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Diagnosis and treatment of xerosis cutis – a position paper

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Summary

Background and rationale: Xerosis cutis (also referred to as xeroderma, dry skin, asteatosis) affects more than 10 million individuals in Germany. It is among the most common dermatological diagnoses and a cardinal symptom of many dermatological, internal and neurological diseases. Even though it has been established that basic skin care plays a significant role in the management of patients with xerosis cutis, there are as yet no evidence-based algorithms for diagnosis and treatment.

Objective: The present position paper provides physicians across all specialties with a practical, symptom-based approach to the prevention, diagnosis and treatment of xerosis cutis.

Methods: Within a structured decision-making process, a panel of experienced dermatologists first defined questions relevant to everyday clinical practice, which were then addressed by a systematic review of the literature. Based on the evidence available as well as expert consensus, diagnostic and treatment algorithms were subsequently developed and agreed upon.

Results: Xerosis cutis is generally diagnosed on clinical grounds. Possible trigger factors must be avoided, and comorbidities should be adequately and specifically treated. Suitable skin care products should be chosen with a view to improving skin hydration and restoring its barrier function. They should therefore contain both

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rehydrating and lipid-replenishing components. The "drier" the skin appears, the greater the lipid content should be (preferably using water-in-oil formulations). The choice of ingredients is based on a patient's individual symptoms, such as scaling (e.g., urea), fissures/rhagades (e.g., urea or dexpanthenol), erythema (e.g., licochalcone A) and pruritus (e.g., polidocanol). Other factors to be considered include the site affected and patient age. Ingredients or rather combinations thereof for which there is good clinical evidence should be preferentially used. The best evidence by far is available for urea, whose efficacy in the treatment of xerosis is further enhanced by combining it with other natural moisturizing components and ceramides. The "xerosimeter" is a tool developed in an effort to facilitate patient management and for training purposes. It not only includes practical tools for diagnosis and follow-up but also a classification of ingredients and a structured treatment algorithm.

Conclusion: The structured symptom- and evidence-based approach proposed herein contains a road map for diagnosis and treatment of xerosis cutis. It aims to raise awareness in terms of prevention and early treatment of this condition and may thus improve quality of life and prevent potential sequelae.

1. Background and rationale

D. Wilsmann-Theis, A. Körber

Definition of xerosis cutis as skin deficient in hydrolipids (ICD 10: L85.3)

Xerosis cutis (synonyms: dry skin, xerosis, xeroderma) is defined as ***skin deficient in hydrolipids.*** *The condition is characterized by decreased quantity and/or quality of lipids and/or hydrophilic substances (the latter is referred to as natural moisturizing factor)* [1].

The ICD 10 lists xerosis cutis (L85.3) as a distinct diagnosis. The beta version of the ICD 11 defines xerosis cutis/asteatosis (code ED 54) as a condition usually caused by a lack in epidermal lipids (as of May 2018). Disease subgroups listed in the ICD 11 include atopic xeroderma, asymptomatic or pruritic xerosis cutis, asteatosis and senile xerosis [2].

It is essential to make a distinction between constitutional xerosis cutis or xerosis cutis triggered by exogenous factors (Table 1) and dermatoses that present with primary skin lesions such as atopic dermatitis (AD), the various forms of psoriasis, or the various types of ichthyosis. Moreover, it is important to differentiate xerosis associated with systemic diseases (e.g., diabetes, renal and biliary disorders) or induced by pharmaceutical drugs, as the condition in those cases is a mere symptom and not a distinct diagnosis (Table 2).

Table 1 Examples of external causes and environmental triggers of xerosis cutis.

Environmental factors	Cold; low humidity/dry indoor heat; intense exposure to sunlight
Occupational factors/ hobbies	"Wet" work or contact with irritant occupational substances (e.g., hairdressers, construction and metal workers, nursing staff); housekeeping
Skin cleansing/ washing	Frequently taking long hot showers or baths. Use of alkaline soaps and cleansing agents

Prevalence and significance as risk factor

Xerosis cutis is one of the most common conditions seen by dermatologists and general practitioners in everyday clinical practice, with an estimated annual prevalence in Germany of at least 10 million affected individuals.

Occupational screening exams in Germany (n = 48,380) have revealed that **approximately every third employee (29.4 %) between the age of 16 and 70 years is affected by xerosis cutis.** There is no gender predilection [3]. The prevalence increases with increasing age (55.6 % at a mean age of 75.1 years) [3, 4]. Older, care-dependent individuals (mean age: 83.6 years) have been shown to develop xerosis cutis in 99.1 % of

Table 2 Endogenous causes (dermatological, internal and psychiatric diseases, diet, drugs) associated with xerosis cutis.

Category	Examples of diseases/triggers
Dermatological diseases	
Inflammatory skin disorders	Atopic dermatitis, allergic contact eczema, irritant contact dermatitis, dyshidrotic eczema, nummular eczema, drug eruption, psoriasis, seborrheic dermatitis, perioral dermatitis
Genodermatoses	Ichthyoses
Infectious dermatoses (chronic stage)	Fungal and bacterial infections, pediculosis, scabies
Neoplasms	Cutaneous lymphoma (e.g., mycosis fungoides)
Internal diseases	
Endocrine and metabolic disorders	Chronic kidney disease, diabetes mellitus, hepatopathies (e.g., primary biliary cholangitis, primary sclerotic cholangitis, drug-induced cholestasis, extrahepatic cholestasis), hyperparathyroidism, hypothyroidism, malabsorption
Inflammatory diseases	Chronic inflammatory bowel disease (gluten-sensitive enteropathy), rheumatic disease
Infections	Diarrheal diseases, helminths, hepatitis B and C virus, HIV
Hormonal changes	Menopause, andropause, pregnancy
Hematological and lymphoproliferative diseases	Myeloproliferative disorders (e.g., polycythemia vera, essential thrombocytosis), Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma
Psychiatric causes	
Obsessive-compulsive disorders	Obsessive skin cleansing/washing
Eating disorders	Anorexia
Addictions	Alcohol and drug abuse
Dietary causes	
Dehydration	Insufficient fluid intake, excessive perspiration
Malnutrition	Hypovitaminosis (vitamin D, vitamin A, niacin deficiency), zinc or iron deficiency
Drug-related causes	
Pharmaceutical drugs (not including erythema)	Retinoids, topical corticosteroids (prolonged use), diuretics, lipid-lowering agents, calcium antagonists, beta blockers, antirheumatic drugs, contraceptives/antiandrogens, cytostatic agents, radiation dermatitis (following radiation therapy), possibly immunomodulators

cases [5]. Data from the KIGGS study (study on the health of children and adolescents in Germany) show a lifetime prevalence of atopic dermatitis among children and adolescents of 13.2 % [6, 7]. While there have been no studies that merely investigated the symptom "dry skin" among children in Germany, the prevalence is assumed to be 15–20 %, with a peak in the first two years of life.

Analysis of statutory health insurance data shows that xerosis cutis as a distinct diagnosis is greatly underrepresented compared to its actual prevalence, with a documented prevalence of 0.3 % among women and 0.2 % among men. This may not only be the result of frequent self-treatment outside the statutory health insurance realm, but also due to common disease-coding practices by which xerosis cutis is coded through associated primary diseases such as atopic dermatitis. Nevertheless, within the statutory health care system, early recognition, diagnosis and treatment of xerosis cutis is of great significance. This is especially true, as the frequently associated/resultant impairment in the epidermal barrier leads to increased sensitivity to environmental factors, irritants, allergens and pathogens. Following relevant exposure, this may facilitate the development of dermatoses such as atopic dermatitis or contact dermatitis [8]. Augustin et al. (2018) have shown that xerosis cutis is associated with an increased risk of developing axillary dermatitis, atopic dermatitis, exsiccation eczematoid, psoriasis, plantar warts

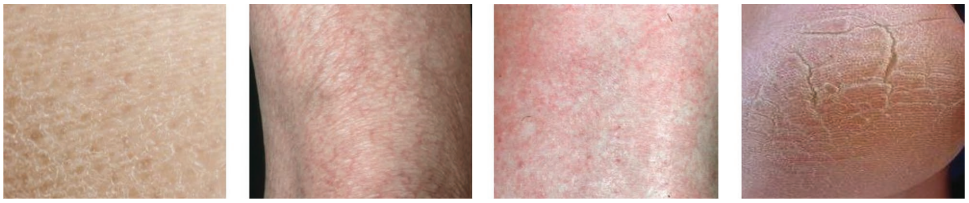

Figure 1 a–d: Clinical examples of xerosis cutis: (a) xerosis cutis with typical fine scaling and coarsening of the skin texture. (b) Senile xerosis with wrinkling and mild scaling. (c) Xerosis cutis with incipient erythema. (d) Atopic "winter feet" with coarse scaling and incipient fissures.

and seborrheic dermatitis [3]. Elderly, care-dependent individuals with dry skin show a diminished defense against external pathogens and an increased risk of developing decubital ulcers [9].

Symptoms and site

Objective signs of xerosis cutis include dry, scaly, rough, wan and somewhat grayish skin (Figure 1a).

In addition, the skin is characterized by decreased elasticity, coarsening of its texture and wrinkling (Figure 1b); erythema (Figure 1c) and fissures (Figure 1d) may also occur. Subjective symptoms include a feeling of tightness and pruritus, which may also be perceived as pain or a burning sensation by some patients.

Xerosis cutis, in particular when associated with pruritus, leads to considerable impairment in patients' quality of life [10, 11]. While all areas of the body may generally be affected, sites with fewer sebaceous glands, such as the lower legs, forearms, hands and feet, are usually more frequently affected.

Causes of xerosis cutis

Xerosis cutis is associated with impairment in the natural barrier function and/or lack of moisturizing factors in the skin, leading to decreased skin hydration.

The **natural skin barrier** comprises 15–20 layers of corneocytes embedded in a lipophilic intercellular substance and arranged in regular columns in the stratum corneum (brick and mortar model) (Figure 2).

Corneocytes originate from keratinocytes that migrate from the basal membrane zone to the skin surface within four weeks. During this time, they differentiate into enucleated, organelle-free cells that are surrounded by a rigid cornified envelope that eventually shed. The conversion of profilaggrin to filaggrin takes place within keratinocytes in the lower stratum corneum. Filaggrins facilitate the formation of disulfide bridges between keratin filaments and play an important structural role in the skin barrier. In the upper layers of the stratum corneum, filaggrin is further degraded to pyrrolidine carboxylic acid, urocanic acid and free amino acids. These components make up the "natural moisturizing factor" (NMF), which is essential for the water-binding capacity of the corneal layer.

The distribution of the moisturizing factor glycerol via aquaporin 3 channels may also be involved in the pathogenesis of xerosis cutis [12, 13]. Healthy skin should normally be able to store a water content of 10–20 %. Both water content that is too high (e.g., "swollen" hands of washwomen) as well as too low an amount of water lead to impaired barrier function. Genetic alterations in filaggrin metabolism are associated both with impaired barrier function and diminished water-binding capacity, and play a pathogenetic role in certain types of ichthyosis and atopic dermatitis [14, 15].

The **size, number and arrangement of corneocytes** also affect the physical barrier function of the skin. Its effectiveness depends on the water content of the corneocytes, patient age and the time of year. Some inflammatory dermatoses (e.g., psoriasis) present with hyperproliferation of smaller yet not fully differentiated corneocytes. Certain drugs, such as vitamin A derivatives, induce an increase in epidermopoiesis and thus also lead to smaller keratinocytes.

