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Stratum corneum hydration : mode of action of moisturizers on a molecular level

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CHAPTER 3

THIS THESIS

1. OBJECTIVES

Dry skin is one of the most common symptoms of dermatological disease, but can also occur in normal skin that has been exposed to excessive washing (Rawlings et al., 1994c) or dry environmental conditions (e.g. in winter xerosis) (Katagiri et al., 2003b; Rogers et al., 1996; Simon et al., 2001). In these cases, low SC water levels are caused by the extraction of NMF by washing or by changes in lipid composition and consequently lipid organization due to environmental influences. It becomes more and more apparent, however, that many dermatological diseases that list dry skin as one of their symptoms are at least partially caused by genetic deficiencies. These deficiencies can cause aberrant lipid organizations, as seen for instance in lamellar ichthyosis and atopic dermatitis (Lavrijsen et al., 1995; Pilgram et al., 2001b), decreasing the barrier properties of the intercellular lipid phase, which may lead to increased water loss. However, the latter disease, atopic dermatitis has also been linked to defects in the genes for (pro-)filaggrin (Morar et al., 2006). These defects imply that only little filaggrin-derived NMF can be produced, rendering the SC unable to retain enough water for a proper functioning.

Low water levels caused by a deficient barrier may be treated using hydrophilic or lipophilic moisturizers. Even though topical applications for the treatments of dry skin have been used for thousands of years, the exact working mechanisms of moisturizers are not yet known. This thesis aims to unravel these mechanisms. For this purpose, several moisturizers were selected. The hydrophilic groups consisted of four humectants: glycerol, the monosaccharide glucose, the disaccharide saccharose and hydroxyethyl urea (HEU). The lipophilic group consisted of the occlusive moisturizer Vaseline® and the non-occlusive moisturizers isostearyl isostearate (ISIS), isopropyl isostearate (IPIS) and glycerol monoisostearate (GMIS) (figure 1).

2. OUTLINE

Chapter 4 describes studies in which sliced cross sections of *ex vivo*, moisturizer treated and untreated human SC are visualized using cryo-SEM. The SC is divided into regions of high and of low water content and the thickness and the number of corneocytes in these regions is measured and counted, respectively. Thus, the location of water in treated and untreated SC, as well as the total increase in water levels is determined.

In Chapter 5 the possibility of using isolated porcine CER in lipid mixtures modelling the SC's intercellular lipid matrix for FTIR studies is explored. Furthermore, effect of glycerol on the lipid organization in such mixtures and in isolated SC is studied.

In Chapter 6, the interaction of lipophilic moisturizers and the SC's intercellular lipid matrix of human skin is reported. The lipid matrix is visualized after *in vivo* moisturizer treatment using a combination of tape-stripping and FFEM. The effect on the lamellar ordering of the lipid matrix is studied *in vitro* by adding the moisturizers to SC lipid mixtures of which the lamellar ordering is determined by SAXD measurements.

In Chapter 7 lipophilic moisturizers are added to SC lipid mixtures and their effect on the lateral organization in these mixtures is determined. Furthermore, a possible working mechanism for non-occlusive lipophilic moisturizers is proposed.

In Chapter 8 the penetration of lipophilic and hydrophilic moisturizers in human skin *in vivo* is described. With a combination of tape-stripping and ATR-FTIR spectroscopy a penetration profile for the moisturizers is determined. Additionally, a profile for the water distribution in the SC is found.

In Chapter 9 the findings described in this thesis are summarized and their impact and the future perspectives of moisturizer research are discussed.

Chapter 10 is a layman's summary in Dutch.

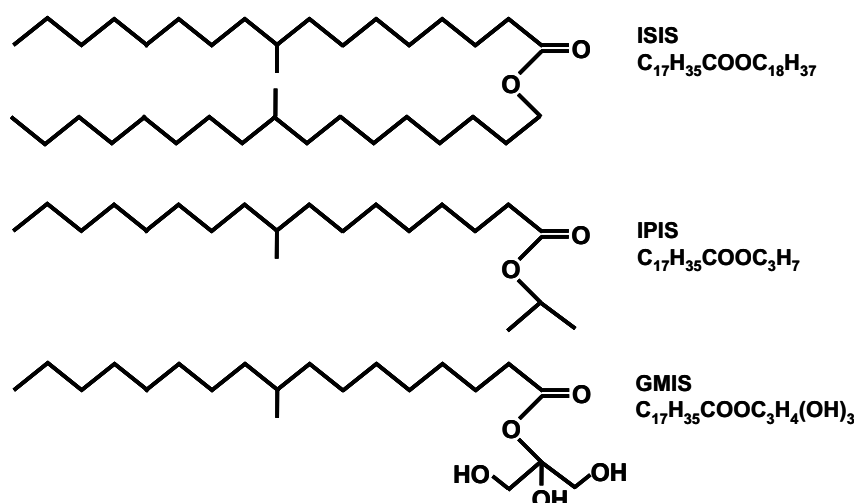


FIGURE 1. Structure formulas of isostearyl isostearate (ISIS), isopropyl isostearate (IPIS) and glycerol monoisostearate (GMIS).

3. REFERENCES

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