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Lipophilic microemulsions as appropriate vehicles for topical delivery of antioxidant vitamins

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Introduction

Microemulsions (ME) are effective and even non-irritant potential vehicles for topical delivery of antioxidants to support skin endogenous antioxidant system. This strategy is a popular approach for protection skin from excessive exposure to free radicals. As the balance between skin antioxidants is very important, a combined therapy with a hydrophilic (vitamin C) and a lipophilic (vitamin E) antioxidant is desirable. For this reason ME as clear, thermodynamically stable dispersions of water and oil, stabilized by an interfacial film of surfactant molecules could be advantageous due to their unique microstructure that allow the incorporation of lipophilic and hydrophilic antioxidant in the same system. Further, their viscosity could be optimized for topical application relatively easily not only by conventional way – addition of suitable thickener but also by an alternative approach - formation of transparent microemulsion gel due to structural transition.

The main purpose of this work was therefore to evaluate the influence of different lipophilic ME (non- thickened o/w and thickened o/w) on release profile and *in vitro* skin bioavailability of vitamins C and E. Skin deposition of drugs is namely influenced by their physical-chemical properties as well as by their carrier system and its impact on the skin.

Results

Total amount of released vitamins was higher for vitamin E than for vitamin C (Fig. 1). For vitamin C delayed release was observed which can be attributed to its partition mostly in inner aqueous phase of ME whereas vitamin E is predominately found in outer lipophilic phase. ME thickened with colloidal silica expressed higher viscosity (≈3900mPas) than ME thickened with white wax (≈1100mPas) explaining higher release rate of both vitamins from the latter.

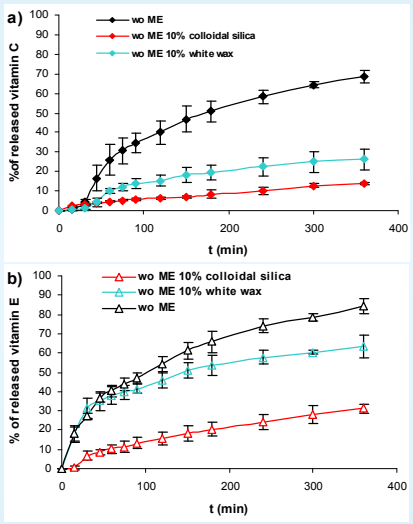

Fig. 1: Release profiles of vitamin C (a) and vitamin E (b) from different lipophilic ME.

All ME were able to deliver vitamins C and E to the skin. Skin concentrations of vitamin E were approximately 100x times higher than of vitamin C (Fig.2) indicating that stratum corneum is an efficient barrier for hydrophilic vitamin.

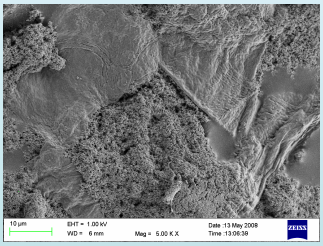

Fig. 3: SEM picture of 2nd tape strip of pig ear skin treated with w/o ME thickened with 10% colloidal silica.

Colloidal silica accumulated to considerable amount in the first layers of stratum corneum (Fig.3) but was not found in deeper layers. We assume that it disturbed the organisation of outer layers of stratum corneum and facilitated passage of hydrophilic vitamin across the skin (Fig. 2a).

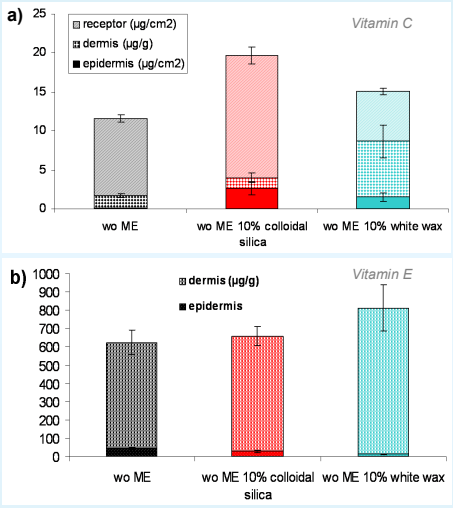

Fig. 2:. Amounts of vitamin C (a) and vitamin E (b) accumulated in epidermis, dermis and receptor fluid after 6 hours.

Conclusions

- **Release profiles of vitamins C and E from lipophilic (w/o) ME are mostly influenced by vitamin location in vehicle and viscosity of formulation.**
- **Permeation studies confirmed tested ME as suitable carriers for simultaneous delivery of hydrophilic and lipophilic vitamin in the skin.**
- **No simple correlation between particular vitamin release and its permeation could be found, mainly due to the fact that formulation can apart from release behaviour change also skin properties.**

Materials and methods

Vitamins C and E (Sigma Aldrich) were incorporated in different w/o ME in 0,4% and 1% concentration respectively. w/o ME consisted of 30% of surfactant mixture (Imwitor 308:Tween40=1:1),10% water and 60% isopropyl myristate as oily phase. w/o ME was thickened by adding either 10% of colloidal silica (Degussa, Aerosil 200) or 10% of white wax (Pharmachem, Slovenia).
Release studies: Franz cells and cellulose acetate membrane under sink conditions.

In vitro permeation studies using pig ear skin: The amounts of vitamins accumulated epidermis and dermis and passed into receptor solution were determined using Franz diffusion cells and infinite dosing after 6 hours of contact. All samples were analysed by HPLC.
Accumulation of colloidal silica inside stratum corneum was investigated by SEM after tape stripping.

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