The **intercellular lipid bilayer** prevents evaporation of water and is primarily responsible for the chemical barrier function of the skin. It contains keratinosomes (Odland bodies) that are composed of ceramides, sterols and free fatty acids. They form broad, parallel, lamellar lipid layers that subsequently seal the intercellular space between keratinocytes. The composition of lipids in the stratum corneum is influenced by age, genetic disposition, time of year, diet (e.g., percentage of essential fatty acids) as well as drugs (e.g., cholesterol-lowering agents). Hormone-mediated sebum production in sebaceous glands also contributes to the amount of skin lipids. Intercellular lipids and NMF are removed from the skin by frequent contact with detergents, water or solvents, thus resulting in impaired barrier function.

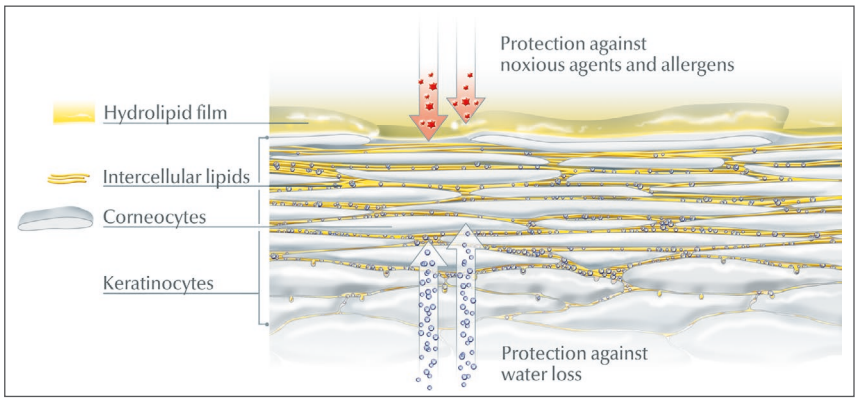

Figure 2 Structure of the skin barrier. For the water content of the skin to be sufficient (10–20 %), it requires a functioning intercellular lipid bilayer as well as orderly arrangement and differentiation of corneocytes with an adequate amount of natural moisturizing factor (NMF).

The **protective acid mantle** of the skin is a thin hydrolipid layer (with a pH of 4.0–6.5) consisting of lipids produced by sebaceous glands, sweat and remnants of keratinocytes that have been sloughed off. A pH that is too high can lead to increased degradation of barrier lipids and a reduced defense against cutaneous infections [16].

It has recently been shown that the skin microbiome has an impact on the condition of the skin, its texture and the development of skin diseases, even though the exact pathogenetic mechanism has not yet been fully elucidated [17]. It is thought that the individual composition and diversity of the microbiome play a role in physiological skin function and defense [17, 18]. Areas of the skin with many sebaceous glands, such as the back and face, tend to be colonized by a large number of propionibacteria. These bacteria break down sebum triglycerides into free fatty acids and thus contribute to lipid replenishment of the skin and also to maintaining the protective acid mantle. Baurecht et al. (2018) have demonstrated that the epidermal lipid composition (the proportion of long-chain unsaturated fatty acids in particular) is associated with the amount of propionibacteria and corynebacteria present [17]. Although these studies show that the makeup of the microbiome has an impact on the composition of skin lipids, the majority of these studies have been conducted in patients with inflammatory disorders such as atopic dermatitis [19, 20], psoriasis [21] and acne [22]. It is therefore still unclear whether the microbiome also has direct effects on xerosis cutis.

In summary, the decreased water content of the skin in patients with xerosis cutis is caused by impairment of the skin's barrier function and/or lack of moisturizing factors.

Potential causes for this include:

- **Altered composition of the intercellular lipid bilayer,** e.g., caused by external (Table 1) or endogenous factors (Table 2).
- **Abnormal keratinocyte differentiation or desmolysis,** e.g., in psoriasis, ichthyosis and others.
- **Decreased content of moisturizing factors in the skin** [23], e.g., caused by environmental factors (Table 1), fluid deficiency or by decreased endogenous production (e.g., inherited filaggrin deficiency [14, 15]) or poor distribution (e.g., aquaporin 3 deficiency [13]).

In addition, numerous other dermatological and internal diseases are associated with xerosis cutis (Table 2).

Rationale

Xerosis cutis is one of the most common conditions seen by dermatologists and general practitioners in routine clinical practice. It affects patients' quality of life and – due to the impaired skin barrier – is a risk factor for the development of atopic or allergic dermatitis and other skin diseases. Currently, there are various guidelines available in Germany, either for specific diseases (e.g., atopic dermatitis, psoriasis), specific symptoms (e.g., chronic pruritus [24]) or for topical treatment in general (S2k guidelines for topical treatment [25]). The 2009 GD (German Society of Dermopharmacy) guidelines for the use of "Dermocosmetic Agents for Skin Cleansing and Skin Care in Patients with Dry Skin" [1] were the first to address practical aspects, albeit without providing a concrete pathway for diagnosis and treatment.

2. Objectives

The objectives of the present position paper are

- To provide a summary of current scientific study data with regard to basic skin care for patients with xerosis cutis ("state of the art") and to fill evidence gaps with clinical practice experience ("expert consensus").
- To raise awareness among physicians of various specialties (dermatologists, allergists, general practitioners, pediatricians and internists, including gerontologists, diabetologists, nephrologists, gastroenterologists) in terms of

prevention and early treatment of xerosis cutis in order to prevent sequelae.
– To provide physicians with concrete practical recommendations, including a structured treatment pathway for managing patients with xerosis cutis in everyday practice.

3. Methods

Relevant questions in terms of management of xerosis cutis in routine clinical practice were developed in the context of an expert consensus process. Systematic reviews and hallmark publications identified through a structured literature search were used to answer these questions. In the first step of this structured, multistage decision-making process, the six experts were asked about their own diagnostic and therapeutic approach.

If a given approach was spontaneously mentioned by > 50 % of the experts, they were considered to be in strong agreement; if > 90 % provided the same answer, agreement was considered to be very strong. For approaches mentioned twice, the agreement was deemed moderate (33 % agreement); any approaches suggested only once were merely mentioned.

Based on these answers, concrete recommendations were developed, which were then assessed in the context of an expert consensus process using a five-point scale (0 = do not agree, 1 = somewhat agree, 2 = tend to agree, 3 = agree, or 4 = agree entirely). Scores of 3 or 4 were considered to be in agreement. Pursuant to AWMF (Association of Scientific Medical Societies in Germany) recommendations for consensus finding [26], a level of agreement among the participants of > 95 % was classified as strong consensus; > 75–95 %, as consensus; 50–75 %, as moderate consensus (majority agreement); < 50 %, as weak consensus. Recommendations with a moderate or weak level of agreement were subsequently modified and voted on again at a consensus conference. Based on evidence and expert opinion, the experts then developed a diagnostic and treatment algorithm containing recommendations for the management of xerosis cutis in routine clinical practice.

4. Diagnosis of xerosis cutis

D. Wilsmann-Theis, A. Körber

Key question: What diagnostic information on xerosis cutis is useful for a treatment decision?

Xerosis cutis is generally a clinical diagnosis. Triggers and/or underlying diseases must be determined and specifically treated (100 % consensus).

History

Table 3 provides an overview of the recommended diagnostic approach in patients with xerosis cutis. When taking the history, patients should be asked about atopic disorders, exogenous factors and endogenous factors/internal diseases as well as disease course. As regards the latter, it is particularly important to enquire about the duration of symptoms and factors that lead to disease exacerbation. Given that a patient's perception of pruritus can vary, it is essential to also ask about symptoms such as a burning sensation or pain.

Assessment of cutaneous findings and symptoms

The choice of a suitable basic skin care preparation for xerosis cutis requires the assessment of scaling, fissures/rhagades, erythema and pruritus. Age-dependent characteristics and physiological features of special sites have to be taken into consideration (100 % consensus).

In the past, there has been no standardized approach to assessing xerosis cutis and grading its severity: in 1993, the EEMCO (European Group of Efficacy Measurement of Cosmetics and other Topical Products) developed the ODS (Overall Dry Skin) score and the specific SRRC (scaling, roughness, redness, cracks) symptom score for assessing the severity of dry skin [27]. The SRRC/ODS score is focused on objective, visible signs only. Subjective symptoms, such as pruritus, or the affected body surface area are not included in these scores. Based on expert consensus, Günther et al. (2012) classified xerosis cutis and its symptoms into four grades of severity (0–3) [28]. Visible signs still included roughness/scaling, erythema and fissures. In addition, Günther et al. included pruritus and pain as subjective symptoms. Moreover, their classification accounted for different body sites (face, trunk, hands/feet). The authors did not systematically incorporate the relevant scientific evidence available at the time; neither did they consider age-specific characteristics.

Severity scores used for atopic dermatitis (Eczema Area and Severity Index, EASI or SCOre of Atopic Dermatitis, SCORAD) or psoriasis (e.g., Psoriasis Area and Severity Index, PASI) merely include xerosis as one symptom among others, and also consider the body surface area (BSA) affected.

The goal of the expert consensus was to develop a diagnostic algorithm that **aids in the selection of suitable ingredients for basic skin care:** scaling (100 % consensus), fissures/rhagades (100 % consensus) and erythema (85 % consensus) were identified as objective signs. The validated five-point EEMCO scale was employed to assess disease severity [27].

State-of-the-art clinical research requires that a comprehensive assessment of disease burden include both **subjective**

Table 3 Diagnostic approach to patients with xerosis cutis.

History	– History of atopy (family, stigmata) – Age – External factors: frequency in terms of washing and use of skin care products, contact with irritants, occupation, recreational activities, living conditions, diet – Pregnancy/menopause – Preexisting conditions (in particular diabetes, kidneys, liver/gall bladder, thyroid, infections) – B symptoms – Past and current medications – Prior management of xerosis cutis
Findings	– Objective cutaneous findings (scaling, fissures/rhagades, erythema) including assessment of severity – Subjective symptoms (pruritus, burning sensation, pain, feeling of tightness) including assessment of severity – Pattern of distribution (trunk/extremities, hand/feet, face/scalp, special sites)
Clinical course	– Duration (acute < six weeks, chronic > six weeks) – Disease course (continuous or intermittent, frequency, trigger factors)
Diagnosis	– Dermatosis with primary skin lesions – Genuine/constitutional xerosis cutis – Comorbidity/adverse drug effects
Decision	– Specific treatment – Further diagnostic workup (allergy/internal diseases/malignancy)

symptoms and objective signs. In this context, the presence and severity of pruritus (as a subjective symptom) were considered key aspects for the choice of ingredients (100 % consensus). Based on current recommendations, a numeric rating scale (0–10) was deemed most suitable to assess pruritus (100 % consensus) and considered preferable to the five-point verbal rating scale and the visual analog scale (0–10). In routine practice, the numeric rating scale from 0–10 is more commonly used and has been shown to yield more reliable results in clinical studies [29]. In addition, assessment of subjective pruritus should always include visible signs such as excoriations.

A majority of experts involved in this publication, did not consider other symptoms such as roughness, wrinkles, feeling of tightness, burning sensation and pain to be relevant for the assessment of disease severity and/or for the choice of suitable treatment.

Assessment of the **overall disease severity of xerosis cutis** should include evaluation of potential impairment in quality of life. Validated assessment forms are available for this purpose (Table 4). Information provided by patients may also be useful in terms of treatment planning, especially when patient needs are assessed and included in the treatment goals. While both can be done during physician–patient consultations,

Table 4 Validated questionnaires for the assessment of health-related quality of life in patients with xerosis cutis.

