doi:10.36849/JDD.7560

 ORIGINAL ARTICLE Journal of Drugs in Dermatology

Promoting a Healthy Skin Barrier Using Skin Care in People With Mature Skin Xerosis

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ABSTRACT

Introduction: Most people are living into their sixties and beyond. Fundamental changes in chronologically aged skin have significant and widespread dermatological implications. This review discusses aging-associated alterations in epidermal function leading to xerosis and related pruritus and the benefits of maintaining or restoring a healthy skin barrier using skincare, specifically ceramide-containing skincare.

Methods: A panel of 7 dermatologists convened for a meeting to review aspects of xerosis in mature skin, skin barrier changes, and nuances in the treatment and maintenance of mature skin using gentle cleansers and moisturizers.

From the selected literature, 13 statements were drafted. During the meeting, the draft statements underwent the panel's evaluation at a workshop, followed by a plenary discussion adopting 5 statements using evidence from the literature coupled with the panel's opinions and experiences.

Results: The exact etiology of xerosis is not entirely understood and likely depends on several genetic and environmental mechanisms. Aging-associated changes in epidermal function include a marked reduction in total lipids in the stratum corneum relative to young skin due to reduced epidermal lipid synthesis. In aging skin, xerosis is significantly associated with pruritus. Studies have shown that lipid-containing skin care, such as a gentle ceramide-containing cleanser and moisturizer, promotes a healthy barrier reducing xerosis and pruritus in individuals with mature skin.

Conclusions: The development of xerosis in mature skin involves several genetic and environmental mechanisms. Skincare, including gentle cleansers and moisturizers, has reduced xerosis and pruritus in mature skin individuals.

J Drugs Dermatol. 2024;23(1):1253-1259. doi:10.36849/JDD.7560

INTRODUCTION

With advances in medical biology and healthcare technology over recent decades, human lifespans are increasing worldwide, resulting in a proportionate increase in the aged population.[1,2] Today, most people can expect to live into their sixties and beyond.[1]

Fundamental dermal and epidermal changes in chronologically aged skin have significant and widespread dermatological implications.[3,4] As early as 50, the frequency of aging-associated skin conditions increases, in parallel with epidermal dysfunction such as compromised permeability homeostasis, reduced stratum corneum (SC) hydration, and elevated skin surface pH.[5-8] Studies have shown that epidermal dysfunction predisposes to xerosis, pruritus, atopic dermatitis, and contact dermatitis.[9,10] Skin conditions affect up to 70% of matured individuals, with xerosis and pruritus as the most common skin disorders.[5] The etiology of xerosis in mature skin is not fully understood but likely involves genetic and environmental factors leading to changes in the keratinization process and lipid content in the SC.

TABLE 1.

Intrinsic Factors for Xerosis	
Category	**Examples**
Dermatological diseases	Atopic dermatitis, allergic contact eczema, irritant contact dermatitis, ichthyoses. Fungal and bacterial infections, pediculosis, scabies. Cutaneous lymphoma (eg, mycosis fungoides).
Internal diseases	Chronic kidney disease, diabetes mellitus, hepatopathies (eg, primary biliary cholangitis, primary sclerotic cholangitis, drug-induced cholestasis, extrahepatic cholestasis), hyperparathyroidism, hypothyroidism, and malabsorption.) Chronic inflammatory bowel disease (gluten-sensitive enteropathy), rheumatic disease. Diarrheal diseases, helminths, hepatitis B and C virus, HIV. Menopause, andropause, pregnancy. Myeloproliferative disorders (eg, polycythemia vera, essential thrombocytosis), Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma.
Psychiatric disorders	Obsessive skin cleansing/washing, anorexia, alcohol, and drug abuse.
Dietary disorders	Insufficient fluid intake, excessive perspiration, Hypovitaminosis (vitamin D, vitamin A, niacin deficiency), zinc or iron deficiency.
Medication-related	Retinoids, topical corticosteroids (prolonged use), diuretics, lipid-lowering agents, calcium antagonists, beta-blockers, antirheumatic drugs, contraceptives/antiandrogens, cytostatic agents, radiation dermatitis (following radiation therapy), and possibly immunomodulators.

