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Stabilisation of a W/O/W Multiple Emulsion using a Natural Polymers

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Introduction

Multiple emulsions are of major interest as potential skin delivery systems and are also known as "emulsions of emulsions". They show high potential for the transport of hydrophilic drugs across the skin and the internal droplets can serve as an entrapping reservoir for hydrophilic drugs. However, multiple emulsions are thermodynamically unstable due to a high tendency of the internal droplets to coalesce, aggregate or rupture. The aim of the present study was to prepare multiple emulsions by a simple one-step emulsification using a natural polymer as a thickener of the external water phase to improve long-term stability and increase the release under shear. Furthermore 5-fluorouracil was incorporated as a model drug to investigate skin penetration properties.

Experimental methods

Formulations

Multiple emulsions using Span 80 as a lipophilic and Tween 80 as a hydrophilic surfactant were prepared using a One-Step Emulsification Method [1]. The total amount of surfactant was kept at 4%. Both surfactants were solved in the oil phase. Oil and aqueous phase containing 1% 5-fluorouracil as a model drug were separately heated up to 50±5°C. Subsequently the water phase was slowly added into the oil phase under moderate stirring. Afterwards the natural polymer Solagum™ AX (Acacia Senegal Gum and Xanthan Gum) was incorporated and stirred for 20 min at 750 rpm.

Optical light microscopy

The characterisation of the multiple droplets was performed using a photo microscope (Zeiss Axis Observer.Z1 microscope system, Carl Zeiss, Oberkochen, Germany).

Stability assessment

Droplet size was determined using a laser diffraction particle size analyser (Mastersizer 3000, Malvern, United Kingdom). The particle size distribution was calculated according to the Mie theory.

In vitro skin penetration

Skin penetration of 5-fluorouracil from W/O/W multiple emulsions was determined by tape stripping experiments. Formulation was applied on full-thickness porcine ear skin for one hour. Subsequently the uppermost layers of the stratum corneum were removed with 20 tape strips. Corneocytes and 5-fluorouracil were quantified by NIR and HPLC, respectively. The entire horny

layer thickness was determined by removing the whole stratum corneum until the limit of detection of the NIR densitometer was reached.

Results

It was possible to create stable W/O/W multiple emulsions using Solagum™ AX as a natural thickener. The use of a thickener led to a decrease of droplet size from approximately 36 µm to 17 µm and an improvement of droplet-stability. Furthermore the number of inner water droplets entrapped in the oil droplets was increased. After 10 weeks of storage there were rarely any entrapped water droplets left in the multiple emulsion without a thickener, whereas the oil droplets of the multiple emulsion with a polymer contained still a lot of inner water droplets. The mean droplet sizes of the thickened multiple emulsion remained largely constant over the whole observation period. The skin penetration of the model drug 5-fluorouracil proved to be excellent from the obtained W/O/W multiple emulsion with a thickener. 5-Fluorouracil could be detected up to 20 strips, which approximates 82% of the entire stratum corneum thickness.

Acknowledgements

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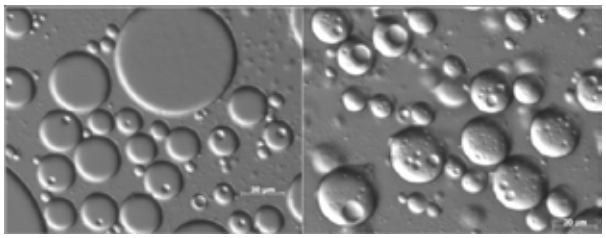

Figure 1: Differential interference contrast microscopic (DIC) images of a W/O/W multiple emulsion. Left: Without a thickener, Right: With a natural polymer as a thickener

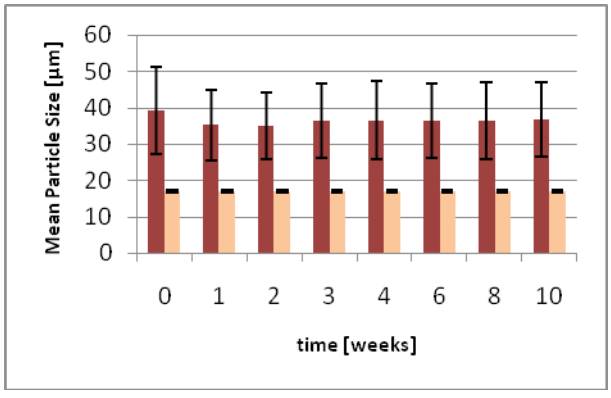

Figure 2: Droplet sizes of the multiple W/O/W emulsions presented as the mean diameter based on the volume distribution D(v,0.5). Red bars: without thickener, orange bars: with thickener

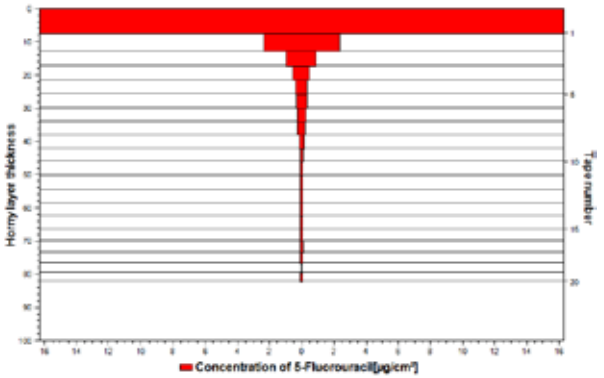

Figure 3: Skin penetration profile of 5-fluorouracil from a W/O/W multiple emulsion using Solagum™ AX as a thickener (n=6)

References

[1] Morais, J.M., Santos, O.D.H., Nunes J.R.L., Zanatta C.F., Rocha-Filho P.A., 2008. W/O/W Multiple Emulsions Obtained by One-Step Emulsification Method and Evaluation of the Involved Variables. J. Dispersion Sci. Technol. 29, 63-69.