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The influence of surface active agents on the bioavailability of the preservative methylisothiazolinone

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SCIENCE & RESEARCH

Bioavailability, determined as skin barrier penetration ability, is one of the most important factors influencing the margin of safety of cosmetic preservatives. A formulation of cosmetic can strongly affect the penetration, and often is a predominant factor influencing the stratum corneum penetration rate.

2-methylisothiazolin-3-one (INCI name: Methylisothiazolinone) is a preservative, for which despite of the well-done toxicological dossier, the problem of topical application-related bioavailability still remains uninvestigated. It is regarding especially an influence of the cosmetic formulation on the ability of the preservative permeation through epidermal barrier, determining possible toxic, both local and general effects. Methylisothiazolinone is widely use in wash out products like shampoos and bathing cosmetics containing anionic surfactants which are well-known strong permeation enhancers. Therefore, investigation of the influence of surface-active agents - especially anionic - on the permeation of the compound through the skin, seemed important.

We carried out permeation research in standard Flynn chambers with ceramide-based sandwich-type liquid crystal membranes. As a model mixture of stratum corneum intercellular cement lipids we applied Cerasome 9005 (Lipoid GmbH).

We discovered that Methylisothiazolinone relatively well penetrates through the model membrane. This phenomenon could be explained by presence of hydrogen bonding lowering the thermodynamic activity coefficient of the permeant in the membrane. It is also indicated by distinct lag time visible in the permeation curve (fig. 1).

Introducing anionic surfactants as Sodium Lauryl Sulphate (SLS), Sodium Laureth-2 Sulphate (SLES-2) and Sodium Laureth-3 Sulphate (SLES-3) into the solution, in contrary to the expectations, lowered down the permeation (fig. 2-4). This effect appeared at surfactant concentrations exceeding the cmc value only and weakens as the concentration increases. It is probably the result of an influence of surfactants on the liquid-crystalline structure of the membrane.

Lowering down the permeation rate seems to be a result of the Methylisothiazolinone binding in micelles causing decline of thermodynamic activity in the donor solution. It is surprising because of relatively high preservative polarity eliminating, to a large extent, its participation in solubilization processes. A structure of Methylisothiazolinone can be here an explanation, enabling to build-in molecules of the preservative into anionic surfactant micelles by forming adequate complexes. This issue will be an object of further research.

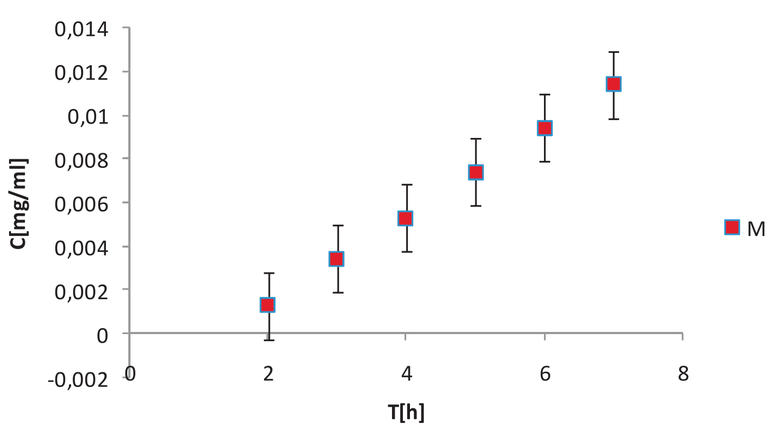

Fig 1. Methtylisothiazolinone (MI) permeation curve

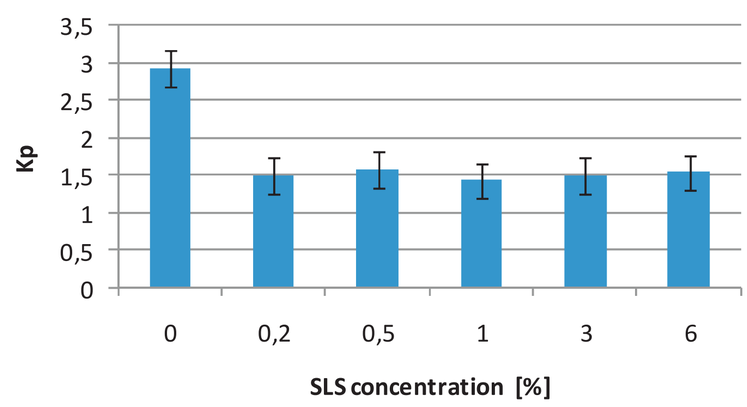

Fig. 2. The influence of SLS on Methylisothiazolinone permeation.