Name	Scope (items)	Specificity	Author	Available from
DLQI	10	Chronic inflammatory skin diseases	Finlay 1993 [30]	CVderm
Skindex 17	17	Chronic inflammatory skin diseases	Chren 1995 [31] GT: Augustin 2011 [33]	CVderm
FLQA	15	Dry skin/ulcers		
FLQA-AH	25	Aging skin	Blome et al.	CVderm
PBI	23	Dry skin; assesses "patient needs"	Augustin 2009 [33]	CVderm

DLQI, Dermatological Life Quality Index; GT, German translation; FLQA, Freiburg Life Quality Assessment; PBI, Patient Benefit Index.

use of short standardized questionnaires is more valid and efficient [30–33].

If patients have certain underlying diseases such as psoriasis or atopic dermatitis, standardized severity scores validated for these conditions (e.g., PASI; SCORAD; EASI) should be used.

By contrast, in the opinion of the experts, neither a summation score combining the various individual symptoms of xerosis cutis (SRRC or Günther et al.) nor assessment of the affected body surface area (BSA) is useful for the individual choice of ingredients or for determining overall disease severity. For instance, severely dry skin of the face or on hands and/or feet might be associated with considerable impairment in quality of life, even though this would not be reflected by BSA or a summation score. On the other hand, standard assessment of the BSA affected by xerosis cutis is useful for follow-up and for determining the quantity of skin care products required.

In routine practice, it is important to **distinguish between different areas of the body** (face, trunk, hands/feet and special sites such as the scalp, eyelids, lips, genital region), as certain sites require a different therapeutic approach. Age-specific characteristics, in the elderly and newborns in particular, also have to be taken into account.

A novel diagnostic approach (Table 3) as well as the newly developed "xerosimeter" (Figure 3) were devised in the context of the present position paper on the management of xerosis cutis. The latter enables physicians to make individual symptom-based treatment decisions and to assess the disease course in a structured manner.

Measurement of skin barrier function and hydration

Measurement of TEWL using "tewametry" or measurement of hydration by corneometry are not required for the diagnosis of xerosis cutis to be made. Both methods are important objective parameters in clinical trials and may be employed, for instance, in cases of inadequate treatment response or severe disease course (100 % consensus).

A series of biophysical, non-invasive in vivo measurement methods are available to objectively assess the subjective feeling of dry skin, respectively the clinical diagnosis of xerosis cutis. Measurement of the barrier function by evaluating **transepidermal water loss (TEWL) using "tewametry" and measurement of skin hydration by means of corneometry** are among the most important parameters for objectively assessing xerosis cutis.

These methods are employed as objective measurement parameters in clinical trials in particular. In addition – if required in certain cases – the amount of surface sebum can be measured using the Sebumeter®; and skin roughness, by using Visioscan®, a profilometry technique. A novel method for measuring hydration in different skin layers, KOSIM IR® is an analytical system that combines infrared spectroscopy and confocal microscopy, thus allowing for assessment of the water content of the skin as a function of depth [34]. For clinical studies, a standardized environment (climate chamber) is required in order to obtain reproducible and conclusive measurements.

The diagnosis of dry skin is typically made on clinical grounds. The aforementioned procedures may be employed if an extended diagnostic workup is required, e.g., in case of inadequate response to treatment, or if requested by the patient, e.g., as individual diagnostic measure.

5. Management of xerosis cutis

P. Staubach, G. Itschert, M. Kerscher, M. Augustin

Key question: Which factors affect the choice of ingredients and what is the scientific evidence?

Definition of "basic skin care" and limitations of assessment

P. Staubach and G. Itschert

Basic skin care products for the treatment of xerosis cutis include topical dermocosmetic agents that contain active ingredients with remoisturizing, lipid-replenishing, film-forming, skin-soothing and/or antipruritic effects.

Regular use of a combination of remoisturizing and lipid-replenishing topical agents to treat xerosis cutis should not only be considered mere skin care; instead, this approach is one of the causal treatment components aimed at restoring the skin's barrier function [35]. These topical agents are therefore also referred to as "basic therapeutic agents".

The majority of basic skin care agents most commonly used are approved through the EU cosmetics regulation (VKVO) [36]. The goal of the cosmetics regulation is to ensure the safety of products that are intended to maintain or "protect" "a good skin condition". Studies on the products' efficacy in terms of skin care and their tolerability are in part conducted by manufacturers themselves. However, these studies only rarely constitute randomized controlled trials (RCTs) of good quality that investigate the effect of an active ingredient in comparison to the vehicle (placebo). These studies were reviewed during the development of this position paper and considered in the decision-making process. The overall challenge in assessing the study data available for individual ingredients arises from the methodology used and the regulatory labeling requirements: due to the

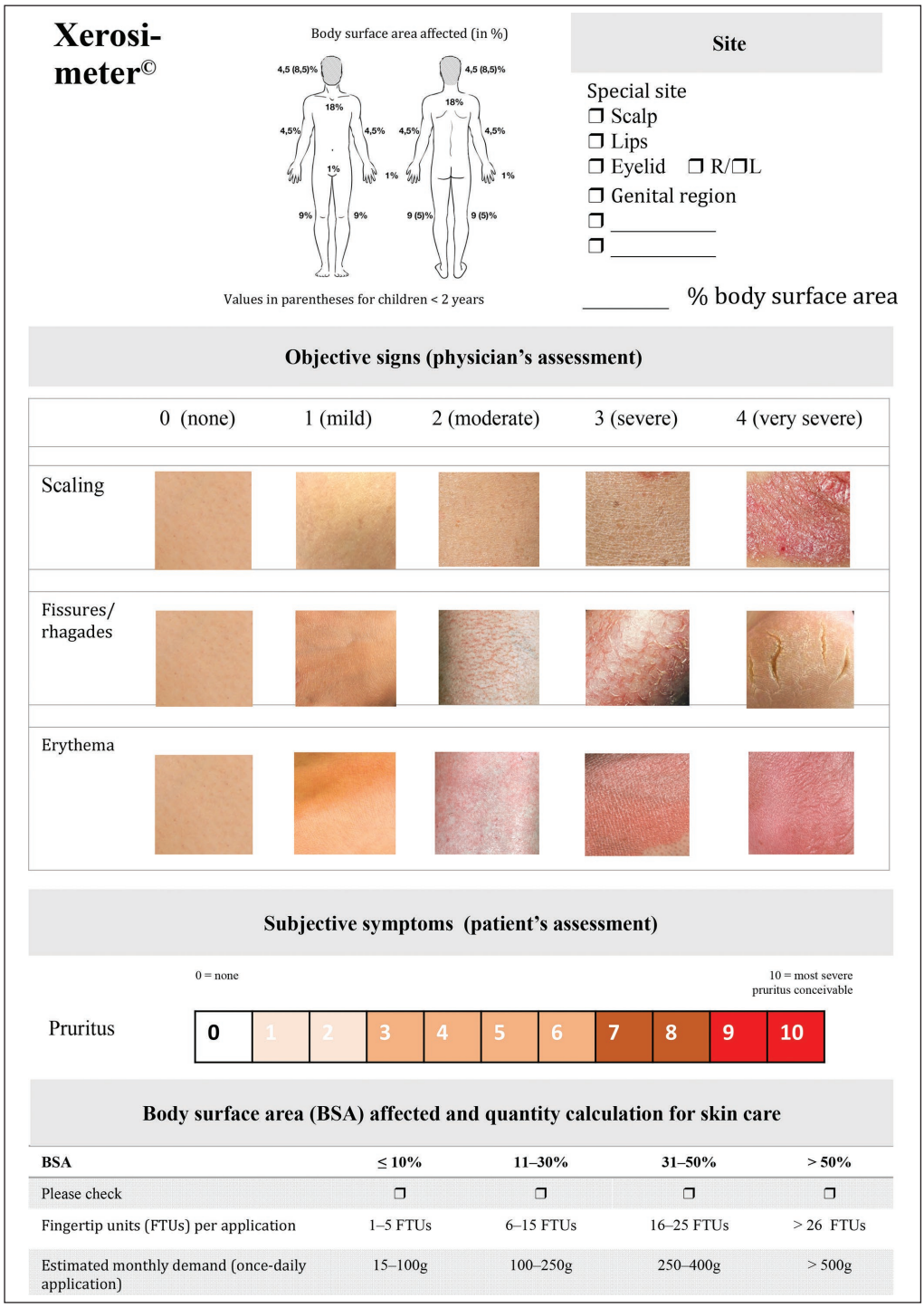

Figure 3 Xerosimeter® for the assessment of disease severity and clinical course in patients with xerosis cutis.

chosen composition of a given topical base, the vehicle itself frequently has an effect of its own. What is more, the exact scientific classification of individual ingredients is rendered even more difficult by the fact that the exact concentration of an ingredient is frequently not declared by the manufacturer and/or the individual substance to be assessed is used in various combinations with other ingredients. Thus, it is difficult conclusively determine an ingredient's individual effect.

In an effort to make a distinction from pharmacological ingredients/agents, there was consensus among the

Table 5 General preventive measures for xerosis cutis.

General measures	Trunk/extremities	Face	Hands/feet
Skin cleansing/contact with water	– Full-body bath for a maximum of 5 min, no bubble baths – Lukewarm, no hot showers – Use of mild, non-alkaline soap, lipid-replenishing syndets or shower and bath oils.	– Cleansing and skin care with products low in fragrances and allergens; no shampoo – Cleansing no more than twice daily	– Avoid contact with water, soap and detergents – Use products low in fragrances and allergens
Clothing	– Cotton clothing, not too tight (avoid friction), – Avoid wool		– Protective cotton gloves (possibly as inner gloves)
Diet	Avoid citrus fruits, very hot and spicy food, large quantities of hot drinks and alcohol.		
Climate/room temperature	Avoid dry, hot or very cold climates as well as significant temperature variations and intense sun exposure.		
General lifestyle	Avoid agitation, tension, stress.		

experts involved to use the term "active ingredients" when referring to dermocosmetic agents. The following effects of active ingredients play a key role in the treatment of dry skin: lipid replenishing, remoisturizing, film forming, skin soothing and antipruritic. A classification based on these aspects was jointly developed by the panel of experts (Table 6).

General principles in the treatment of xerosis cutis

Preventive measures

P. Staubach and G. Itschert

General preventive measures, such as using gentle cleansing agents, constitute the basis of successful xerosis cutis treatment.

Xerosis cutis can be triggered or aggravated as a result of excess or improper skin cleansing, clothes that are overly tight or that chafe, certain dietary habits as well as climatic and environmental factors. Table 5 provides an overview of general recommendations intended to assist patients in the management of xerosis cutis.

Basic principles of topical treatment

P. Staubach and G. Itschert

The use of basic skin care products is an internationally recognized approach to treating xerosis cutis. This includes skin diseases associated with xerosis cutis such as atopic dermatitis or ichthyosis. Basic skin care targets the stratum corneum, including the NMF found in corneocytes and the associated intercellular lipid bilayer.

Basic skin care in the treatment of xerosis cutis is intended to improve skin hydration, compensate ***the lack in barrier lipids and improve the skin's barrier function****. Thus, a combination of hydrophilic and lipophilic components is preferable (100 % consensus).*

Optimal topical skin care for xerosis cutis should, to the greatest extent possible, mimic the various components of the skin barrier or restore its function. Products to be used should therefore contain lipophilic (lipid-replenishing, film-forming) and hydrophilic (remoisturizing) ingredients (Figure 4).

Hydrophilic (remoisturizing) ingredients primarily include low-molecular-weight, water-binding substances such as glycerol or urea. Given their low molecular weight, they are able to penetrate the stratum corneum, where they assume the role of NMF or act as "humectants". "Humectants" are polyvalent, short-chain alcohols that are used as moisture-binding agents in many dermocosmetic products due to their outstanding hydrophilic and hygroscopic properties. Not only do they slow down TEWL, they also prevent the formulation from drying out too soon.

