Research Communication

Changes in levels of omega-O-acylceramides and related processing enzymes of sun-exposed and sun-protected facial stratum corneum in differently pigmented ethnic groups

Anthony V. Rawlings1 | Rotraut Schoop2 | Christian Klose3
Jean-Marc Monneuse4 | Beverley Summers5 | Rainer Voegeli2

1AVR Consulting Ltd, Northwich, UK
2DSM Nutritional Products, Kaiseraugst, Switzerland
3Lipotype GmbH, Dresden, Germany
4Phylogene SA, Bernis, France
5Sefako Makgatho Health Sciences University, Medunsa, South Africa

Correspondence
Rainer Voegeli, DSM Nutritional Products, Kaiseraugst, Switzerland
Email: rainer.voegeli@dsm.com

Funding information
DSM Nutritional Products

Abstract
Introduction: We report on the differences in ceramide composition and levels of omega-O-acylceramide processing enzymes of sun-exposed and sun-protected facial stratum corneum (SC) among Albino African, Black African and Caucasian women living in South Africa.

Methods: Tape strippings were taken from the sun-exposed cheek and the sun-protected postauricular site (PA). In two subsets proteomic (n = 18) and lipidomic (n = 24) analysis were performed using mass-spectrometry-based shotgun platforms.

Results: No significant differences in total ceramide levels or ceramide subtypes were found between the Black African and Caucasian women in either the cheek or PA samples. Compared to the other two groups the levels of total ceramide as well as selected omega-O-acylceramide species were increased in Albino Africans. On the cheek, ceramide (CER) EOS, EOH along with CER AS were increased relative to the Caucasian women, while CER EOP and EOdS were elevated relative to the Black African women. Moreover, on the PA site CER EOP and EODS were elevated compared with the Black African women and CER EOdS in Caucasians. Decreases in mass levels of 12R-LOX and eLOX3 were observed on cheeks compared with the PA sites in all ethnic groups. On the PA sites 12R-LOX was particularly lower in the Albino Africans compared with the Black African and Caucasian women. On the cheeks mass levels of SDR9C7 was also lower in the Albino Africans.

Conclusion: The mass levels of the ceramides were similar between Black African and Caucasian women. However, elevated total ceramides and excessively elevated selected omega-O-acylceramides were apparent in the Albino African women. The findings in the Albino African women were unexpected as these participants suffer from impaired skin barrier function. However, the elevated levels omega-O-acylceramides can contribute to barrier insufficiency by directly...

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2022 DSM Nutritional Products AG. International Journal of Cosmetic Science published by John Wiley & Sons Ltd on behalf of Society of Cosmetic Scientists and Societe Francaise de Cosmetologie.
impacting SC lipid phase behaviour and/or secondly elevated omegaO-acylceramide levels may indicate a reduced attachment of ceramides to the corneocyte lipid envelope and reduced corneocyte maturation that can also impair the barrier. Indeed, differences in the mass levels of omega-O-acylceramide processing enzymes were observed for 12R-LOX and SDR9C7 for the Albino Africans. This indicates a corneocyte lipid scaffold disorder in this population.

**KEYWORDS**
chemical analysis, corneocyte envelope, ethnic, lipidomics, proteomics, skin barrier, skin physiology/structure

**Résumé**

**Introduction:** Nous décrivons les différences de composition en céramides et de niveaux des enzymes du métabolisme des oméga-O-acylcéramides du stratum corneum facial (SC) photo-exposé et photo-protégé chez des femmes Albinos Africaines, Noires Africaines et Caucasiennes vivant en Afrique du Sud.

**Méthodes:** Les prélèvements ont été effectués sur la joue photo-exposée et sur le site post-auriculaire (PA) photo-protégé à l’aide de disques adhésifs. Dans deux sous-groupes, des analyses protéomiques (n = 18) et lipidomiques (n = 24) ont été réalisées à l’aide de plateformes de spectrométrie de masse non-ciblées.

**Résultats:** Aucune différence significative de quantité globale de céramides ou dans les différentes classes de céramides n’a été observée entre les femmes Noires Africaines et les femmes Caucasiennes, quels que soient les échantillons (Joue ou de PA). Comparativement aux deux autres groupes, les quantités de céramides totales, ainsi que certaines espèces d’oméga-O-acylcéramides, étaient plus élevés chez les femmes Albinos Africaines. Sur la joue, les céramides (CER) EOS, EOH et CER AS étaient plus élevés que chez les femmes Caucasiennes, tandis que les CER EOP et EOdS étaient plus élevés que chez les femmes Noires Africaines. De plus, sur le site PA, les CER EOP et EOdS étaient plus élevés que chez les femmes Noires Africaines et les CER EOdS chez les Caucasiennes. Des diminutions des niveaux d’enzymes 12R-LOX et eLOX3 ont été observées sur les joues par rapport aux sites PA dans tous les groupes ethniques. Sur les sites PA, le niveau de 12RLOX était notablement plus faible chez les femmes Albinos Africaines comparativement aux femmes Noires Africaines et Caucasiennes. Sur les joues, le niveau de SDR9C7 était également plus faible chez les Albinos Africaines.