This review discusses aging-associated alterations in epidermal function leading to xerosis and related pruritus and maintaining or restoring a healthy skin barrier using skincare, specifically ceramides-containing (CER-containing) skincare.

MATERIALS AND METHODS

The project used a modified Delphi process comprising face-to-face discussions followed up online.[11,12]

Literature Review

The structured literature searches (01-August 2022) on PubMed and Google Scholar, as a secondary source, of the English-language literature (2010 – July 30, 2022) were performed by a dermatologist and a physician/scientist (searchers). Additionally, the searchers manually reviewed the selected literature for additional resources. The searches prioritized studies on mature skin xerosis, SC barrier function, and skincare benefits using cleansers and moisturizers. The searches for mature* skin included senile xerosis, xerosis in aging skin, and xerosis in the elderly, and explored present clinical guidelines, treatment options, and therapeutic approaches addressing mature skin xerosis using the following terms:

Mature skin xerosis AND skin barrier physiology OR function OR dysfunction OR depletion of stratum corneum lipids OR atopic dermatitis.*

Mature skin xerosis AND skincare OR cleansers OR moisturizers OR emollients OR ceramides OR ceramides containing skincare OR efficacy OR safety OR tolerability.*

The searches yielded 42 papers deemed clinically relevant to mature skin xerosis and skin care to promote a healthy skin barrier and potential mitigation of xerosis using over-the-counter (OTC) skincare and CER-containing cleansers and moisturizers.

Role of the Panel

The panel of 7 dermatologists (panel) convened for a meeting (September 3, 2022) to review unique aspects of xerosis in mature skin and the skin barrier changes and to discuss nuances in the treatment and maintenance of mature skin using gentle cleansers and moisturizers.

From the selected literature, the searches (AA and TE) and MG drafted 13 statements. During the meeting, the draft statements underwent the panel's evaluation at a workshop, followed by a plenary discussion adopting 5 statements using evidence from the literature coupled with the panel's opinions and experiences. The second step consisted of a post-meeting review by individual advisors of the manuscript.

Statement 1: *The exact etiology of xerosis is not entirely understood and likely depends on several genetic and environmental mechanisms.*

A healthy skin barrier function depends on the complex interplay among SC pH, desquamation rate, and the appropriate ratio of intrinsic lipids.[13,14] The lipids comprise approximately 20% of the volume of the healthy SC and are composed of CERs (40-50%), cholesterols (20-33%), and free fatty acids (7-13%).[13,14] Further lipids include cholesterol-3-sulfate (0-7%) and cholesteryl esters (0-20%).[13,14] The slightly acidic surface of healthy skin is required to maintain the SC barrier, inhibiting the growth of pathogenic microorganisms.[13] Skin acidification plays a vital role in SC barrier health and activates enzymes in the extracellular processing of SC lipids.[13] The SC pH influences barrier homeostasis, integrity, cohesion, and antimicrobial defense mechanisms.[13,15,16]

Occupational screening studies (n = 48,380) showed that approximately every third employee (29.4 %) between the ages of 16 and 70 years is affected by xerosis.[14] The prevalence of xerosis increases in mature skin at 55.6 % at a mean age of 75.1 years.[14] Xerosis is characterized by decreased quantity and quality of lipids and/or moisturizing factors and is generally diagnosed on clinical presentation.[9,10,13,14-16] It is essential to distinguish between constitutional xerosis and xerosis due to dermatoses such as atopic dermatitis (AD), psoriasis, or ichthyosis and xerosis triggered by exogenous factors.[9,10,13,14] Xerosis may be due to systemic diseases such as diabetes, renal and biliary diseases, infections, and hormonal changes, or triggered by medication (Table 1).[13,14]

Statement 2: *Xerosis in older adults is multifactorial and may include: intrinsic age-related changes, use of diuretics and similar medications, systemic conditions, hypothyroidism, and overuse of heaters or air conditioners.*