As regards lipophilic ingredients, a distinction is made between lipid-replenishing and film-forming substances. While oils, fats or waxes based on mineral oil or silicone do not penetrate the skin because of their high molecular weight and thus form a thin lipophilic layer on the skin surface [37],

physiological skin lipids, such as e.g., ceramides, cholesterol, free fatty acids and certain components of natural oils, are able to replenish the intercellular lipid matrix, thereby augmenting the skin's barrier function.

If the skin is erythematous or if there is pruritus, additional ingredients with skin-soothing or antipruritic properties can be used (Table 6).

Table 6 Classification of commonly used active ingredients for basic skin care* in patients with xerosis cutis.

Class	Mode of action	Active ingredients (examples)
Remoisturizing		
NMF (natural moisturizing factor)	Physiologically formed by the breakdown of filaggrin in the skin; occurs in sweat; binds water in the skin.	Urea, lactic acid derivatives, pyrrolidine carboxylic acid (PCA), amino acids (alanine, arginine, citrulline, glycine, histidine, leucine, lysine, serine, threonine), inorganic salts
Other moisturizing factors (humectants) and swelling agents	Hydrophilic and hygroscopic substances that reduce transepidermal water loss and/or improve water distribution.	Glycerol, glyceryl glucoside (GG), hyaluronic acid, glycosaminoglycans, glycols (propylene glycol, polyethylene glycol/macrogols (PEG), butylene glycol), various sugars and sugar alcohols**
Film forming		
Hydrocarbon mixtures based on mineral oil	Form a hydrophobic film on the surface of the skin, thus reducing water loss.	Vaseline (petroleum jelly), liquid paraffin, wax, microcrystalline ozokerite
Silicone oils	Form a thin hydrophobic, semi-occlusive (permeable to water vapor) film on the surface of the skin; positive effects on spreadability	Dimethicone, methicone, polysiloxane, cyclomethicone
Lipid replenishing		
Physiological barrier lipids	Replenish the intercellular lipid matrix	Ceramides, sterols, cholesterol derivatives, squalenes, triglycerides, free fatty acids
Naturally occurring oils, fats and waxes	Provide numerous polyunsaturated omega-6 fatty acids (linoleic acid, γ-linolenic acid), phytosterols and sterols for the formation of skin barrier lipids; form a hydrophobic film on the surface of the skin.	e.g., evening primrose oil, grape seed oil, safflower oil, canola oil, sunflower oil, flaxseed oil, almond oil, borage oil, jojoba oil, shea butter, lanolin#, beeswax#
Skin soothing		
	Inhibit, for example, the secretion of mediators of inflammation; capture free radicals and/or promote wound healing	Licochalcone A, glycyrrhizic acid, dexpanthenol, oat extract# bisabolol#, vitamins A, E, B (niacinamide), witch hazel
Antipruritic		
	Act as local anesthetic, relieve pain and/or activate cold receptors	Polidocanol, menthol, menthoxypropanediol, N-palmitoylethanolamide, camphor, tannins

*No claim to being exhaustive; many ingredients could be assigned to more than one group.
**Fructose, glucose, inositol, mannitol, sorbitol, butylene.
#Note: sensitization potential.

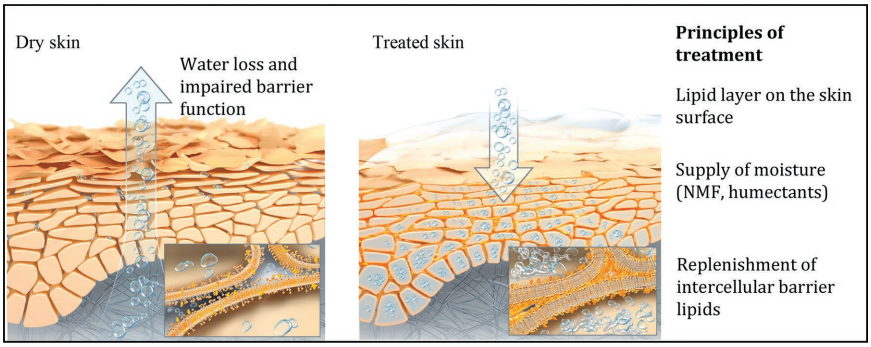

Figure 4 Basic principles of topical treatment of xerosis cutis: optimal treatment involves the supply of moisture in the form of the natural moisturizing factor (NMF) or humectants, replenishment of barrier lipids and the prevention of water loss through the formation of a lipid layer on the skin surface.

Choice of formulation

The drier the skin, the more lipids the base should contain (moderate, 83 % consensus). For acute, inflammatory disease stages, vehicles with a higher water content are preferable.

Skin-soothing and antipruritic substances can be added (strong, 100 % consensus). Pure fats/oils are generally NOT suited for long-term basic skin care (strong, 100 % consensus).

Topical bases are divided into four groups that should be applied based on the condition of the skin: oil-in-water (hydro) lotion, water-in-oil (lipo)lotion, hydrophilic and lipophilic creams. The choice of bases for dermatological use depends on the condition of the skin and the disease stage. Water-in-oil lotions or lipophilic creams are better suited for dry skin, as their bases prevent increased water loss, resulting in improved hydration. The lower the lipid content of the stratum corneum, the better a topical lipid-rich preparation can penetrate. While pure oils/fats may generally be recommended for scale removal, they are not suited as bases or for long-term basic skin care. For acute, inflammatory disease stages or intense pruritus, bases with a higher water content are preferable [25] (Figure 5).

In a study of 154 individuals, Weber et al. (2012) investigated the efficacy of various combinations of lipophilic and hydrophilic ingredients for the treatment of xerosis cutis [38]. They compared a ceramide-containing lipophilic base (vehicle) with the same base supplemented with urea, lactic acid, and sodium lactate (vehicle plus) and a study formulation that additionally included 14 NMF components, glycerol and glyceryl glucoside (GG) for optimal water distribution. Both an oil-in-water lotion (light) and a water-in-oil lotion (rich) were investigated. It was shown that the base cream

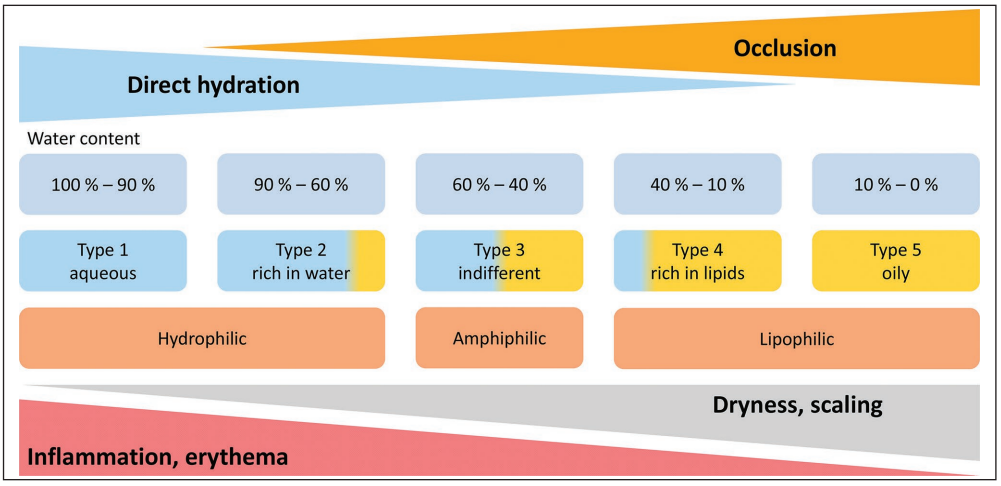

Figure 5 Background information regarding the choice of a suitable vehicle based on the condition of the skin (according to the German S2k guidelines for topical treatment). Types 2–4 are generally used for xerosis cutis. Modified after [25].

(vehicle) alone resulted in a significant increase in hydration compared to the untreated side.

The addition of urea and lactate to these bases (vehicle plus) resulted in a significant increase in skin hydration and a decrease in TEWL compared with the vehicle alone. When other NMF and humectant components were added for optimal water distribution (study formulation), the greatest possible increase in skin hydration was achieved (significantly better than the vehicle plus) while maintaining skin barrier stability. This study shows that the combination of NMF and humectant components with lipophilic ingredients results in significant improvement in barrier function and skin hydration compared to the vehicle alone.

In a double-blind randomized trial (2016) of 80 adult xerosis patients [39], Shim et al. **investigated five different water-in-oil formulations containing various hydrating and lipid-replenishing ingredients** (four of five products also contained ceramides). After **four weeks of twice-daily application, all five study formulations showed comparable improvement in the condition of the skin and in transepidermal water loss** – irrespective of whether the preparations contained ceramides, pseudoceramides or an endothelial growth factor (original test substance). This study too confirmed that basic skin care products consisting of a combination of remoisturizing and lipophilic substances are able to improve the skin barrier. However, the study did not compare said effects with those of the vehicle alone.

Ingredients: classification and evidence in the treatment of xerosis cutis

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Given the lack of a universally accepted classification and overview of ingredients of topical preparations used for the treatment of xerosis cutis, the expert panel agreed on a classification of the most commonly used ingredients based on their underlying mode of action. Due to the large number of substances in the various categories, the list below does not claim to be exhaustive (Table 6).

The choice and composition of ingredients should be based on substances that have been clinically shown to restore the skin barrier (strong, 100 % consensus)

Urea – a natural moisturizing factor (NMF)

The term "natural moisturizing factor" (NMF) refers to a group of water-binding components in the epidermis that result from the breakdown of filaggrin in the stratum corneum [40] or are derived from sweat. The NMF of the skin includes urea, lactic acid derivatives, pyrrolidine carboxylic acid (PCA), amino acids (alanine, arginine, citrulline, glycine, histidine, leucine, lysine, serine, threonine), ammonia, uric acid and inorganic salts. A decrease in the amount of NMF in the epidermis has been observed in xerosis cutis, atopic dermatitis, ichthyosis vulgaris and advanced age [41]. Besides, regular cleansing with soap, overly hot baths or showers and UV exposure may also lead to a reduction in the amount of NMF in the skin. Clinically, a lack in NMF gives rise to roughness, scaling, fissures and rhagades.

The best-known representatives of NMF used in topical preparations include urea [42], lactic acid [43] and PCA [44]. The best evidence from studies is available for urea, which will be briefly discussed below:

Based on available scientific data, urea (synonym: carbamide) is the gold standard in the treatment of xerosis cutis. Not only does urea effectively hydrate the skin, it also improves the barrier function as well as the skin's own defense and hydration mechanisms. It increases the penetration of active ingredients into the skin and has antipruritic and – at higher concentrations – keratolytic effects.

For topical application, the urea concentration and type of vehicle used should be based on the individual condition of the skin, patient age, and the underlying dermatosis. It should not be used on open skin or inflammatory lesions or in children < 2 years of age (stinging effect). In terms of the hydrating effects of urea, its combination with ceramides and NMF is superior to treatment with a vehicle (base) alone or topical preparations that only contain urea. The effect is longer when used in water-in-oil formulations than in oil-in-water formulations.

Effects of topical urea

In 2016, Friedman et al. published a comprehensive review on the effects of topical urea [42]:

- **"Humectant" (provider of moisture)**: it retains water and forms hydrogen bonds with non-polar, aromatic protein amino acids, which additionally increases the water-binding capacity of the corneal layer. It is believed that the observed antipruritic effect is associated with improved skin hydration (secondary effect).
- **Maintaining the barrier function of the skin.** By accumulating in the inner liquid phase of the intercellular lipid bilayer, urea improves elasticity and protects against transepidermal water loss.
- **Maintaining the skin's own defense and hydration mechanisms** by modulating the expression of genes responsible for improving epidermal lipid synthesis, keratinocyte

differentiation, desmolysis, defense against pathogens (AMPs) as well as urea transport [45, 46].