**Conclusion:** La masse des céramides totaux était similaire entre les femmes Noires Africaines et Caucasiennes. Cependant, des niveaux élevés de céramides totaux et excessivement élevés des oméga-O-acylcéramides sélectionnés, ont été observés chez les femmes Albinos Africaines. Les résultats obtenus chez les femmes Albinos Africaines étaient surprenants car ces participantes souffrent d’une altération de la fonction de la barrière cutanée. Néanmoins, les niveaux élevés d’oméga-O-acylcéramides peuvent en premier lieu contribuer à l’insuffisance de la barrière en ayant un impact direct sur le comportement de la phase lipidique du SC et/ou, deuxièmement, peuvent indiquer une fixation réduite des céramides à l’enveloppe lipidique des cornéocytes et une maturation réduite des cornéocytes pouvant aussi altérer la barrière. En outre, des différences
INTRODUCTION

The molecular anatomy together with the cellular and lipid architecture of stratum corneum (SC) is now well established for healthy skin barrier function [1]. Ethnic differences in SC structure, biochemical composition and function were recently reviewed with the aim of identifying the need for ethnically targeted skin care solutions [2–4]. However, there are limited data on ethnic differences in facial skin, especially in relation to the biochemistry of the SC.

We have recently published on the physiology of facial skin (photodamaged cheek and postauricular (PA) sites) among mainly Albino African, Black African and Caucasian women using a variety of bioinstrumental and biochemical approaches (Figure 1) as well as a unique colour-mapping approach examining 30 carefully selected sites on the faces of Black African, Chinese, Indian and Caucasian women for skin barrier function, skin hydration and skin surface pH [5–9]. These studies highlighted the complexity of barrier function, barrier repair and hydration of facial skin and that the darkly pigmented skin does not necessarily have a better barrier physiology or a lower skin surface pH but has a higher hydration status [5–9]. In contrast, Albino Africans had both a weaker skin barrier and much lower skin hydration and yet faster barrier recovery [5]. Black African women had more pyrrolidone carboxylic acid (PCA) levels on their cheek SC compared with Caucasian women, consistent with their better skin hydration status, but the Albino African women had a low skin hydration despite elevated PCA levels [8]. Moreover, cheek samples in all ethnic groups had a greater prevalence of more immature corneocyte envelopes (CEf) as measured by reduced Nile red/involucrin staining compared with the PA site, possibly indicating lowered lipid hydrophobicity of the corneocyte protein envelope (CPE), due to alterations in linoleoyl-omega-O-acylceramide processing. However, Albino Africans had dramatically reduced levels of mature corneocyte envelopes on both test sites together with corneocyte parakeratosis [8,13–18]. As a result, we were interested...
in the SC omega-O-acylceramides and associated lipid processing enzyme biochemistry in Albino African, Black African and Caucasian women living in South Africa.

The 12 main intercellular ceramides observed in human SC are depicted in Figure 2 [10]. These are classified according to the original nomenclature of Motta et al [11]. The omega-O-acylceramides (CER EOS, CER EOP, CER EOds and CER EOH) have their linoleoyl esterified fatty acid components modified, de-esterified and the resulting omega-hydroxy acylceramide is attached to the corneocyte protein envelope, e.g. CER OS, etc. [12]. The enzymes responsible for linoleoyl-omega-hydroxy acylceramide processing are shown in Figure 3 [10,13–18]. 12R-lipoxygenase (12R-LOX) oxygenates the linoleic acid attached to the omega-O-acylceramide species (CER EOX) [14,15], epidermal lipoxygenase-3 (e-LOX3) then isomerizes the resulting hydroperoxide [16], which is then dehydrogenated by short-chain dehydrogenase/reductase family 9C member 7 (SDR9C7) [17] or converted to a linoleoyl triol by (EPHX3) [18] and cleaved by an unknown esterase. The latter two products are then attached to the corneocyte envelope by transglutaminase 1 (TG1) [13,17]. The SDR9C7 product may also attach to the corneocyte protein envelope (CPE) through a reversible covalent binding [17].

Decreased ceramide levels and altered biochemistry together with lamellar ultrastructure are known to occur in seasonally dry, diseased and aged skin [19–29]. Equally, seasonal and dry skin-induced changes in CE maturation and associated covalently bound ceramide content are also described [30–33]. However, as far as we are aware there is a no study examining facial ceramide biochemistry on SC among different ethnic groups. Nevertheless, some report differences in SC lipid levels on the forearms among different ethnic groups, with reduced levels in African American women compared with Asian and Caucasian women living in the United States while others report on subjects of African and Asian descent together with Caucasian women living in Denmark [34–36]. The largest study of these studies identified a reduction in a highly selective class of ceramides (C18 phytosphingosine ceramides and the assumption was that all other ceramide species declined) in African American women [35]. Similar findings were observed by Sugino et al. [34]. The most recent study in Europe found no ethnic differences in the ceramide subtypes measured at that time, but there was a reduced total ceramide/cholesterol ratio in the African and an increase in this ratio in Asian study participants [36]. However, these analyses again were based on forearm SC samples, and we have recently shown no differences in the major 12 classes of ceramides on cheek samples from Black African and Caucasian women living in South Africa (the same subjects in this study) [37]. There are no studies examining SC ceramides in Albino African SC.