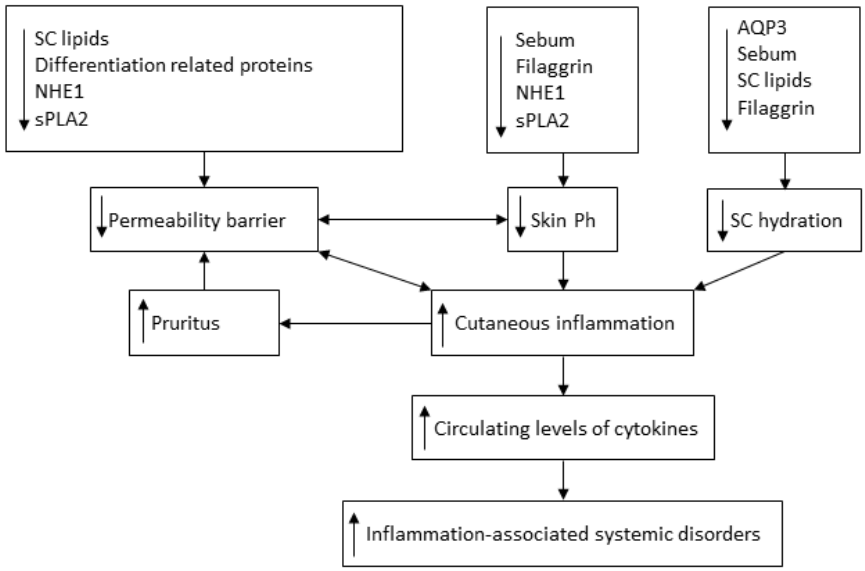
Xerosis is a common skin condition in matured skin characterized by xerosis, and pruritic, excoriated, and exfoliated skin.[17-24] The exact etiology of mature skin xerosis is not understood and likely depends on several genetic and environmental mechanisms.[17-19]

Intrinsic aging is a fundamentally unsustainable process that affects the entire body, including sun-protected sites.[16] Intrinsic skin aging is primarily characterized by atrophy, as the number of cells that make up the skin and the amount and quality of the extracellular matrix decrease.[16] Further, the amount and the conduction of blood vessels and nerves that supply the skin deteriorate or decrease.[16] Xerosis in older adults is multifactorial: intrinsic changes in keratinization and lipid content, use of diuretics and similar medications, systemic conditions, hypothyroidism, medications, and overuse of heaters or air conditioners can all contribute to the disease.[19-24] Skin is a target of reactive oxygen species (ROS) and oxidative stress from both extrinsic (solar radiation) and intrinsic sources (oxidative metabolism).[17] Chronic exposure to extrinsic factors, such as ultraviolet radiation, air pollution, smoking, alcohol consumption, or malnutrition, induces an age-associated skin microenvironment, including inflammation and reduced collagen production.[17,18]

Changes in the keratinization process and lipid content in the SC probably represent the main factors in mature skin xerosis.[19-24] From about 50 years of age, epidermal dysfunction may occur, such as compromised permeability homeostasis, SC hydration reduction, and skin surface pH elevation.[19-23] The reduction of epidermal growth factors, keratinocyte proliferation, and increased keratinocyte apoptosis has been shown to lead to a thinner epidermis and SC.[7] Further aging-related skin changes included a decline in the levels of structural proteins for the epidermal permeability barrier, including filaggrin, loricrin, and other late cornified envelope proteins.[8] In mature skin, the barrier function weakens, leading to increased transepidermal water loss (TEWL) and decreased protective functions (Figure 1).[20-23]

The speed of the aging process depends mainly on individual genetic factors.[16] Women develop these signs earlier due to a decrease in the protective effects of estrogen hormones during menopause.[14-16]

FIGURE 1. Mature-skin-associated stratum corneum function changes.



SC, stratum corneum; NHE1, sodium-hydrogen antiporter 1; *PLA2*, phospholipase A2; *AQP-3*, aquaporin.
Adapted with permission from Wang et al.[16]

Statement 3: *Aging-associated changes in epidermal function include a 30% reduction in total lipids in the stratum corneum relative to young skin due to reduced epidermal lipid synthesis.*

