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The influence of cationic compounds on the bioavailability of 5-hydroxyproline

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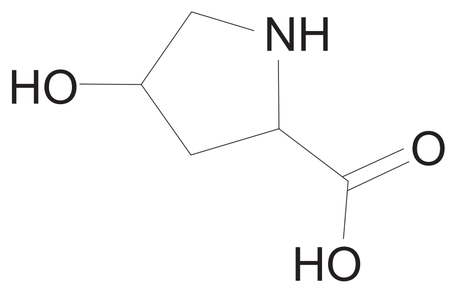
SCIENCE & RESEARCH

Quaternary ammonium salts are more and more often applied as ingredients of skin care cosmetics, above all on account of its skin conditioning effects. Change of the skin sensory parameters caused by their activity is an effect of the stratum corneum surface nanostructurization. These ingredients have a significant influence on the penetration rate of active substances, many authors recognize it as penetration enhancers, however available scientific data are far from the explicitness.

The aim of this study was to investigate the effect of quaternary ammonium compounds on the skin penetration by the 5-hydroxyproline.

Hydroxyproline is an important component of anti-age cosmetics. Apart from moisturising properties it stimulates collagen synthesis by fibroblasts probably by enhancing procollagen proline hydroxylation. As most of aminoacids 5-hydroxyproline belongs to substances of low bioavailability during topical application.



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 found, that hydroxyproline, as expected, penetrates through stratum corneum modelling membranes relatively poorly, at values of the permeation coefficient order of magnitude 10^{-7} cm·s^{-1}. In addition a distinct dependence of the permeation rate on the pH of the environment is being observed (Fig. 1a-b).

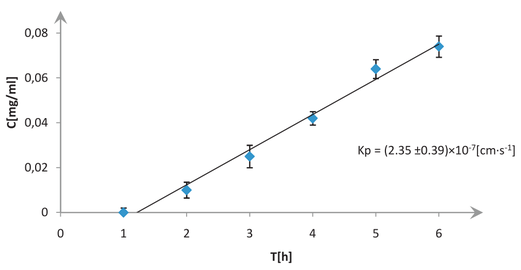


Fig. 1a. Hydroxyproline permeation through model membrane at pH 7.4.

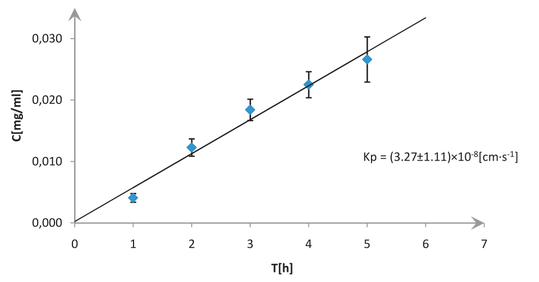


Fig. 1b. Hydroxyproline permeation through model membrane at pH 5.5.

We observed a distinct lag-time at the pH of 7.4 pointing at strong influence of the permeant on the membrane. In the investigated range of pH values 5-hydroxyproline exists exclusively in the form of ampholyte ion (Fig. 2), therefore influences with the membrane at higher pH values are probably a result of the dissociation of membrane lipids, free fatty acids above all.

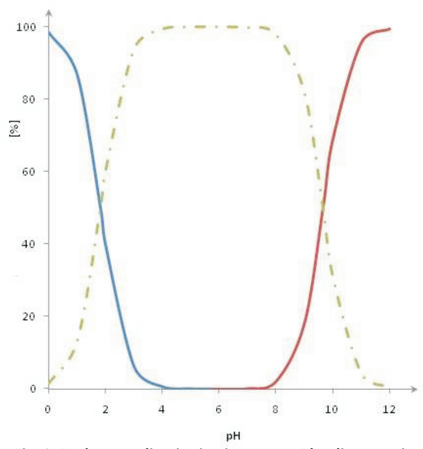


Fig. 2. Hydroxyproline ionization curve. Blue line – cations, red line – anions, green dotted line – ampholyte ions

Introduction of 0,5% quaternary ammonium salts into the solution strongly hampers 5-hydroxyproline permeation (Fig.3). The strongest hampering activity demonstrated trimethylbenzylammonium chloride, reducing the permeation rate almost five times. The weakest - strongly sterically hindered tetrabutylammonium chloride. We did not find any dependence of hampering ratio with simple physico-chemical parameters of quats like basicity, lipophilicity or molecular weight.

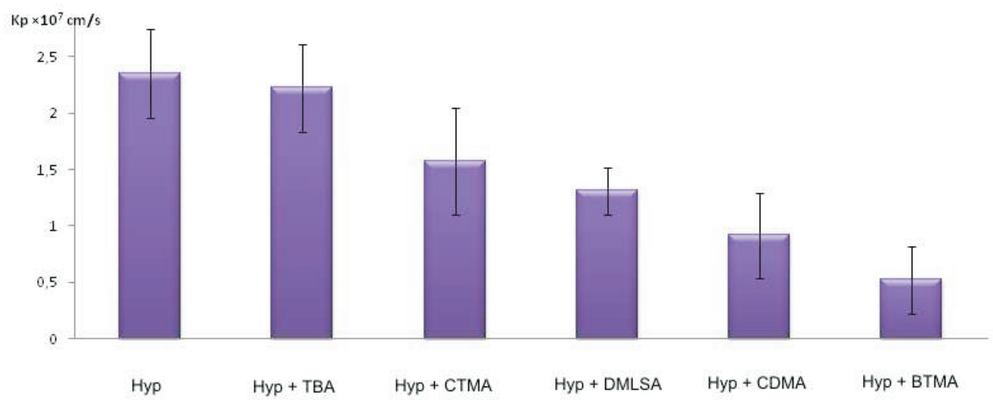
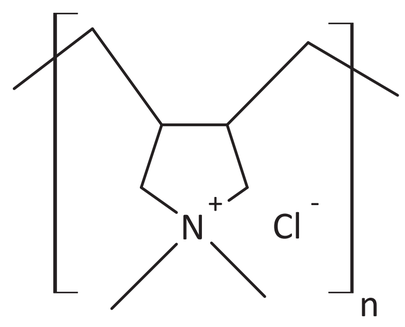