On photodamaged cheeks of Caucasians, we have previously reported decreased mass levels of 12R-LOX and eLOX3 but increased mass levels of TG1 and SDR9C7 measured by proteomics [38]. However, like 12R-LOX activity, transglutaminase activity was reduced despite its increased mass levels [39,40]. These lowered activities of these enzymes are likely contributing to the presence of immature corneocyte envelopes on their cheek samples compared with the PA site [8,41]. To date, there is no information on the levels and/or activities of these SC enzymes in Black African especially Albino African women who have the most dramatically lowered levels of mature corneocyte envelopes as far as we are aware [8].

Here, we report on the ceramidomic and proteomic analysis of SC samples taken from the cheek and PA areas of Albino African, Black African and Caucasian women living in South Africa. Proteomics data from the cheeks of Black African and Caucasian participants previously reported are included for completeness [37].
METHODS

Study population and methods

The study was a cross-sectional study and was approved from the School of Health Care Sciences Research and Ethics committee (SREC) together with the Medunsa Campus Research and Ethics Committee (MREC), South Africa, and was conducted in accordance with the Declaration of Helsinki Principles. Written, informed consent was obtained from all participants before enrolment as previously reported [5].

As part of a larger study, sixty healthy female volunteers, living in Pretoria, South Africa, participated in this observation [5]. There were three age- and count-matched groups (twenty subjects per group) of Albino African (40.3 ± 2.9 years old), Black African (38.2 ± 2.3 years old) and Caucasian women (44.6 ± 3.1 years old). The participants did not apply any dermatological or cosmetic products to their faces for 3 days before the start of the study. For the 3-day conditioning phase, the subjects cleansed the face with tepid water in the morning as well as in the afternoon. Before the evaluation, the skin was cleaned by gentle swabbing with a cotton pad soaked with distilled water of ambient temperature and allowed to dry for 20 min. Before any measurements and tape stripplings, the participants were acclimatized for 30 min in a room at a temperature of 21 ± 1°C and 35 ± 10% relative humidity [5].

A subset of 24 participants (eight per ethnic group) was selected for the lipidomics and one of 18 participants (six per ethnic group) for proteomics analysis. One standard D-Squame® disk (Cuderm Corporation, Dallas, US) with a diameter of 2.2 cm was taken on the cheek (3 cm below the outer corner of the eye) and the PA area for the lipidomic analysis [42], and nine were taken for the proteomic analysis [38]. The tapes were applied with 225 g cm⁻² of pressure with a pressure device (Cuderm Corporation, Dallas, US) for 5 s and then removed by a single stroke movement. To minimize variations, the procedure was conducted by the same technician for all volunteers, throughout the study. In order to enable the normalization of the samples, the SC protein content of the tape...
strippings was quantified by infrared absorption measurements at 850 nm with SquameScan™ 850A (Heiland electronic, Wetzlar, DE) [43].

The tape strippings of each participant were analyzed by a mass spectrometry–based shotgun lipidomics platform to define the facial ceramidome together with mass spectrometry–based proteomics to define the facial SC corneome, but in this case, only corneocyte envelope lipid processing enzymes are reported [38,42]. Omega-esterified hydroxy acylceramide fatty acids cannot be determined using the lipidomics method.

Ceramide measurements were normalized using the respective participant’s SC protein mass of the facial site of the measurement (check or PA). A linear mixed model was fit to the log-transformed normalized data (pmol/µg protein) with ethnic group, facial site and its interaction as fixed effects and participant as random effect. We tested the impact of facial site per ethnic group, and the difference between ethnic groups per facial site and pooled across both sites. Due to the small sample size and the exploratory nature of the research, we refrained from any adjustments for multiplicity.

RESULTS AND DISCUSSION
SC lipidomics and ceramidomics

The total ceramide levels of the Albino Africans were higher than those from normally pigmented Black African and Caucasian women with the differences being statistically significant (p < 0.05) (Figure 4). This is in marked contrast to the increased basal TEWL in the Albino African group as reported earlier [5] and points to abnormalities in ceramide composition, localization and/or utilization for corneocyte lipid envelope (CLE) attachment as we previously observed in our corneocyte maturation studies [8]. There were minor differences between the PA and the cheek sites, but these were not statistically different.

The findings between the Black African and Caucasian women are similar to that of Jungersted et al. [36] but completely different to that of Sugino et al. [34] and Muizzuddin et al. [35]. The differences to the latter two studies may be due to effects of the exposome on the skin and differences in test sites and ethnicity, but methodological differences may also be contributing. Although the study of Muizzuddin et al. was larger, it was conducted on forearm SC [35]. Aside from the anatomical location differences, they used a highly selective approach to measuring just C18 phytosphingosine ceramide bases. Phytosphingosine bases represent approximately 30–35% of ceramides [12] and the C18 sphingoid chain length is only 25% of these [44]. As a result, these findings are not representative of both the total SC ceramides as well as their subtypes levels. Nevertheless, the findings of elevated total ceramides in the Albino Africans cannot account for their impaired barrier function.