Ceramides, cholesterol, and free fatty acids are essential constituents of the SC.[14,16] They form a highly ordered matrix called the lipid lamellae and fill the space between the corneocytes.[14,16] The composition and structure of the lipid lamellae are critically important to the permeability barrier function of the skin and form an effective waterproof barrier.[14,16] The composition of SC lipids is influenced by age, genetic disposition, time of year, diet, hormone-mediated sebum production, and medication such as cholesterol-lowering agents.[14,16] Reductions in SC lipid content may be due to the delayed barrier recovery in mature skin.[6,16] In aged skin, the number and function of sebaceous glands reduce, leading to xerosis.[20-23] In mature skin, along with the gradual degeneration of the innervation of the skin and the decrease in the number of sweat glands, the heat balance and cold tolerance of aging individuals deteriorates.[20-23]

Studies have shown that baseline TEWL rates on several body sites are lower in matured vs young skin.[6] The demonstrated TEWL rates on the décolleté region correlated positively with age, but TEWL rates on the neck, forearm, and hand were comparable between young and aged women.[6]

Studies from the mid-nineties have shown that the aged SC displays a >30% reduction in total lipid content compared with young SC due to reduced epidermal lipid synthesis, particularly in cholesterol synthesis, both under basal conditions and after barrier disruption.[25,26] Studies have further shown that epidermal dysfunction predisposes to various cutaneous abnormalities, including atopic dermatitis, contact dermatitis, pruritus, and xerosis.[9,10,20-23,27]

In support of evidence that reduced lipid levels contribute to aging-associated dysfunction in the skin barrier, topical applications of SC physiologic lipid mixtures such as ceramides may improve epidermal permeability barrier function.[14]

Statement 4: *In older people, xerosis is significantly associated with pruritus.*

Pruritus is common in matured skin and has been attributed partially to a decline in normal physiology due to advanced aging.[24,27-31] Pruritus significantly impacts the quality of life and is reported by patients to be as bothering as skin pain or even worse.[31] Changes in mature skin structure and its ability to regenerate, along with cumulative effects of the environment, diminish the SC barrier function and hydration.[21,24] These changes make the elderly more susceptible to the entry of irritants and allergens through the skin, leading to inflammation and pruritus.[24]

A cross-sectional study including 756 patients aged 65 and older reported a prevalence of xerosis of 56%.[19] Of these patients, 9% had moderate to severe xerosis associated with a significant disease burden, including pruritus and feelings of very dry or unbearably dry skin.[19] Another cross-sectional study of a population of 11,730 showed that the prevalence of chronic pruritus was 20.3% in people between 60 and 70 years.[30] The large study demonstrated significant xerosis-associated risk factors for pruritus, including older age, female sex, atopic dermatitis, or concomitant treatment that may be associated with xerosis.[30] Additional causes of pruritus may include various comorbidities, such as renal failure, cholestasis, systemic infections, diabetes mellitus, liver failure, malignancies, or certain hematological disorders.[28-30]

Xerosis is often associated with pruritus, mainly involving the extremities, and is more prominent at low temperature and humidity conditions.[19,30] Scratching can lead to secondary infections, ulcerations, and chronic wounds.[24,27-29]

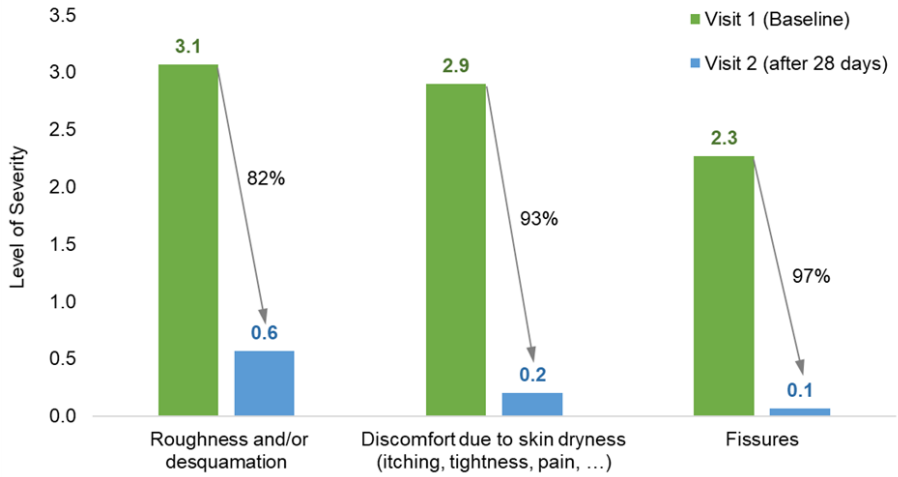
SC lipids containing moisturizers such as ceramides combat xerosis and may reduce pruritus.[13] Components of topical products such as polidocanol, menthoxypropanediol (derivate of menthol and an agonist of the TRPM8 receptor), or N-palmitoylethanolamide, a fatty acid, may have antipruritic effects.[32-35] A double-blind, vehicle-controlled study including patients with xerosis and pruritus (N=70) showed that those topically treated for 6 weeks with menthoxypropanediol combined with cyclohexane carboxamide reported a significantly more robust and longer-lasting antipruritic effect than those receiving the placebo.[34] A study on topically applied N-palmitoylethanolamide demonstrated antipruritic effects in patients with xerosis.[35]