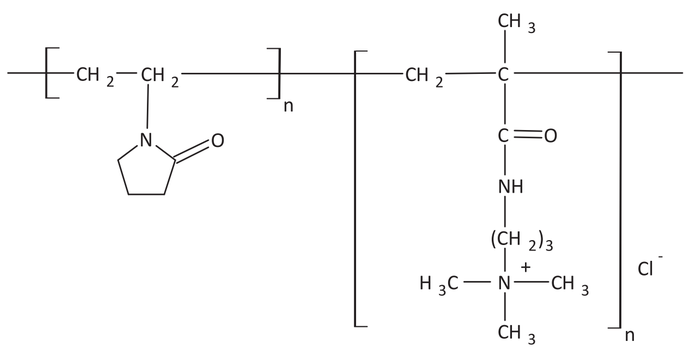
Fig. 3. The influence of cationic surfactants on the hydroxyproline (Hyp) penetration rate. TBA – tetrabutylammonium cation, CTMA – cetyltrimethylammonium cation, DMLSA – dimethyllaurylstearylammonium cation, CDMA – cetyldimethylammonium cation, BTMA – benzoyltrimethylammonium cation

The mechanism of the hindering influence of these compounds on the permeation of the hydroxyproline is difficult to explain on the base of available data. The hampering of the permeation can be an effect of creating complexes in the donor solution lowering the thermodynamic activity of the permeant. The alternative mechanism can be associated with interaction of quaternary ammonium salt with elements of the membrane and creating barrier structures hampering penetration of the hydroxyproline into membrane lipid phase.

The hindering effect exhibit also cationic polyeloctrolytes, so Polyquaternium-6 and Polyquaternium-28



Polyquaternium-6
Kp = 0.785 ± 0.30 cm·s^{-1}, ER=66,9



Polyquaternium-28
Kp=2.09 ± 0.37 cm·s^{-1},
ER=-11,1

Polyquaternium-6 is a sterically nonhindered cationic polymer of high charge density, it hampers hydroxyproline permeation by over 50% (ER=-66.9). The influence of strongly hindered, low charged Polyquaternium-28 is much lower (ER=11.1).

The effect of these substances is probably a result of the alteration of the membrane surface by quaternary ammonium salt absorption. It is pointed by results of experiments carried with membranes pretreated with Polyquaternium-6. As a result of the reaction of material of the membrane with the polyelectrolyte it barrier properties dramatically increase (fig. 4). The hydroxyproline permeation rate through Polyquaternium-6-pretreated diaphragms decreases over three times. Important difference into Polyquaternium-6-based hampering permeation rate in the donor solution and pretreated membranes can point at the mixed mechanism of action connected to both hampering and promoting the permeation.

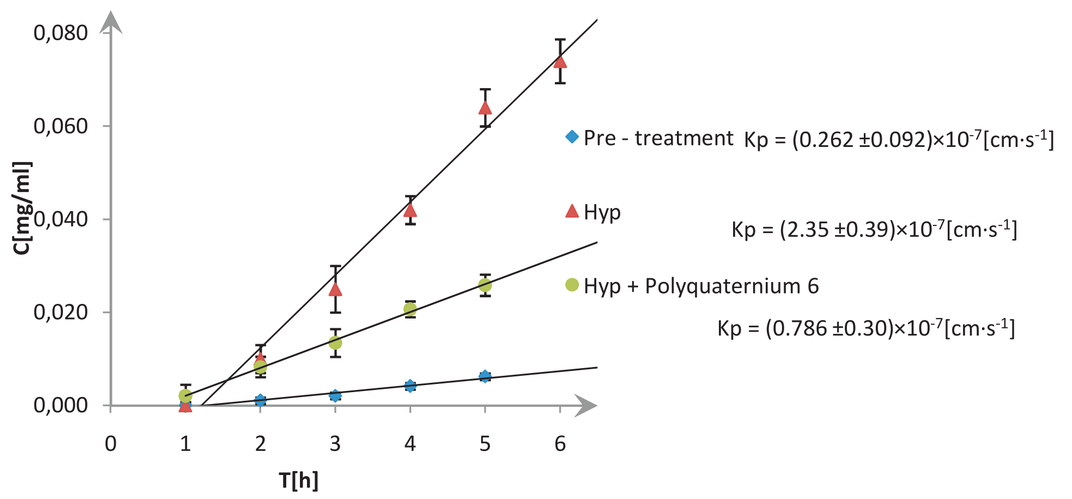


Fig. 4. The influence of membrane pretreatment by Polyquaternium-6 on the hydroxyproline permeation rate.

Summary

The results obtained indicate that contrary to the documented data, quaternary ammonium salts may have an inhibitory effect on the penetration of substances capable of ionization. This effect is particularly strong in the case of cationic polymers. It can be probably used in the modulation of bioavailability of the ingredients of the cosmetic effect, and potentially toxic compounds such as some dyestuffs used in hair dyes. The issue requires further research, above all in the mechanism of permeation hampering connected with interactions between membrane lipids and quaternary ammonium salts.

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