Comparing the different 12 types of ceramides between the Black African and Caucasian women, their profiles were largely similar on both testing sites, but on examining to the Albino African women, CER AS was elevated compared with the Caucasian women (p < 0.05). However, greater differences were observed for the long-chain omega-O-acylceramides. On the cheek compared with the Black African women, CER EOP and EOds were elevated, whereas CER EOS and EOH were elevated compared with the Caucasian women (p < 0.05). On the PA sites, only CER EOP when compared with the Black African women and EOds compared with both ethnicities reached significance (p < 0.05) (Figure 5).

Comparing within the cheek and PA sites for each ethnicity, differences were also observed with decreasing CER NP and AdS levels for the Caucasian and Black African participants together with decreasing CER NdS for the Black Africans (p < 0.05) (not shown). Although not statistically significant, numerical increases in the levels of all omega-O-acylceramides in the Albino Africans together with CER EOP and EOds in the Black Africans were observed on their cheeks. No differences in ceramide chain lengths were observed in any comparison.

The lack of statistical differences for the ceramide subtypes between the Black African and Caucasian women is similar to that of Jungersted et al. [36], even though the methodology at that time could only measure seven ceramide subtypes but the findings of elevated levels in the Albino Africans are novel. They did, however, find reduced ceramide/cholesterol levels in the participants of African descent in their study compared with the other ethnic groups. Nevertheless, although the ratios were
OMEGA-O-ACYLCERAMIDES AND PROCESSING ENZYMES

OMEGA-O-ACYLCERAMIDES AND PROCESSING ENZYMES

Raised in the Albino and Black Africans, they were not significantly different (not shown).

The importance of CER EOS levels for barrier function is well established [45]. However, if CER EOS is replaced with CER EOP, a disrupted barrier structure is apparent [46]. Indeed, CER EOP is reported as a weaker barrier component [47]. Moreover, too high a concentration of acyl ceramide levels is also associated with a weaker barrier [48,49]. Furthermore, the types of fatty acids esterified to the omega-hydroxy groups of such omega-O-acylceramides also dictate their behaviour [50,51]. However, this was beyond the scope of our analysis.

SC proteomics of corneocyte lipid envelope processing enzymes

The elevated omega-O-acylceramides observed in the Albino African women may indicate one of the reasons for additional corneocyte lipid scaffold and corneocyte maturation abnormality we observed in the Albino Africans previously, namely elevated levels of immature corneocytes [8]. Omega-O-acylceramides, especially the linoleate-containing ones, are used in a complex enzymatic process to attach ceramides to the corneocyte protein envelope (CPE) [13–18]. Reduced levels of 12R-LOX and eLOX3 were reported in photodamaged cheek SC previously from Caucasian women and 12R-LOX in Chinese subjects [38–40]. In this study, we observed that the mass levels of 12R-LOX and eLOX3 were equivocal in all three ethnic groups indicating a lipoxygenase-relevant corneocyte maturation insufficiency in all ethnicities (Table 1A-C). Not only can these differences possibly contribute to the presence of immature and fragile CEs on the photodamaged SC site from all three ethnicities that we reported previously [8], but the excessive amounts of fragile CEs in the Albino Africans are not solely related to these particular enzyme levels. SDR9C7 is also purported to be involved in the linoleoyl-omega-O-acylceramide transformation process, and its mass levels were equally reduced in the Albino African subjects compared with the other two ethnicities (Table 1C) [13–18]. A reduction of at least these three enzymes involved in the process of corneocyte lipid envelope (CLE) formation are probably contributing to the clear lipid scaffold disorder in the Albino African subjects. These changes could be related to the extra photodamage on these subjects [5]. Indeed, similar to our previous results [5], a thickening of the SC is known in subjects with Albinism [52]. Moreover, following UV irradiation, Meguro et al. [53] has shown elevated TEWL associated with reduced covalently bound ceramides while Takagi et al. [54] has shown increased levels of CER EOS and EOH together with CER AS and AP and also reductions in corneocyte covalently bound ceramide levels.

Takagi et al. [54] have shown decreased TG1 expression following UV irradiation, but Lee et al. have shown increased activity [55]. However, overall, 12-LOX expression is reported to be decreased [56]. This latter study did not consider 12R-LOX. Reductions in 12R-LOX are expected to be associated with reduced filaggrin processing [57], but at the phenotype levels the Albino Africans have greater quantities of NMF [8]. These increases are more likely to be associated with their excessive photodamage that is known to increase filaggrin levels [55]. Activity measurements of the enzymes need to be conducted to decipher these differences as well as the fatty acid composition of

**FIGURE 5** Distribution of the 12 major ceramide classes in cheek and PA sites among the three ethnic groups. a: Cheek site. b: PA site. *p < 0.05 Albino Africans vs Black Africans, **p < 0.05 Albino Africans vs Caucasians