Treating pruritus with systemic medication is outside the scope of this review and is not discussed here.

Statement 5: *Moisturizers containing urea, ceramides, and lactate have shown benefits in promoting a healthy skin barrier structure and function in older people with xerosis.*

Skincare using gentle cleansers and moisturizers can promote a healthy skin barrier and is crucial for mature skin to reduce TEWL and minimize exposure to irritants and allergens.[14,36-42] Acidification of the SC may improve epidermal structure and function in chronologically aged humans. In aged subjects, using a moisturizer at pH 4.0 for 29 days improved SC hydration and lamellar bilayer structure, along with increased resistance to challenges from topical sodium dodecyl sulfate.[36] Following acute SC barrier disruption in aged subjects, a topical pH 4.0 moisturizer improved SC barrier recovery faster while significantly improving SC integrity after 28-day treatments compared with a pH 5.8 moisturizer.[37]

FIGURE 2. Physician evaluation of roughness/desquamation, discomfort, and fissures.

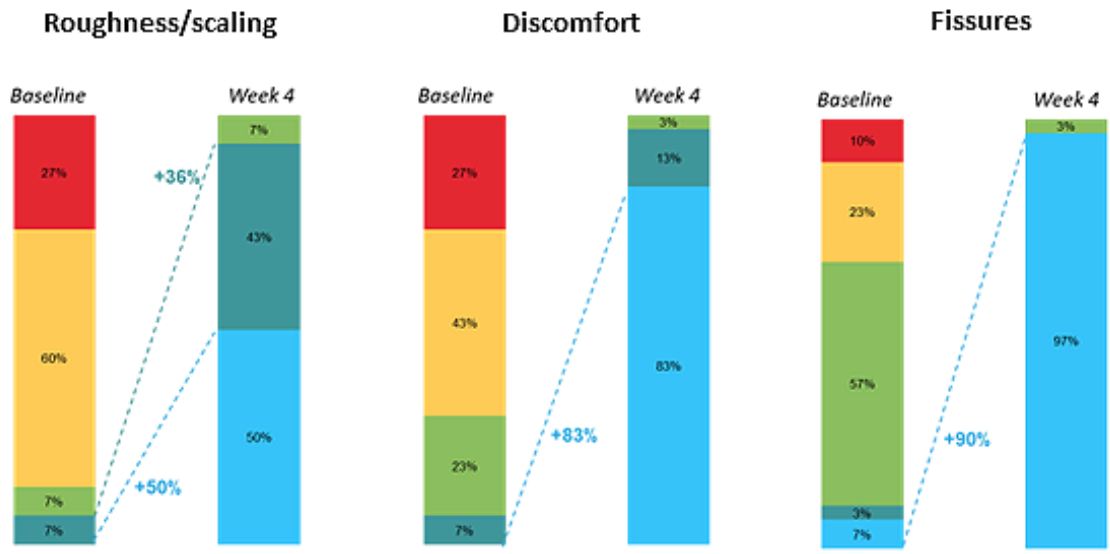


N = 30 men (63%) and women (37%) age ≥ 70 years with xerosis and/or scaly skin.
Treatment: ceramides-containing cleanser and moisturizer at least once per day.