– **Smoothing and desquamative – at concentrations > 20 % – also keratolytic effects** by unfolding cohesion proteins between corneocytes. This also explains the enhanced penetration of drugs into the skin when given together with urea.

The vehicle determines the duration and depth of action of urea

The water-binding activity of urea in skin care products is also determined by the formulation used. For instance, a water-in-oil emulsion is associated with a longer and stronger hydrating effect than an oil-in-water emulsion [47]. It has been shown by corneometry that a combination consisting of urea 10 %, ceramides, other NMF components, glycerol and glyceryl glucoside in a water-in-oil formulation leads to significantly higher moisture levels compared to the vehicle, even 48 hours after the last application. After six days, 20 % of the moisture levels originally achieved were still detectable [38].

The choice of urea concentration depends on the individual condition of the skin and the site affected

Dry skin contains up to 50 % less urea than is physiologically found in healthy skin [48]. Regular skin care with products containing urea at the proper concentration is able to compensate the lack in urea and rehydrate the skin.

As regards facial treatment, urea concentrations of up to 5 % are usually used; however, we were unable to identify specific clinical studies on this topic. In clinical **skin care** trials of healthy individuals (trunk and extremities), **concentrations of 2 to 10 %** were used for a period of two weeks or less [49–55], whereas in studies on **xerosis cutis,** urea concentrations of 10 % [38, 56–59] – 15 % [60] were used for a period of two to four weeks. Urea has been shown to reduce skin dryness, pruritus and roughness as well as TEWL: in a vehicle-controlled trial (n = 72, mean age: 70 years), Schölermann et al. (1999) investigated the effect of urea 10 % alone vs. the combination of urea 10 %, panthenol 1 % and bisabolol 0.07 %. Both urea-containing preparations showed significantly enhanced hydration of the stratum corneum compared to the vehicle [61]. In another study, Danby et al. also showed that the addition of urea 5 %, ceramide NP and lactate resulted in significantly improved hydration and barrier function in older individuals with dry skin compared with the primarily paraffin-based vehicle [62]. The hydrating effects of urea can be further amplified by using a suitable combination partner: the combination of urea with vitamins and ceramides has proved to be more effective in this regard than treatment with urea alone (n = 10) [63]. Likewise, the combination of urea with ceramides, other NMF components, glycerol and glyceryl glucoside has been shown to result in significantly improved hydration than the vehicle or the vehicle plus urea (n = 154) [38].

In a review by Parker et al. [64], urea **at a concentration of 10–25 %** (in some cases, 35–40 %) was associated with impressive outcomes in the treatment of **xerosis of the feet**: the combination of urea 10 % with paraffin was superior to a purely paraffin-based emollient [65, 66]. The combination of urea 10 % with other NMF components, lactate, glycerol, glyceryl glucoside and ceramides has been shown to be superior to treatment with the vehicle alone [67]. In other studies, a urea 25 % cream was shown to be superior to a urea 10 % cream [68] and also to topical agents that contained unspecified concentrations of urea [69]. While a urea 10 % cream was equivalent to treatment with ammonium lactate 12 % [70], a urea 40 % cream was superior to the 12 % cream containing ammonium lactate [71]. A urea 5 % cream in combination with carnosine and arginine was superior to a glycerol 15 % cream in terms of skin hydration [72]. In a multicenter, double-blind, vehicle-controlled trial, 167 diabetic patients with deep pedal fissures were treated with a cream consisting of glycerol 10 %, urea 5 % and petroleum jelly 8 %: the dry skin and pedal fissures improved significantly more on this treatment than on the vehicle alone; no significant difference was found after four weeks in terms of complete healing of the fissures [73].

Tolerability

Higher urea concentrations (usually ≥ 10 %) may be associated with an unpleasant burning sensation when treating mildly irritated skin or inflammatory lesions. At least for the initial treatment of mildly irritated, atopic skin, it is therefore recommended to use urea at concentrations of no more than 5 %. Given that urea causes a stinging effect in infants younger than two years of age, it should only be given to children after that age and only at concentrations of up to 5 %.

Glycerol

A humectant, glycerol improves skin hydration in combination with lipid-replenishing, occlusive components such as petroleum jelly, paraffin or jojoba oil. Skin hydration can be further increased through combination with glyceryl glucoside, urea and NMF.

Glycerol is one of the most important representatives of the group of compounds referred to as humectants. It increases hydration of the stratum corneum and creates a feeling of "soft" skin [74]. It has been shown that dry, scaly skin is improved by increased degradation of desmosomes in the corneal layer [75]. Aquaporin channels are required to ensure adequate distribution of moisture even in deeper epidermal layers

[12, 13]. These channels distribute water and glycerol (and thus moisture) within the various skin layers. Glyceryl glucoside is known to increase the number of aquaporin 3 channels in the skin. It has been shown that the addition of glyceryl glucoside – unlike glycerol alone – further improves the distribution of glycerol (and thus water) and also reduces TEWL [13]. While a glycerol concentration of 5–10 % is usually used in creams, it is well tolerated up to a concentration of 20 %.

In two vehicle-controlled studies of 63 and 58 patients with xerosis cutis, Christman et al. (2012) investigated the effect of a combination consisting of glycerol and niacinamide compared to glycerol alone in various vehicles (paraffin base or petroleum jelly base). Adding glycerol improved the effect on hydration and TEWL compared to the vehicle alone. The combination of glycerol and niacinamide resulted in even better and quicker results in terms of skin hydration and TEWL compared to the other test substances [76]. In a vehicle-controlled trial of patients with uremic xerosis cutis, seven-day treatment with an emollient consisting of glycerol and petroleum jelly showed a significantly better clinical response than the vehicle alone [77]. In a vehicle-controlled study of 154 xerosis cutis patients, the combination of glycerol, glyceryl glucoside and other NMF components with either 5 % or 10 % urea showed greater improvement in skin hydration than urea or the vehicle alone [38]. In a small study of patients with senile xerosis cutis (n = 10), the combination of skin cleansing with water and a washing solution containing glycerol (2 %) and petroleum jelly showed the best effect on skin hydration and TEWL [78]. In an investigator-blinded study of 122 nursing-home patients (mean age: 83.8 years), Kottner et al. [79, 80] examined two structured skin care regimens (group I: water-in-oil emulsion with shea butter and glycerol; group II: water-in-oil emulsion with urea 4 % and liquid paraffin) in comparison to the standard skin care regimen previously employed (group III). While groups I and II showed greater improvement in terms of skin dryness compared to group III, there were no differences in functional parameters (TEWL/hydration) between groups. Cristaudo et al. too reported a positive effect of glycerol in a paraffin-based cream for the treatment of older patients [81].

Compared to urea, there is significantly less evidence for glycerol in the treatment of xerosis of the feet: a glycerol 15 % cream was less effective than a urea 5 % cream [72]. In a multicenter, double-blind and vehicle-controlled study of 167 diabetic patients with deep pedal fissures, the combination of glycerol 10 %, urea 5 % and petroleum jelly 8 % was associated with significantly greater improvement in both fissures and dry skin than the vehicle. However, there was no significant difference in terms of complete healing of the fissures after four weeks [73].

In their study of infants with an increased risk of atopy, Horimukai (2014) et al. showed that daily skin care with a lotion containing glycerol and jojoba significantly reduced the risk of developing atopic dermatitis in the first six months of life [82].

Mineral oil hydrocarbons

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Mineral oil hydrocarbons are not absorbed by healthy skin. They form a thin lipophilic layer on the surface of the skin that leads to improvement in the skin's barrier function and to increased water content of the skin. They are very stable and possess no allergenic potential.

Based on current scientific data, the German Federal Institute for Risk Assessment (BfR) has concluded that there are no health risks to consumers due to transdermal absorption of mineral oils from cosmetics [83].

Mineral oil-based oils, fats, and waxes include the following substances: white and yellow petroleum jelly, liquid paraffin, paraffin (paraffin wax), microcrystalline wax, ozocerite and ceresin.

In their 2012 review, the Society of Cosmetic Scientists described the benefits of mineral oil [84]: not only is the lack of transdermal penetration the reason for the safety of these lipid compounds, the resultant very good occlusive effect also reduces TEWL.

It has been shown that this occlusive effect is associated with an effective increase in the water content of the stratum corneum and thus provides emollient and protective effects [85]. Another advantage is the inert chemical behavior of mineral oils in comparison to vegetable oils, given their antioxidant stability and the fact that they form no degradation products, even after prolonged storage. They contain no allergenic components and contribute to the stability of any preparation. However, prolonged use of paraffin ointments for daily skin care is not recommended, as they form a greasy film on the skin and may be associated with local accumulation of heat.

Safety

Mineral oil-based oils, fats and waxes consist of a complex mixture of aliphatic, branched-chain hydrocarbons of varying chain lengths (MOSH – mineral oil saturated hydrocarbons) as well as aromatic compounds (MOAH – mineral oil aromatic hydrocarbons). MOAH may contain a small percentage of polycyclic aromatic compounds (PAC), which are suspected of being carcinogenic.

Pursuant to the EU cosmetics regulation, mineral oils in cosmetics are only permitted if the refining process is entirely known and the manufacturing process ensures that

these carcinogenic components are removed, so that the raw material used (e.g., liquid paraffin) is demonstrably not carcinogenic. Evidence for this is provided through specific test methods during and after the manufacturing process.

A 2017 review of 13 in vivo (healthy individuals, animals) and in vitro studies summarized the available data regarding transdermal absorption of mineral oils and waxes [86]. All studies reviewed arrived at the uniform conclusion **that mineral oils and waxes used in cosmetic products penetrate healthy skin only superficially.** Human studies showed that there was no penetration into "living" skin layers. The substances remained in the stratum corneum and were not detected systemically.

In February of 2018, the German Federal Institute for Risk Assessment (BfR) updated its position on highly refined mineral oils in cosmetics. It was determined that, based on current scientific data, health risks were not to be expected for consumers of cosmetics if these products are used on healthy skin [83]. There were no reports of negative health effects caused by mineral oil compounds in cosmetic products, despite many years of – frequently daily – use. The validity of the relevant scientific data is now considered to be "high" in the current version of the BfR assessment report.

Silicone oil products

Silicone oil products form a fine hydrophobic, usually water-vapor-permeable (semipermeable), non-occlusive film on the surface of the skin. They protect the skin from harmful external factors, such as water and irritants, and promote wound healing. They are very well tolerated, very stable, non-comedogenic and characterized by high cosmetic acceptance due to their great spreadability. There is currently no evidence as to their specific effects on xerosis cutis (hydration or TEWL).

The chemically inert silicone oils (including dimethyl siloxane/dimethicone; phenyl methyl siloxane and the cyclic methyl siloxanes/cyclomethicone) are characterized by their extremely good spreadability. Moreover, they are very well tolerated and enjoy high cosmetic acceptance: they are non-comedogenic and make the skin feel "velvety and smooth" [87]. Silicone oils form a hydrophobic, yet water-vapor-permeable film on the surface of the skin, which has been shown not to interact with the lipids of the stratum corneum [88]. The permeability to water vapor depends on the number of long-chain alkyl groups (C18 or longer). Thus, certain long-chain alkyl silicone polymers may be similarly occlusive as petroleum jelly.

Silicone oil derivatives are used as "barrier creams" to prevent skin irritation [89] and dermatitis in patients with incontinence [90, 91]; they have a positive effect on scar formation and keloids [92].

In a study of 24 healthy women, De Paepe et al. (2014) compared the effects of three silicone oils of different viscosities as well as three silicone-containing water-in-oil creams (in combination with glycerol 5 %) and petroleum jelly on TEWL and skin hydration. Only the highly spreadable silicone oil and petroleum jelly lowered TEWL after four hours. By contrast, skin hydration improved only with the silicone oil-glycerol creams and with petroleum jelly but not with silicone oils [93].