**FIGURE 5** Distribution of the 12 major ceramide classes in cheek and PA sites among the three ethnic groups. a: Cheek site. b: PA site. *p < 0.05 Albino Africans vs Black Africans, **p < 0.05 Albino Africans vs Caucasians
TABLE 1  Fold changes in 12R-LOX, eLOX3, SDR9C7 and TG1 between (A) cheek and postauricular sites for each ethnicity; (B) differences among postauricular site for all ethnicities; and (C) differences among cheek site for all ethnicities. Data are mean ±SEM

| Protein names                                                                 | Gene names | Albino African | Black African | Caucasian |
|-------------------------------------------------------------------------------|------------|----------------|---------------|-----------|
| (A) Comparison cheek vs postauricular                                           |            |                |               |           |
| Arachidonate 12-lipoxygenase (12R-LOX)                                        | ALOX12B    | 0.72 n.s.      | <0.05         | 0.25 n.s. | 0.31 <0.001 |
| Hydroperoxide isomerase (eLOX3)                                               | ALOXE3     | 0.73 n.s.      | <0.05         | 0.56 n.s. | 1.02 n.s.   |
| Short-chain dehydrogenase/reductase family 9C member 7 (SDR9C7)               | SDR9C7     | 0.97 n.s.      | <0.05         | 0.97 <0.01| 1.52 <0.001 |
| Transglutaminase 1 (TG1)                                                      | TGM1       | 1.48 n.s.      | n.s.          | 1.93 n.s. | 1.47 <0.01  |

| Protein names                                                                 | Gene names | Albino African vs Black African | Albino African vs Caucasian | Black African vs Caucasian |
|-------------------------------------------------------------------------------|------------|---------------------------------|-----------------------------|---------------------------|
| (B) Comparison A vs B vs C, postauricular                                       |            |                                 |                             |                          |
| Arachidonate 12-lipoxygenase (12R-LOX)                                        | ALOX12B    | 0.30 <0.01 <0.01 n.s.           | 0.37 <0.05 <0.05 n.s.       | 1.24 n.s. n.s.           |
| Hydroperoxide isomerase (eLOX3)                                               | ALOXE3     | 0.68 n.s. n.s.                  | 1.00 n.s. n.s.              | 1.48 n.s. n.s.           |
| Short-chain dehydrogenase/reductase family 9C member 7 (SDR9C7)               | SDR9C7     | 0.58 n.s. n.s.                  | 0.85 n.s. n.s.              | 1.46 n.s. n.s.           |
| Transglutaminase 1 (TG1)                                                      | TGM1       | 1.14 n.s. n.s.                  | 1.05 n.s. n.s.              | 0.92 n.s. n.s.           |

| Protein names                                                                 | Gene names | Albino African vs Black African | Albino African vs Caucasian | Black African vs Caucasian |
|-------------------------------------------------------------------------------|------------|---------------------------------|-----------------------------|---------------------------|
| (C) Comparison A vs B vs C, cheek                                             |            |                                 |                             |                          |
| Arachidonate 12-lipoxygenase (12R-LOX)                                        | ALOX12B    | 0.86 n.s. n.s.                  | 0.86 n.s. n.s.              | 1.00 n.s. n.s.           |
| Hydroperoxide isomerase (eLOX3)                                               | ALOXE3     | 0.88 n.s. n.s.                  | 0.72 n.s. n.s.              | 0.81 n.s. n.s.           |
| Short-chain dehydrogenase/reductase family 9C member 7 (SDR9C7)              | SDR9C7     | 0.58 <0.05 n.s.                 | 0.55 <0.05 n.s.             | 0.94 n.s. n.s.           |
| Transglutaminase 1 (TG1)                                                      | TGM1       | 0.88 n.s. n.s.                  | 1.05 n.s. n.s.              | 1.20 n.s. n.s.           |
the omega-O-acylceramides that are found to be increased in these study participants.

One of the limitations of this study is its small sample size, but it is the first, to our knowledge, comparing the SC ceramidome among these three ethnic groups living in South Africa. More work is needed to study other facial locations especially as these are reported to be different physiologically and biochemically [5–9,41]. Moreover, intercellular lipid structure and lipid biophysical behaviour need to be determined. Nevertheless, to fully understand the impact of our findings, we need to determine the precise composition of the corneocyte lipid envelope (CLE), resolve the composition of esterified fatty acid component of the omega-O-acylceramides and measure the enzyme activities, rather than just their mass levels, of the relevant enzymes in the different ethnicities.

CONCLUSIONS

Using shotgun mass spectrometry lipidomics, we demonstrate that there is no ethnic difference in facial ceramide levels or ceramide subtypes between Black African and Caucasian women living in South Africa. However, elevated total ceramides and excessively elevated omega-O-acylceramides are apparent in the Albino African women. The former was unexpected as these participants have an impaired skin barrier function, but the latter can contribute to this deficiency by directly impacting SC lipid-phase behaviour for the worse or indicating a reduced lipid attachment and corneocyte maturation process. Indeed, differences in the mass levels of omega-O-acylceramide processing enzymes were observed for 12R-LOX and SDR9C7 for the Albino Africans. These differences are likely to account for the reduced corneocyte maturation in these subjects. This indicates that induction/activation of these enzymes is required to correct the corneocyte lipid scaffold disorder in these subjects and topical use of all omega-O-acylceramide subtypes may not be advisable for all skin types.