Danby and colleagues included 2 cohorts (N=21) of patients with senile xerosis 60 years and older and one test group.[38] The comparative 28 days study treated group 1 with the test emollient (Urea 5%, ceramide NP) on the forearm vs no treatment on the other arm. Group 2 received the test emollient on the forearm vs the control emollient (soft white paraffin, liquid paraffin) on the other arm. Effects on the skin barrier were evaluated by measuring skin barrier function, hydration, and skin surface pH, and by analyzing Fourier transform infrared spectra before and after treatment. Group 3 (6 young adults) applied the test emollient once and, with a tape-stripping technique, the effect on the skin barrier's molecular structure was measured. The test emollient showed significantly better and longer-lasting results and addressed the pathological features of xerotic mature skin, supporting its use as first-line therapy for xerotic skin conditions in this population.[38]

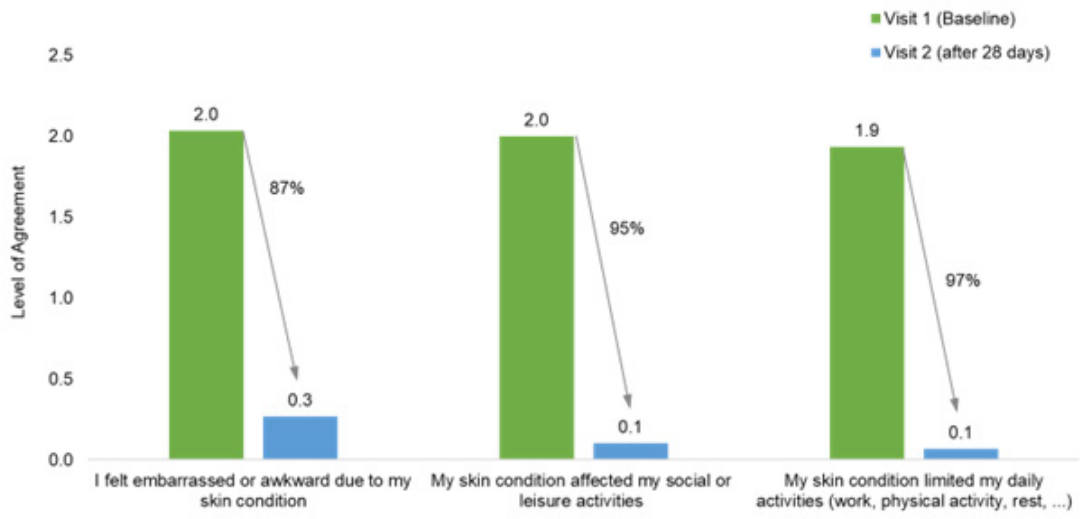
Another study included 20 patients with senile xerosis aged 62 to 82 years who received 10% urea cream for 14 days. Pruritus (Visual Analog Scale) scores and dermoscopy were used for evaluation. At the end of the study, all scores showed a significant improvement (P<0.05). The Pearson's test showed a correlation

FIGURE 3. Patient evaluation of roughness/desquamation, discomfort, and fissures.



5-point scale: 4 (intense), 3, 2, 1, 0 (none)
N = 30 men (63%) and women (37%) age ≥ 70 years with xerosis and/or scaly skin.
Treatment: ceramides-containing cleanser and moisturizer at least once per day.

FIGURE 4. Improvement in patient quality of life after four weeks of treatment.



Average calculated on the scale of level of severity: Strongly disagree (0) - Strongly agree (3)

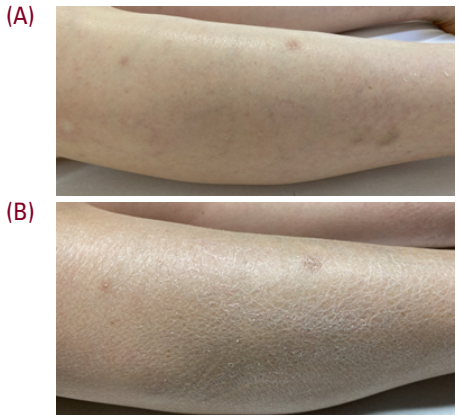
between clinical and dermoscopy evaluation both at baseline, day 7, and day 14 ($r = 0.73$, $r = 0.76$, $r = 0.71$, respectively).[39]