Ceramides

Ceramides represent essential components of the physiological lipid barrier. In the treatment of xerosis cutis, they achieve better barrier-stabilizing effects in combination with urea, NMF and glycerol than when used alone.

Apart from cholesterol and free fatty acids, ceramides (sphingolipids) constitute the main components (approximately 40 %) of the extracellular lipid matrix of the stratum corneum. The individual percentage of certain lipids in the lipid matrix is a crucial factor in terms of a functional skin barrier [94–96]: not only does the amount of ceramides decrease with age, it also depends on gender and endocrine factors such as female sex hormones. The lower proportion of long-chain ceramides [97] in older individuals or patients with atopic dermatitis [98] and psoriasis [99] is also thought to play a pathogenetic role with regard to the impaired barrier function [100–102]. When using ceramides in topical preparations, it is essential to bear in mind that the sheer ceramide content of a given emollient is less important than its **physiological lipid composition of ceramides, fatty acids and sterols** [100].

The majority of clinical trials using ceramides only have been carried out in patients with atopic dermatitis [103] and psoriasis [104]; only few studies are available for xerosis cutis:

In a study by Weber et al. (2012) a ceramide 3-containing vehicle in a water-in-oil and in an oil-in-water formulation was compared with the same formulations that additionally contained urea, other NMF components, glycerol and glyceryl glucoside (GG). In comparison to untreated skin, only the ceramide 3-containing vehicle in the water-in-oil formulation resulted in significant improvement of skin hydration; there was no positive effect on TEWL, though. By contrast, the combination of both ceramide-3-containing vehicles with urea 5 % or 10 %, other NMF components, glycerol and GG showed a significant improvement in skin hydration and TEWL compared both to the vehicle alone as well as to untreated skin [38]. In another study in which one side of the body was treated with a combination of ceramides, urea and vitamins and the other with urea alone, the former yielded better results with regard to TEWL and hydration [50].

In the treatment of xerosis of the feet, a ceramide-containing topical preparation that also contained urea 10 %, glycerol, fatty acids, allantoin and panthenol showed more rapid reorganization of the lipid lamellae in the stratum corneum as well as greater improvement in TEWL and skin hydration than the vehicle [105].

In newborns with an increased risk of atopy, daily skin care with either sunflower oil or various paraffin, petroleum jelly or ceramide-based emollients significantly lowered the risk of developing atopic dermatitis in the first six months of life [106]. The authors did not comment on the individual effect of the ceramide-based preparation.

Natural oils

Natural oils in topical preparations should contain a high percentage of omega-6 fatty acids (linoleic acid in particular). A high proportion of monounsaturated fatty acids (e.g., oleic acid) seems to have an unfavorable effect on skin barrier function.

Many oils also differ in their vitamin and phytosterol content as well as their antimicrobial effects. However, the clinical significance in the treatment of xerosis cutis has not been sufficiently investigated.

In general, the combination of oils and remoisturizing substances is better than the use of oils alone.

Natural oils differ in their content of triglycerides, free polyunsaturated omega-3 fatty acids (eicosapentaenoic acid and docosahexaenoic acid) and omega-6 fatty acids (including linoleic acid, gamma linolenic acid (GLA), eicosadienoic acid, arachidonic acid), monounsaturated oleic acids (e.g., oleic acid) and saturated fatty acids (e.g., lauric acid and caprylic acid) as well as in their content of vitamins (vitamin E, vitamin A), flavonoids, triterpenes and phytosterols (see ceramides) [107] and in their antiseptic properties (e.g., lauric acid) [108–110] (Table 7). Important cosmetic issues to be considered include the speed with which a given oil spreads on the skin, how rapidly it is absorbed and how long its emollient effect persists. All of these factors depend on its spreadability. When used for facial skin care, it is essential to consider the extent of any comedogenic effects.

Similar to paraffin oils, many natural oils form a water-repellent layer on the surface of the skin, thereby reducing TEWL. Almond oil, soybean oil, avocado oil and coconut oil [115] have a strong occlusive effect similar to that of paraffin oil [116].

Table 7 Selection of oils based on their linoleic acid content [111–113].

Substance (INCI)	Linoleic acid (18:2)	Linolenic acid GLA (18:3 n-6)[1] ALA (18:3 n-3)[2]	Oleic acid (18:1) (monounsaturated)	Reference
Evening primrose oil (*Oenothera biennis*)	74 %–80 %	7–14 %[1]	8 %	[127]
Safflower oil *(Carthamus tinctorius)*	53.5 %–83 %	0–0.1 %	8.4–21.3 %	
Grapeseed oil *(Vitis vinifera)*	58 %–78 %	0–1.0 %	12–28 %	[114]
Sunflower seed oil *(Helianthus annuus)*	48–74 %	0–0.3 %	14–39 %	[120–124]
Soybean oil *(Glycine soya)*	48–59 %	4.5–11.0 %[2]	17–30 %	
Wheat germ oil *(Triticum vulgare)*	55–60 %	4.0–10.0 %[2]	13–21 %	
Blackcurrant seed oil *(Ribes nigrum)*	46 %	12–16 %[2]	10–15 %	
Borage oil (*Borago officinalis*)	45 %	18–25 %[1]	20 %	[128]
Argan oil *(Argania spinosa)*	34 %	0.1 %	45 %	[125]
Avocado oil *(Persea gratissima)*	8.6 %		72.8 %	
Almond oil *(Prunus dulcis)*	8–28 %	0–0.2 %	64–82 %	[115]
Jojoba oil*(*Simmondsia chinensis)*	5 %		11.2 %	[114]
Castor oil *(Ricinus communis)*	4.3–9.7 %	0–1 %	1.8–7.7 %	
Olive oil *(Olea europea)*	3.5–21 %	0–1.0 %	55–83 %	[116–118]
Coconut oil (*Cocos nucifera)*	1.0–2.5 %	<1.1 %	5–8 %	[114, 132, 133]

*Jojoba is a wax consisting of up to 50 % of wax esters, very similar to human sebum.

Table 8 Possible clinical applications of urea based on various concentrations.

Urea concentration	≤ 5 %	≤ 10 %	> 10 %–40 %
Effects	Hydrating and smoothening effect	Strong hydrating effect; in addition, antimicrobial and antipruritic effects	Additional keratolytic effect
Range of application	– Daily skin care for hands, feet and body – Smoothens moderately scaly skin – Relieves mild pruritus	– Daily skin care for severely scaly or fissured hands/feet, body – Basic skin care for aging skin, foot xerosis, AD, psoriasis, ichthyosis, pruritus	Short-term use – In patients with severely scaly, hyperkeratotic feet* – To dissolve nails affected by onychomycosis.

*not to be used on rhagades; AD, atopic dermatitis.

The composition of saturated, mono- and polyunsaturated free fatty acids plays a significant role in terms of skin barrier restoration: a large proportion of monounsaturated fatty acids (e.g., oleic acid in olive oil) weakens the skin barrier [117–119]. By contrast, a large percentage of polyunsaturated omega-6 fatty acids, such as linoleic acid, which are preferably used to provide skin barrier lipids (linoleoyl ceramides), strengthens the skin barrier [120]. This effect has been shown for sunflower oil in particular both in adults [121] and infants [122–125]. In a study of 60 postmenopausal women, oral and topical use of argan oil had a positive effect on skin hydration [126].

Given that the epidermis is unable to desaturate essential fatty acids, it depends on the supply of gamma linolenic acid (GLA; e.g., evening primrose oil, borage oil) from dietary intake or through the skin. GLA is an important precursor of eicosanoids. These tissue hormones exert immunomodulatory effects thought to be involved in a number of inflammatory skin disorders such as atopic dermatitis. In a meta-analysis of patients with atopic dermatitis, oral administration of GLA-rich **evening primrose or borage oil** showed no significant added value [127]; topical use has been shown to be only mildly effective [128, 129]. The combination with other ingredients has been reported to result in clinical improvement in skin parameters [126, 127], as well as a reduction in *Staphylococcus aureus* colonization [130, 131]. In this context, coconut oil has also been shown to be effective due to its high lauric acid content [132, 133]. To date, the effects of GLA or lauric acid on xerosis cutis have not been conclusively elucidated.

Skin-soothing substances

M. Kerscher and M. Augustin

In patients with severe skin dryness, the impaired skin barrier and the associated secretion of proinflammatory cytokines may give rise to inflammatory erythema. In addition to lipid-replenishing and remoisturizing therapy, this also requires symptomatic (skin-soothing, anti-inflammatory) treatment. Substances that have demonstrated skin-soothing effects in clinical studies and that were most frequently mentioned by the experts during the consensus process include licochalcone A, dexpanthenol, bisabolol and oat extract. These compounds are briefly discussed below.

Licochalcone A

A natural ingredient derived from the roots of the Chinese licorice plant (*Glycyrrhiza inflata*), **licochalcone A** inhibits the secretion of inflammatory mediators such as NF-κB, IL-6 and TNFα by various skin cells and protects the skin from free radicals [134]. Due to these anti-inflammatory properties, licochalcone A has soothing effects on irritated skin and visibly decreases erythema, as has been shown in studies of patients with atopic dermatitis [135] and facial erythema [136].

Dexpanthenol

Given its high tolerability, **dexpanthenol**, the precursor of vitamin B5, is primarily used in products intended for sensitive skin [137]. The substance improves hydration of the stratum corneum and reduces TEWL [138–140]. Moreover, it promotes wound healing due to increased fibroblast proliferation and epithelialization [141]. The clinical fields of application range from atopic dermatitis, diabetic feet, diaper dermatitis to fissures and scars (in combination with silicone oil) following burn injuries or skin grafts [137].

Oat extract

Oat extract (*Avena sativa*) is used in its colloidal form for the treatment of dermatitis and pruritus. Clinical studies have provided evidence of its anti-inflammatory and immunomodulatory

effects in topical preparations [142]. Colloidal oatmeal extracts have been shown to reduce proinflammatory cytokines in vitro and to result in clinical improvement in terms of skin dryness, roughness and scaling in vivo [143]. The skin barrier is strengthened due to its content of oat lipids (omega-3 linoleic acid and omega-6 linolenic acid). Phenolic flavonoids and saponins exert anti-inflammatory effects by inhibiting the release of NF-kB and IL-8 in a dose-dependent manner. In vitro, oat extract stimulates keratinocyte differentiation, increases filaggrin expression and promotes synthesis and excretion of epidermal lipids. Oat extract has been shown to promote wound healing and to result in significant clinical improvement in children and adults with atopic dermatitis and in elderly patients with chronic pruritus [142]. Despite good clinical results and common usage, many studies have reported sensitizations to occur due to the amount of oat proteins (approximately 15 % in extracts). In rare cases, these sensitizations led to food allergies in children [144–146]. The risk-benefit profile should therefore be carefully weighed in children in particular.

Bisabolol

Bisabolol is an important component of the essential oil of chamomile, which, for centuries, has been one of the most popular medicinal plants [147]. A sesquiterpene with anti-inflammatory, skin-soothing and barrier-stabilizing properties, bisabolol is used for skin regeneration and wound healing, for instance, following sunburns or burn injuries. While there have been reports of contact sensitization, they have been primarily attributed to contamination with other plant proteins (especially mayweed) due to poorly controlled farming conditions [148, 149].