ACKNOWLEDGEMENTS

This study was financially supported by DSM Nutritional Products., Kaiseraugst, Switzerland. We would like to thank Lebogang Kgatuke, Marlize Lategan, Caroline Moletsi and Lee Ann Raaff of the Photobiology Laboratory, Sefako Makgatho Health Sciences University, Pretoria, South Africa, for their enthusiasm in conducting the study. Most importantly, we would like to thank all the subjects for their willing and valuable participation in this study. The proteomics was performed at Phylogene SA and lipidomics at Lipotype GmbH. AVR is a consultant to DSM.

CONFLICT OF INTEREST

There is no conflict of interests.

ORCID

Anthony V. Rawlings https://orcid.org/0000-0003-4740-6502

Rainer Voegeli https://orcid.org/0000-0002-3951-0329

REFERENCES

1. Rawlings AV. Molecular basis for stratum corneum maturation and moisturization. Br J Dermatol. 2014;171(Suppl 3):19–28.
2. Rawlings AV. Ethnic skin types: are there differences in skin structure and function? Int J Cosmet Sci. 2006;28(2):79–93.
3. Iwuala C, Taylor SC. Structural and functional differences in skin of colour. Clin Exp Dermatol. 2021;47(2):247–50.
4. Alexis AF, Woolery-Lloyd H, Williams K, Andriessen A, Desai S, Han G et al., Racial/ethnic variations in skin barrier: implications for skin care recommendations in skin of color. J Drugs Dermatol. 2021;20(9):932–8.
5. Voegeli R, Rawlings AV, Summers B. Facial skin pigmentation is not related to stratum corneum cohesion, basal transpidermal water loss, barrier integrity and barrier repair. Int J Cosmet Sci. 2015;37(2):241–52.
6. Voegeli R, Rawlings AV, Seroul P, Summers B. A novel continuous colour mapping approach for visualization of facial skin hydration and transpidermal water loss for four ethnic groups. Int J Cosmet Sci. 2015;37(6):595–605.
7. Raj N, Voegeli R, Rawlings AV, Gibbons S, Munday MR, Summers B et al., Variation in stratum corneum protein content as a function of anatomical site and ethnic group. Int J Cosmet Sci. 2016;38(3):224–31.
8. Raj N, Voegeli R, Rawlings AV, Summers B, Munday MR, Lane ME. Variation in the activities of late stage filagrin processing enzymes, calpain-1 and bleomycin hydrolase, together with pyrrolidone carboxylic acid levels, corneocyte phenotypes and plasmin activities in non-sun-exposed and sun-exposed facial stratum corneum of different ethnicities. Int J Cosmet Sci. 2016;38(6):567–75.
9. Voegeli R, Gierschendorf J, Summers B, Rawlings AV. Facial skin mapping: from single point bio-instrumental evaluation to continuous visualization of skin hydration, barrier function, skin surface pH, and sebum in different ethnic skin types. Int J Cosmet Sci. 2019;41(5):411–24.
10. Voegeli R, Rawlings AV. Moisturizing at a molecular level - The basis of Corneocare. IFSCC Magazine. 2021;24(4):187–202.
11. Motta S, Monti M, Sesana S, Caputo R, Carelli S, Ghidoni R. Ceramide composition of the psoriatic scale. Biochim Biophys Acta. 1993;1182(2):147–51.
12. Moore DJ, Rawlings AV. The chemistry, function and (patho)physiology of stratum corneum barrier ceramides. Int J Cosmet Sci. 2017;39(4):366–72.
13. Tyrrell VJ, Ali F, Boeglin WE, Andrews R, Burston J, Birchall JC et al., Lipidomic and transcriptional analysis of the linoleoyl-omega-hydroxyceramide biosynthetic pathway in human psoriatic lesions. J Lipid Res. 2021;62:100094.
14. Zheng Y, Yin H, Boeglin WE, Elias PM, Crumrine D, Beier DR et al., Lipoxigenases mediate the effect of essential fatty acid in skin barrier formation: a proposed role in releasing
omega-hydroxy-ceramide for construction of the corneocyte lipid envelope. J Biol Chem. 2011;286(27):24046–56.

15. Chiba T, Thomas CP, Calcutt MW, Boeglin WE, O'Donnell VB, Brash AR. The precise structures and stereochemistry of trihydroxy-linoleates esterified in human and porcine epidermis and their significance in skin barrier function: implication of an epoxide hydrolase in the transformations of linoleate. J Biol Chem. 2016;291(28):14540–54.

16. Krieg P, Rosenberger S, de Juanes S, Latzko S, Hou J, Dick A et al., Alox3 knockout mice reveal a function of epidermal lipoxygenase-3 as hepoxilin synthase and its pivotal role in barrier formation. J Invest Dermatol. 2013;133(1):172–80.

17. Takeichi T, Hrabavashti T, Miyasaka Y, Kawamoto A, Okuno Y, Taguchi S et al., SDR9C7 catalyzes critical dehydrogenation of acylceramides for skin barrier formation. J Clin Invest. 2020;130(2):890–903.

18. Edin ML, Yamanashi H, Boeglin WE, Graves JP, DeGraff LM, Lih FB et al., Epoxide hydrolase 3 (Ephx3) gene disruption reduces ceramide linoleate epoxide hydrosylation and impairs skin barrier function. J Biol Chem. 2021;296:100198.