A randomized, investigator-blinded, split-leg study treated xerosis in 53 women using a ceramides-containing cleanser and moisturizer for 4 weeks. Skin hydration, visible signs of xerosis, subject sensory discomfort, ceramides, cholesterol, and free fatty acid levels in the SC were evaluated. The skincare regime improved skin water content through corneometry, a reduction in the subject's perceived sensory discomfort, and the dermatologist investigator-assessed resolution of the signs of dry skin. Improvement continued for 48 hours after moisturizer withdrawal.[40]

Another study in matured skin subjects showed that topical applications of a moisturizer containing SC lipids improved SC hydration and reduced skin surface pH and circulating levels of proinflammatory cytokines.[41] A further investigator-blinded randomized clinical trial of 52 patients with moderate-to-severe xerosis treated group 1 ($n = 39$) with a mild cleanser and moisturizer twice daily for 2 weeks and group 2 ($n = 13$) with a gentle cleanser without moisturizer. Total Clinical Score (TCS; erythema, scale, and fissures), Visual Dryness Score (VDS), and subjective itch-related quality of life (ItchyQoL) were assessed at week 2. Group 1 showed more improvement in TCS and VDS compared with group 2. ItchyQoL (symptoms, functioning, and emotions) showed significantly greater improvements for group 1 compared with group 2.[42]

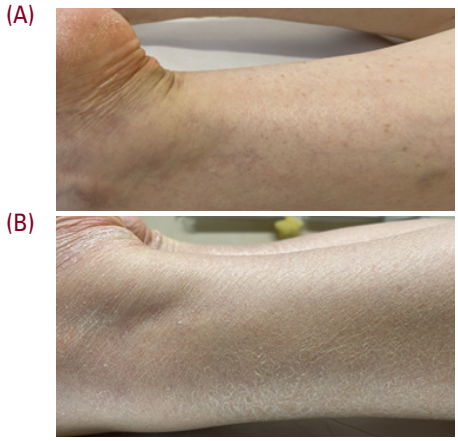
In an unpublished study by Filippi and colleagues, 30 men and women over 70 years of age with xerosis, applied a ceramides-containing cleanser and a ceramides-containing moisturizing

FIGURE 5. Case 1 (A) before (B) after 28 days of skincare.



Case courtesy of Filippi et al.

FIGURE 6. Case 2 (A) before (B) after 28 days of skincare.



Case courtesy of Filippi et al.

cream at least once daily for 4 weeks. Physician and patient evaluation (5-point scale) were at baseline and after 28 days, scoring dryness, roughness and/or desquamation, discomfort, fissures, and cracks. Patients scored the quality of life (4-point scale) aspects at baseline and 4 weeks. The mean physician scores at week 4 decreased for roughness and desquamation from 3.1 to 0.6 (-82%), discomfort due to xerosis from 2.9 to 0.2 (-93%), and fissures from 2.3 to 0.1 (-97%) (Figure 2).

The patients reported that xerosis improved for all parameters (Figure 3). In addition, patient quality of life (QoL) improved, with 77% no longer feeling embarrassed due to their condition, and ≥ 90% not feeling that their condition affected their social/leisure activities or daily activities (Figure 4). Two typical patients are shown to illustrate these results (Figures 5 and 6).

Limitations

The exact etiology of mature skin xerosis is not understood and requires more research. The small number of studies specifically addressing skincare in mature skin did not allow for rating the evidence and recommendations on skincare preferences.

CONCLUSION

Aging-associated alterations in epidermal function lead to xerosis and related pruritus. The development of xerosis in mature skin involves several genetic and environmental mechanisms. Daily use of skincare offers the benefits of maintaining or restoring a healthy skin barrier. Skincare, including gentle cleansers and moisturizers, specifically CER-containing products, have reduced xerosis and pruritus in mature skin individuals.

DISCLOSURES

The authors disclosed receipt of an unrestricted educational grant from CeraVe International for support with the research of this work. The authors also received consultancy fees for their work on this project.

ACKNOWLEDGMENT

All authors participated in the project's steps, reviewed the manuscript, and agreed with the content. All authors read and approved the final version of the manuscript.

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