Antipruritic substances

M. Kerscher and M. Augustin

Pruritus is defined as an unpleasant sensation that triggers the desire to scratch [24]. Clinically, it may be associated with skin disorders with (e.g., atopic dermatitis) or without inflammatory skin lesions (e.g., xerosis cutis) as well as in the context of psychosomatic disorders. Xerosis cutis is one of the most common causes of chronic pruritus [150, 151]. Topical treatment options available have been reviewed by Elmariah et al. and – for elderly patients – by Pierreira et al. [152, 153]. The substances most commonly used for xerosis cutis by the expert panel are briefly discussed below.

Polidocanol

A polyalkylene glycol ether, polidocanol (synonym: laureth 9, macrogol lauryl ether, lauromacrogol 400) is a nonionic surface molecule with local anesthetic properties. Pursuant to information contained in the DAC/NRF (German Pharmaceutical Code/New German Formulary) on the "dosage of active ingredients for topical application: normal concentrations, pediatric concentrations and maximum concentrations of active ingredients used in dermatology", a therapeutic concentration of 3–10 % polidocanol is recommended both for adults and children. The substance can be expected to be well tolerated, as there is no specified maximum concentration. In an open multicenter trial of 1,611 pediatric and adult patients with atopic dermatitis, contact dermatitis, psoriasis and idiopathic pruritus, the combination of urea 5 % and polidocanol 3 % resulted in significant improvement or resolution of pruritus in 50 % of the patients [154]. At concentrations of 2–10 % in combination with urea 5 %, polidocanol has proved to be effective in the treatment of large areas of skin affected by urticaria [155]. A scalp tonic containing urea, lactate, polidocanol and licochalcone A has been clinically shown to improve scalp dryness and pruritus [156].

Cold (TRPM8) receptor activation

Active ingredients that activate the TRPM8 cold receptor have a cooling and antipruritic effect by superimposing the pruritus signal through sensory conduction.

Menthol is one example of a cooling agent that binds to the TRPM8 receptor and has a transient cooling effect. A derivative of menthol, **menthoxypropanediol (MPD)** is a highly potent agonist of the TRPM8 receptor. It has a stronger cooling effect than menthol. In a double-blind, vehicle-controlled comparative trial (n = 70), patients with dry, pruritic skin were treated with either MPD in combination with a cyclohexanecarboxamide (CHC) derivative, another cooling agent, or the corresponding vehicle; treatment duration was six weeks. Patients on MPD in combination with CHC experienced significantly stronger and longer-lasting antipruritic effects than individuals in the placebo group [157].

N-palmitoylethanolamide

Palmitoylethanolamide (PEA) is an endogenous, fatty acid amide that agonistically binds to an intranuclear receptor. The substance has numerous biological functions, including positive effects on chronic pain, cutaneous inflammation and pruritus. Topically applied, it has antipruritic effects in patients with xerosis cutis [158].

Treatment algorithm for xerosis cutis

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Based on the above remarks and a review of the literature, the expert panel used a consensus process to develop a symptom-based treatment algorithm (Figure 6).

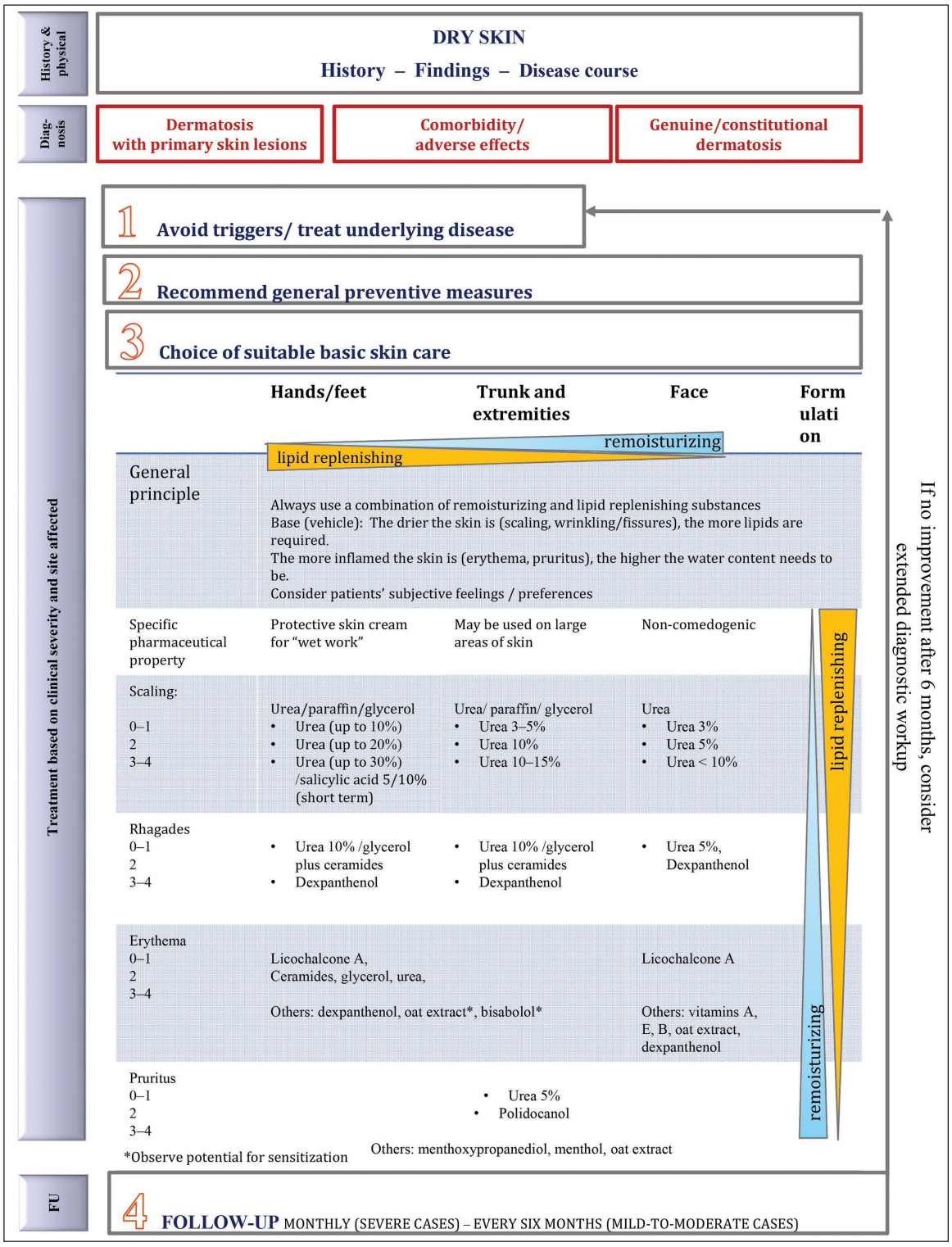

Figure 6 Algorithm for the diagnostic and therapeutic approach to xerosis cutis.

Scaling

The stratum corneum is a layer that continually renews itself and is subject to a natural and usually **invisible desquamative process** that involves dissolution of corneodesmosomes in the uppermost skin layer and enzymatic degradation of the intercellular lipid bilayer. Scaling becomes visible only when corneocytes are shed in large groups of at least 100 cells. This can be the case if there is a lack of NMF (e.g., atopic dermatitis, ichthyosis), in case of increased epidermopoiesis with a shortened turnover time (hyperproliferative keratosis, psoriasis) or in case of a disruption of the intercellular lipid bilayer (retention hyperkeratosis).

For the treatment of scaling, the expert consensus recommends the use of urea, irrespective of clinical severity (strong consensus, 100 %). The choice of concentration depends on the site affected and on the underlying skin disease. Urea should not be used on open lesions or on atopic skin in children <2 years of age (stinging effect).

Urea is among the best-studied and most important ingredients for the treatment of xerosis cutis [159].

The combination of urea with ceramides, NMF and glycerol/GG is significantly more effective than treatment with urea or the vehicle alone [50, 38].

For topical use, it is essential to consider various aspects, including the urea concentration, the individual condition of the skin, the nature of the underlying disease as well as the age of the patient. In clinical studies of patients with generalized or senile xerosis, atopic dermatitis, psoriasis and ichthyosis as well as palmoplantar hyperkeratosis and severe pruritus (e.g., aging skin), a concentration of 10 % was used in most cases. A concentration of 5 % is recommended for sensitive skin (baby skin, fragile aging skin or facial skin) or if there is only mild xerosis.

Other remoisturizing substances to be considered include glycerol 5–10 % (spontaneously mentioned by 33 % of the experts) or lactic acid 5 % (mentioned only once). Lactic acid (lactic acid-lactate buffer) stabilizes urea-containing topical preparations and thus ensures an optimal pH. Occlusive or lipid-replenishing components mentioned by the experts primarily included paraffins (spontaneously mentioned by 33 % of the experts) and ceramides (mentioned only once).

Fissures, rhagades

Urea-containing topical preparations are primarily recommended to be used for the prevention of rhagades.

The combination of urea with glycerol and ceramides is also recommended. Urea should not be used on open lesions. Dexpanthenol may be used in such cases.

Small cracks and fissures in the skin may be the result of impaired cutaneous elasticity and smoothness. The clinical correlate is eczéma craquelé. If these fissures become deeper (rhagades), they may not only become quite painful but they may also give to pathological bacterial colonization. Rhagades most commonly develop at sites with few or no sebaceous glands, e.g., hands, feet, lips and lower legs. Individuals with filaggrin mutations have also been shown to more commonly develop fissures on the hands [160].

A recent systematic review on the treatment of foot xerosis revealed that urea-containing topical preparations were the best-evaluated treatment options for this condition [64]. Liquid cyanoacrylate has also been investigated in the treatment of deep pedal rhagades [161]. Basic skin care ingredients to be used for rhagades and recommended by the expert panel included urea 10 % (spontaneously mentioned by 67 % of the experts), glycerol (spontaneously mentioned by up to 60 % of the experts), lactic acid or salicylic acid (mentioned only once); ceramides and shea butter (spontaneously mentioned by up to 50 % of the experts) were mentioned as lipid-replenishing components to be used.

Dexpanthenol (spontaneously mentioned by 33 % of the experts) and madecassoside (mentioned only once) were mentioned for the treatment of deep rhagades. If there is no clinical improvement on the aforementioned basic skin care measures, pharmaceutical agents (e.g., class 3 corticosteroids and ammonium bituminosulfonate) may be used.

Erythema

If patients develop erythema, the etiology/underlying disease should be investigated (e.g., atopic dermatitis, allergic dermatitis, psoriasis or infections) and individually treated. Apart from effective remoisturizing (urea, glycerol) and lipid-replenishing (ceramides, shea butter) therapy, treatment may also include skin-soothing ingredients such as licochalcone A (spontaneously mentioned by 40–100 % of the experts, depending on the site affected), dexpanthenol, bisabolol, and oat extract (each mentioned once). With regard to the latter two substances, it is important to observe their potential for sensitization (depending on the quality of the ingredients).

There is strong consensus (100 %) for the use of licochalcone A for erythema, depending on the site involved.

Severe erythema that cannot be managed with basic skin care should be treated with anti-inflammatory agents. Corticosteroids or topical calcineurin antagonists are potential candidates.

Pruritus

Effective remoisturizing and lipid-replenishing skin care can generally also have antipruritic effects. Urea in particular has been shown to be effective in this regard. If this approach is not sufficient, topical antipruritic ingredients such as polidocanol (therapeutic concentration: 3–10 %) may be added in the treatment of both adults and children.

Urea (strong consensus, 83 %) and polidocanol (moderate consensus, 67 %) are used for the treatment of xerosis-related pruritus.

Menthoxypropanediol, menthol, licochalcone A and oat extract were also mentioned by the experts. Various circumstances warrant an extended diagnostic workup and possibly the use of systemic agents: 1) The pruritus does not improve in the medium or long term, 2) there is generalized pruritus also occurring at sites not affected by xerosis, and 3) no triggers have been found. For more information, the reader is referred to the recently published guidelines for chronic pruritus by Ständer et al. [11].