19. Fulmer AW, Kramer GJ. Stratum corneum lipid abnormalities in surfactant-induced dry scaly skin. J Invest Dermatol. 1986;86(5):598–602.

20. Denda M, Koyama J, Horii J, Horii I, Takahashi M, Hara M et al., Age- and sex-dependent change in stratum corneum sphingolipids. Arch Dermatol Res. 1993;285(7):415–7.

21. Akimoto K, Yoshikawa N, Higaki Y, Kawashima M, Imokawa G. Quantitative analysis of stratum corneum lipids in xerosis and age-related changes in a senescent murine model. J Clin Invest. 1993;92(2):167–76.

22. Rawlings AV, Watkinson A, Rogers J, Mayo AM, Hope J, Scott IR. Abnormalities in stratum corneum structure, lipid composition and desmosome degradation in soap-induced winter xerosis. J Soc Cosmet Chem. 1994;45(4):203–20. https://library.scconline.org/v045n04/29

23. Ghadially R, Brown BE, Sequeira-Martín SM, Feingold KR, Elias PM. The aged epidermal permeability barrier. Structural, functional, and lipid biochemical abnormalities in humans and a senescent murine model. J Clin Invest. 1995;95(5):2281–90.

24. Conti A, Rogers J, Verdejo P, Harding CR, Rawlings AV. Seasonal influences on stratum corneum ceramide 1 fatty acids and the influence of topical essential fatty acids. Int J Cosmet Sci. 1996;18(1):1–12.

25. Rogers J, Harding C, Mayo A, Banks J, Rawlings A. Stratum corneum lipids: the effect of ageing and the seasons. Arch Dermatol Res. 1996;288(12):765–70.

26. Ishikawa J, Shimotoyodome Y, Ito S, Miyachi Y, Fujimura T, Kitahara T et al., Variations in the ceramide profile in different seasons and regions of the body contribute to stratum corneum functions. Arch Dermatol Res. 2013;305(2):151–62.

27. Ishikawa J, Yoshihara H, Ito S, Naoe A, Fujimura T, Kitahara T et al., Dry skin in the winter is related to the ceramide profile in the stratum corneum and can be improved by treatment with a Eucalyptus extract. J Cosmet Dermatol. 2013;12(1):3–11.

28. Wei KS, Stella C, Wehmeyer KR, Christman J, Altemeier A, Spruell R et al., Effects of season stratum corneum barrier function and skin biomarkers. J Cosmet Sci. 2016;67(3):185–203.

29. Vyumuvohe R, Michael-Jubeli R, Verzeaux L, Boudier D, Le Guillou M, Bordes S et al., Lipid organization in xerosis: the key of the problem? Int J Cosmet Sci. 2018;40(6):549–54.

30. Kikuchi K, Tagami H, Japanese Cosmetic Scientist Task Force for Skin Care of Atopic D. Noninvasive biophysical assessments of the efficacy of a moisturizing cosmetic cream base for patients with atopic dermatitis during different seasons. Br J Dermatol. 2008;158(5):969–78.

31. Akutsu N, Ooguri M, Onodera T, Kobayashi Y, Katsuyama M, Kunizawa N et al., Functional characteristics of the skin surface of children approaching puberty: age and seasonal influences. Acta Derm Venereol. 2009;89(1):21–7.

32. Harding CR, Long S, Richardson J, Rogers J, Zhang Z, Bush A et al., The cornified cell envelope: an important marker of stratum corneum maturation in healthy and dry skin. Int J Cosmet Sci. 2003;25(4):157–67.

33. Fujiwara A, Morifiji M, Kitade M, Kawahata K, Fukasawa T, Yamaji T et al., Age-related and seasonal changes in covalently bound ceramide content in forearm stratum corneum of Japanese subjects: determination of molecular species of ceramides. Arch Dermatol Res. 2018;310(9):729–35.

34. Sugino K, Imokawa G, Maibach HI. Ethnic difference of stratum corneum lipid in relation to stratum corneum function. J Invest Dermatol. 1993;100:587.

35. Muizuddin N, Hellemans L, Van Overloop L, Corstjens H, Declercq L, Maes D. Structural and functional differences in barrier properties of African American, Caucasian and East Asian skin. J Dermatol Sci. 2010;59(2):123–8.

36. Jungersted JM, Hogh JK, Hellgren LI, Jemec GB, Agner T. Ethnicity and stratum corneum ceramides. Br J Dermatol. 2010;163(6):1169–73.

37. Rawlings AV, Lane ME, Summers B, Voegeli R. Response to ‘Structural and functional differences in skin of colour’. Clin Exp Dermatol. 2021;47:247-50.

38. Voegeli R, Monneuse JM, Schoop R, Summers B, Rawlings AV. The effect of photodamage on the female Caucasian facial stratum corneum corneome using mass spectrometry-based proteomics. Int J Cosmet Sci. 2017;39(6):637–52.

39. Guneri D, Voegeli R, Munday MR, Lane ME, Rawlings AV. 12R-lipoxygenase activity is reduced in photodamaged facial stratum corneum. A novel activity assay indicates a key function in corneocyte maturation. Int J Cosmet Sci. 2019;41(3):274–80.