In order to check the practical usefulness of the described above phenomenon a permeation of Methylisothiazolinone from typical cosmetic bathing preparation (Form. 1) through model membranes was examined.

Formulation 1

Sodium Laureth-3 Sulfate	8
Decyl Glucoside	5
Cocamide DEA	2
Ceteareth-12	1
NaCl	1,5
Methylisothiazolinone	0,01
Aqua	to 100%

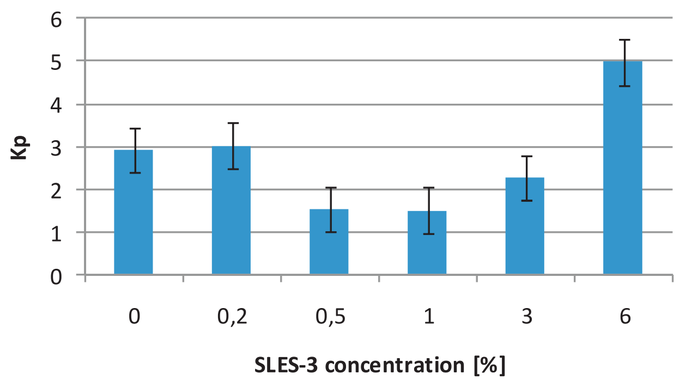

Fig. 4. The influence of SLES-3 on Methylisothiazolinone permeation

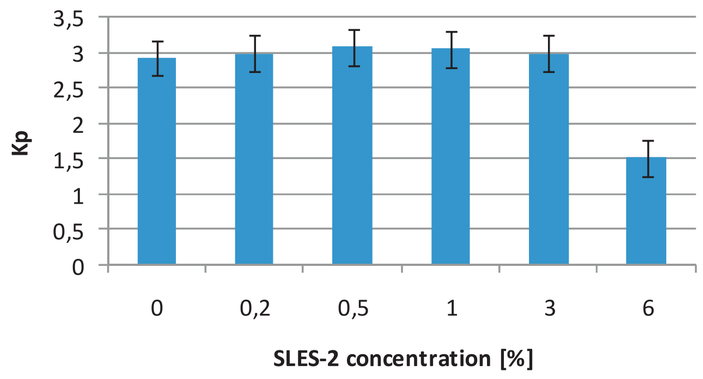

Fig. 3. The influence of SLES-2 on Methylisothiazolinone permeation.

We found that the used mixture of surfactants was reducing the preservative permeation through the model membrane by almost a 50% (fig. 5). Dilution of surfactant mixture (bathing preparation) influences the permeation coefficient only to a little extent.

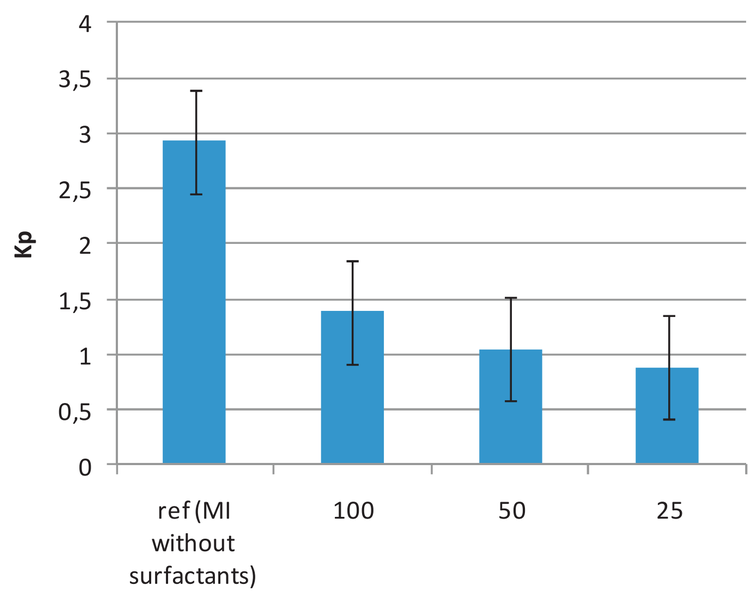

Fig. 5. Influence of bathing product concentration in solution on Methylisothiazolinone (MI) permeation coefficient

Conclusions

Anionic surfactants hamper the Methylisothiazolinone permeation through membranes modelling the horny layer of the epidermis. Probably the reason is building-in Methylisothiazolinone into the micellar structures in solutions of surface-active agents. This phenomenon appears both in solutions of individual surfactants as well as in the case of mixtures of anionic and nonionic surfactants which form mixed micelles in solutions. Contrary to the expectations, applying Methylisothiazolinone in bathing preparations is lowering down its bioavailability and is increasing the safety of application.

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