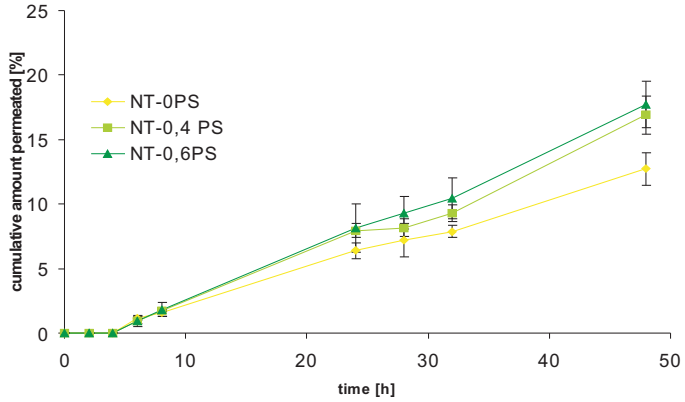


Fig. 3

The cumulative amount of permeated fludrocortisone-acetate through excised porcine skin was influenced by the addition of the cationic PS. An addition of 0.6 % PS is able to increase the cumulative amount about 1.4-fold compared to the control after 48 hours of diffusion time.

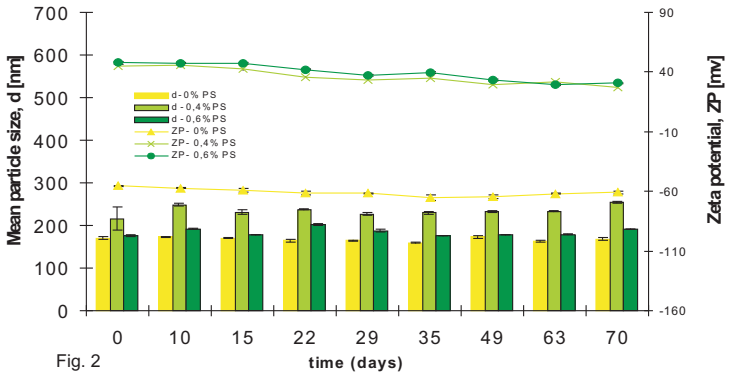


Fig. 2

The stability assessments of the nanoemulsions show constant ZP and uniform particle sizes in the PS free as well in the PS containing formulations over the whole observation period of 10 weeks (Fig. 2).

Conclusion

Overall we succeeded in creating physically stable nano-emulsions with skin compatible ingredients and in enhancing skin permeation of the model drug fludocortisone-acetate by addition of phytosphingosine. The results of this study show that phytosphingosine is a promising canditate for enhancing skin permeation and above all, it is an interesting multifunctional additive for drug delivery systems.

References

[1] M.P.Y. Piemi et al., Positively and negatively charged submicron emulsions for enhanced topical delivery of antifungal drugs, J. Contr. Release 58, 117-187 (1999)