40. Guneri D, Voegeli R, Doppler S, Zhang C, Bankousli AL, Munday MR et al., The importance of 12R-lipoxygenase and transglutaminase activities in the hydration-dependent ex vivo maturation of corneocyte envelopes. Int J Cosmet Sci. 2019;41(6):563–78.

41. Guneri D, Voegeli R, Gurgul SJ, Munday MR, Lane ME, Rawlings AV. A new approach to assess the effect of photodamage on corneocyte envelope maturation using combined hydrophobicity and mechanical fragility assays. Int J Cosmet Sci. 2018;40(3):207–16.

42. Sadowski T, Klose C, Gerl MJ, Wojcik-Maciejewicz A, Herzog R, Simons K et al., Large-scale human skin lipidomics by quantitative, high-throughput shotgun mass spectrometry. Sci Rep. 2017;7:43761.

43. Voegeli R, Heiland J, Doppler S, Rawlings AV, Schreier T. Efficient and simple quantification of stratum corneum proteins on tape strippings by infrared densitometry. Skin Res Technol. 2007;13(3):242–51.

44. Wertz PW, Mietheke MC, Long SA, Strauss JS, Downing DT. The composition of the ceramides from human stratum corneum and from comedones. J Invest Dermatol. 1985;84(5):410–2.
45. Bouwstra JA, Gooris GS, Dubbelaar FE, Weerheim AM, Ijzerman AP, Ponec M. Role of ceramide 1 in the molecular organization of the stratum corneum lipids. J Lipid Res. 1998;39(1):186–96.
46. de Jager M, Gooris G, Ponec M, Bouwstra J. Acylceramide head group architecture affects lipid organization in synthetic ceramide mixtures. J Invest Dermatol. 2004;123(5):911–6.
47. Opalka L, Kovacik A, Pullmannova P, Maixner J, Vavrova K. Effects of omega-O-acylcereamide structures and concentrations in healthy and diseased skin barrier lipid membrane models. J Lipid Res. 2020;61(2):219–28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6997605/
48. Opalka L, Kovacik A, Maixner J, Vavrova K. Omega-O-acylcereamides in skin lipid membranes: effects of concentration, sphingoid base, and model complexity on microstructure and permeability. Langmuir. 2016;32(48):12894–904. https://pubs.acs.org/doi/pdf/10.1021/acs.langmuir.6b03082
49. Uche LE, Gooris GS, Bouwstra JA, Beddoes CM. High concentration of the ester-linked omega-hydroxy ceramide increases the permeability in skin lipid model membranes. Biochim Biophys Acta Biomembr. 2021;1863(1):183487.
50. Bouwstra JA, Gooris GS, Dubbelaar FE, Ponec M. Phase behavior of stratum corneum lipid mixtures based on human ceramides: the role of natural and synthetic ceramide 1. J Invest Dermatol. 2002;118(4):606–17.
51. de Sousa ND, Gooris G, Bouwstra J. Effect of the omega-acylcereamides on the lipid organization of stratum corneum model membranes evaluated by X-ray diffraction and FTIR studies (Part I). Chem Phys Lipids. 2011;164(3):184–95.
52. Semkin VI, Mikhailov IN. Skin changes in albinism in persons of the Negroid race light- and electron-microscopy studies. Arkh Patol. 1984;46(6):52–6.
53. Meguro S, Arai Y, Masukawa Y, Uie K, Tokimitsu I. Relationship between covalently bound ceramides and transepidermal water loss (TEWL). Arch Dermatol Res. 2000;292(9):463–8.
54. Takagi Y, Nakagawa H, Kondo H, Takema Y, Imokawa G. Decreased levels of covalently bound ceramide are associated with ultraviolet B-induced perturbation of the skin barrier. J Invest Dermatol. 2004;123(6):1102–9.
55. Lee DS, Quan G, Choi JY, Kim SY, Lee SC. Chronic ultraviolet radiation modulates epidermal differentiation as it up-regulates transglutaminase 1 and its substrates. Photodermatol Photoimmunol Photomed. 2005;21(1):45–52.
56. Yoo H, Jeon B, Jeon MS, Lee H, Kim TY. Reciprocal regulation of 12- and 15-lipoxygenases by UV-irradiation in human keratinocytes. FEBS Lett. 2008;582(21–22):3249–53.
57. Epp N, Furstenberger G, Muller K, de Juanes S, Leitges M, Hauser I et al., 12R-lipoxygenase deficiency disrupts epidermal barrier function. J Cell Biol. 2007;177(1):173–82. https://rupress.org/jcb/article/177/1/173/34612/12R-lipoxygenase-deficiency-disrupts-epidermal

How to cite this article: A.V. Rawlings, R. Schoop, C. Klose, J.-M. Monneuse, B. Summers, R. Voegeli, Changes in levels of omega-O-acylcereamides and related processing enzymes of sun-exposed and sun-protected facial stratum corneum in differently pigmented ethnic groups. Int. J. Cosmet. Sci. 44, 166–176 (2022). doi:10.1111/ics.12765