Sufficient quantity and frequency of application

Calculating the required quantity of basic skin care products is an important aspect in terms of effective as well as economic skin barrier restoration. The "fingertip unit" and "palm of the hand" rule are the most commonly used and readily understandable bases for calculation [162] (Table 9).

A fingertip unit (corresponds to approximately 0.55 grams) is sufficient

- for one palm (= 1 % of the body surface area) and twice-daily application
- for two palms (= 2 % of the body surface area) and once-daily application

Adherence and preference

M. Augustin

Compliance and adherence play a key role [163, 164] in the treatment and prevention of xerosis cutis. The success of any treatment regimen depends on how consistently and diligently the required measures are applied. Conversely, the effectiveness of xerosis treatment can be considerably impaired if measures that have been agreed upon are not implemented.

Research on patient adherence has shown that no more than 40 %–60 % of recommended topical treatment measures are actually carried out by patients. There are numerous reasons for why patients are non-adherent, some of which can be specifically addressed. The following factors in particular have a negative impact on adherence as regards topical skin care [165–167]:

- Poor tolerability of the topical preparation or an unpleasant odor
- Organizational reasons that prevent the practical implementation or the chosen formulation is difficult to apply to the skin
- Lack of information regarding the required measures
- Lack of trust in the physician's recommendations
- Negative attitude on the part of the patient ("it won't help", "it is bad for me")
- Lack of consensus between patient and physician regarding the measures to be taken
- Lack of treatment success as perceived by the patient
- Patient is not burdened by the skin condition

The following measures may help improve adherence [165, 168]:

- Selection of a well-tolerated topical preparation that meets the patient's clinical needs
- Positive attitude on the part of the physician towards the measures to be taken

Table 9 Calculated quantity requirement of basic skin care products used for the treatment of xerosis cutis. The quantities given are based on the affected body surface area and twice-daily application (modified after [162]).

Body region	Affected BSA (%)	FTUs per single application	Daily quantity (twice-daily application)	Weekly quantity (twice-daily application)	Monthly quantity (twice-daily application)
Both palms	2 %	1 FTU	1.1 g	7.7 g	33.0 g
Both soles	3 %	1.5 FTUs	1.65 g	11.6 g	49.5 g
Face and neck	5 %	2.5 FTUs	2.75 g	19.3 g	82.5 g
Trunk (front and back)	16 %	8.0 FTUs	8.8 g	61.6 g	264 g
Entire leg (including the foot)	16 %	8.0 FTUs	8.8 g	61.6 g	264 g

FTU, fingertip unit, g, gram, BSA, body surface area.

- Simplification of the topical treatment regimen
- Lower frequency of applications
- Repeatedly providing the patient with information
- Feedback and recall
- Involvement of relatives as regards the treatment of difficult-to-reach sites (e.g., the back)
- Clear instructions for use (e.g., written treatment plan)
- Electronic reminders

These factors require that sufficient information be given to patients and that they have a good understanding regarding the implementation of the required measures. To this end, the following tools are available to the physician:

- Explain to the patient the relevance of xerosis cutis in plain language
- Explain the benefits of treating the condition using illustrations and diagrams
- Let the patient try out various products at the office during the consultation
- Provide the patient with multiple samples of dermocosmetic products and let the patient participate in the decision
- Actively inquire about potential problems associated with the application of the dermocosmetic product prior to and during the course of treatment
- In case of non-adherence, do not lecture the patient but rather inquire about possible reasons

Discussion

Xerosis cutis is one of the most common findings in everyday clinical practice – not only for dermatologists but also for office-based pediatricians, general practitioners, internists and geriatricians as well as for physicians working in hospitals. However, the diagnosis of "xerosis cutis" is only very **rarely made as a distinct diagnosis**. Instead, "dry skin" is frequently considered to be an associated symptom that is addressed merely peripherally or not recognized as such at all [3].

In the opinion of the expert panel, this approach does not match the potential risk xerosis cutis poses if left treated inadequately. For this is not just a question of "cosmetically enhancing" the appearance of the skin or of relieving pruritus. In all phases of life, the skin functions as a barrier against noxious external factors. Xerosis cutis is associated with an impairment in barrier function, which makes the skin more permeable to allergens and harmful external factors. Potential sequelae include sensitizations as well as allergic disorders or conditions associated with chronic irritation. These aspects are particularly important for infant care and in occupational dermatology. In elderly individuals, the natural regenerative mechanisms of the skin slow down. Consequently, cutaneous fissures as well as moisture- and pressure-related ulcers develop, which could be avoided through adequate skin care. Such measures not only have positive effects on quality of life but may also be crucial in terms of prolonging life in care-dependent patients.

The goal of the present position paper was to provide physicians across all specialties with a practical approach to the diagnosis and treatment of patients with xerosis cutis. The intention was to integrate both the available evidence and expert opinions in the development of a useful diagnostic and treatment pathway.

Assessing the available evidence and limiting the scope of the subject matter were important components in terms of addressing the topic of "diagnosis and treatment of xerosis cutis". Given that xerosis cutis is frequently discussed in the context of skin disorders such as atopic dermatitis or psoriasis, the expert panel deemed it necessary to focus only on select aspects. A structured literature search on the topic of "dry skin" yielded many nonspecific hits, whereas the search for "xerosis" resulted in only few relevant studies being found. Many publications retrieved for "emollients" or "moisturizers" referred to atopic dermatitis or psoriasis, which, however, are based on a different pathogenesis. While there is a certain amount of evidence for many individual ingredients as it relates to atopic dermatitis (as presented by van Zuuren in a 2017 Cochrane review) [169], there are only few studies on xerosis cutis. It was therefore decided to focus on "xerosis cutis" and the associated impairment of the skin barrier.

The diagnostic tools currently available for xerosis cutis are either only useful in the context of clinical trials [27] or they do not assess objective, subjective or treatment-relevant individual symptoms at specific sites [27]. The **xerosimeter** developed by the panel of experts meets all of these criteria and can help make a customized treatment choice based on symptoms and site affected. Moreover, it is crucial to consider age-related characteristics, such as baby skin or aging skin, as well as special sites such as the lips, eyelids, scalp and genital region. This will be the topic of a future publication.

The classification of select active ingredients presented in Table 6 was jointly developed by the panel of experts. In this context, the focus should be on incorporating as many different physiological skin components and functions as possible when selecting substances for basic skin care in patients with xerosis cutis. A distinction was therefore made between remoisturizing, lipid-replenishing and film-forming agents, which should all be components of basic skin care for xerosis cutis. Other specific active ingredients may be used for additional symptoms such as pruritus or erythema in particular. This classification, which is based on physiological and symptom-based aspects, can therefore assist in selecting and assessing the composition of skin care products. Advising patients on proper skin care is an integral part of everyday

clinical practice for any dermatologist. Experience gathered over the course of many years is useful in selecting appropriate products in this regard. Evidence-based selection of any product should preferably include published, vehicle-controlled trials. The expert panel used a multistage DELPHI procedure, during which every expert first stated his/her choice of ingredients based on the clinical findings as determined by the "xerosimeter". The choice of ingredients was subsequently compared with the relevant existing evidence, which constituted the basis for the development of consensus-based recommendations. The recommendations proposed herein and the choice of ingredients are therefore based both on expert experience as well as existing evidence. However, the authors do not claim that the ingredients discussed in this paper represent an exhaustive summary of all substances used in dermocosmetic products.

The best-studied substance, **urea is certainly the gold standard in the treatment of xerosis cutis** [42, 64, 159]. It therefore plays a crucial role in the treatment recommendations presented herein, especially with respect to scaling, fissures and, to a certain extent, also pruritus. The combination of urea with ceramides, other NMF components and glycerol increases the effectiveness even further [38]. This confirms the concept of incorporating different physiological components in skin care products. Unlike urea, there is only very limited study data available for many other well-established ingredients such as safflower oil or almond oil. There are neither studies that compare the individual ingredient with its vehicle or another commonly used skin care product, nor are there studies that provide any evidence for its efficacy compared to untreated skin. What is more, many trials merely investigated combinations of ingredients without specifying the exact percentage of each individual substance. Hence, it is impossible to conclusively and scientifically determine the effectiveness of an individual ingredient beyond the effect of the combination product investigated in the respective trial. Clinicians should therefore demand that the efficacy of any substance used in skin care products be confirmed in clinical trials, ideally with a vehicle control group and a non-treatment control group.

Finally, considering the primary tenet of medicine ("first do no harm"), the question arises as to whether and how inadequate skin care may be harmful. One such example was shown in a study that compared the effects of olive oil and sunflower seed oil on the skin barrier, with the former resulting in degraded barrier function [121]. Likewise, purely lipid-based vehicles can lead to an impaired skin barrier and facilitate deeper penetration of allergens into the skin. The same potential risk has to be observed for a number of natural – partly insufficiently purified – ingredients such as bisabolol, oat extract or lanolin when used in patients with damaged skin [144–146, 148].

The treatment algorithm developed herein is based on evidence and expert experience. It is intended to assist physicians in everyday clinical practice in selecting skin care agents that target the patient's symptoms and stabilize the skin's barrier function. As with all therapies, individual patient preferences must be considered. Particularly relevant aspects in this regard include the spreadability of the skin care product, its scent and the subjective feeling of "soft skin" [168].

Conclusion

The present position paper provides a summary of the existing scientific data relating to basic skin care for xerosis cutis and fills evidence gaps with practical experience. The article aims to raise awareness in terms of prevention and early treatment of xerosis cutis in order to prevent potential sequelae. The "xerosimeter" presented herein is meant to standardize the diagnostic approach to xerosis cutis and to facilitate the practical implementation of diagnosis and follow-up. In line with this approach, the expert panel developed a structured treatment algorithm that matches the various clinical symptoms and specific sites of the body with appropriate active ingredients and suitable formulations for basic skin care. The choice of ingredients was compared with the existing evidence, which constituted the basis for the development of consensus-based expert recommendations. Data from clinical trials and the expert consensus show that optimal basic skin care for xerosis cutis consists of a topical preparation that both provides the skin with moisture and stabilizes the skin barrier. A combination of such ingredients is superior to their individual application. Urea is the substance that has been most extensively studied in the treatment of xerosis cutis. Studies have shown very good hydrating effects, especially in combination with glycerol and other NMF components [38, 50]. The most effective ingredients for lipid replenishment are physiological skin lipids such as ceramides or omega-6 fatty acid-containing oils. Mineral oils enhance the barrier-stabilizing effect. In case of erythema and skin irritation, skin-soothing ingredients such as licochalcone A or dexpanthenol are recommended. Polidocanol or TRPM8 antagonists may be added as antipruritic substances. Ingredients or combinations thereof for which there is solid evidence from studies should be preferred in the management of xerosis cutis.

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Conflicts of interest

A. Körber has received lecture and consultancy fees as well as honoraria for participation in clinical trials from Abbvie, Biogen Idec, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Janssen-Cilag, MSD, Novartis, Pfizer, Grünenthal, and Almirall.

D. Wilsmann-Theis has received lecture and consultancy fees, travel grants as well as honoraria for participation in clinical trials from Abbvie, Almirall, Amgen, Beiersdorf, Biogen, Boehringer Ingelheim Pharma, Celgene, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Leo, Lilly, Medac, Merck Sharp & Dohme Corp., Novartis, Pfizer, UCB Pharma, VBL.

G. Itschert has received lecture and consultancy fees as well as travel grants from Beiersdorf AG, LEO Pharma and Janssen Pharma.

M. Augustin has received lecture and consultancy fees from Almirall, Beiersdorf AG and LEO Pharma.

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