REVIEW ARTICLE

Gerontodermatology: the fragility of the epidermis in older adults

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Abstract The proportion of adults over 60 years of age is rapidly increasing and is estimated to reach approximately one-sixth of the global population by 2030. An ageing population is a real challenge for healthcare resources, including dermatologists and geriatricians, as age-related changes in skin integrity and barrier function make older adults more susceptible to developing skin pathologies such as pruritus, dermatitis and infections. Fragile skin arises from several interlinked causes, including age-related changes in skin barrier integrity, previous and current lifestyle choices, skin pathologies and medical interventions. Dermo-cosmetics can play a key role in enhancing skin care regimens and preventing pathologies in this age group. *In vitro* studies, clinical, and in-daily clinical practice studies of dermo-cosmetics have shown them to be effective in many skin conditions in older adults, like xerosis and pruritus. Incontinence-associated dermatitis (IAD), a common condition arising from contact with irritants such as urine and faeces which can significantly impact the quality of life of sufferers, can also be improved with a barrier cream in incontinent patients aged 70 years and older. This supplement focuses on the increased fragility of older skin, the development of common skin pathologies and the efficacy and tolerance of dermo-cosmetic products in older adults.
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Conflict of interests

NK is a professor of Dermatology in Kyoto Prefectural University of Medicine, DT is a professor of Dermatology at St. Luc Universitary Hospital in Brussels, GAvK provides consultancy servicese to Pierre Fabre Dermo-Cosmétique, MSA is Medical Director of A-DERMA Dermatological Laboratories and an employee of Pierre Fabre, AL is an employee of Pierre Fabre Dermo-Cosmétique, DB, LD, BG, SB-T and HD work in the Research Center of Pierre Fabre Dermo-Cosmétique.

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Introduction

Both the proportion and absolute number of older adults are increasing in nearly every country.[1] By 2030, the number of people aged 60 years and older is predicted to rise to 1.4 billion worldwide, accounting for one-sixth of the global population.[1] The skin, the major barrier between the internal and external environment, which aids in homeostatic regulation, hydration and protection against external aggressors, is visibly affected by age-related changes. As the skin ages, it becomes 'fragile' and consequently less effective at protecting against external bacterial, chemical and physical aggressors.[2] The concept of fragile skin is broad, ranging from perceived weakening and increased fragility of the epidermis, to severe pathological diseases.[3] The origins of this fragile skin can be broadly grouped into four categories: physiological (age-related), pathological (disease-related), circumstantial (environment-related) or iatrogenic (medical-related). These factors often interplay to create a complex background to fragile skin, as age, lifestyle choices (e.g. smoking,

alcohol consumption and sun exposure), medical procedures (e.g. surgery) and underlying pathologies can all contribute to the development of fragile skin. While not necessarily associated with disease per se, most patients presenting to dermatologists with fragile skin have pathological conditions such as acne, psoriasis and atopic dermatitis.[4] However, surveys reveal that a substantial proportion of people have perceived fragile skin, which, while not associated with disease, can cause redness, tightness, dryness and itching.[5,6] Globally, the incidence of fragile skin in adults has been estimated as 25–52%, across skin types and age groups.[4–6]

In older adults, skin ageing makes individuals more vulnerable to develop fragile skin and associated pathologies resulting from impaired skin barrier function. The mechanisms and clinical relevance of age-related skin deterioration, the prevalence of skin disorders in older adults in Europe and recent *in vitro*, clinical and in-daily clinical practice studies of fragile skin in this age group will be covered in this supplement.

Section 1: Fragile skin in older adults

In addition to internal age-related changes in skin structure and functionality, physiological, circumstantial, pathological and iatrogenic fragile skin causes also contribute to the weakening of the epidermis and skin barrier in older adults.

Physiological fragile skin

Older adults experience physiological fragile skin, as declines in the immune system function within the epidermis, and changes in epidermal and dermal structure contribute to a reduction in the effectiveness of the skin barrier function.[7] During adulthood, the skin layers gradually become thinner, with a faster decrease in skin thickness occurring with increased age, related to a decrease in the epidermal turnover rate.[8] Atrophy of the epidermal layer, together with flattening of the dermal-epidermal junction, leaves the skin more vulnerable to tears,[9] and the overall loss of skin thickness and subcutaneous fat provides less cushioning and support, increasing the risk of pressure ulcers and bruising.[8] The reduced epidermal turnover rate also slows the rate at which the skin heals from mechanical trauma, such as after injury or surgery.[10] Additionally, as vitamin D is produced cutaneously, a thinner skin layer leads to a decreased capacity of production in older adults, contributing to an increased risk of osteoporosis and bone fractures.[8,11]

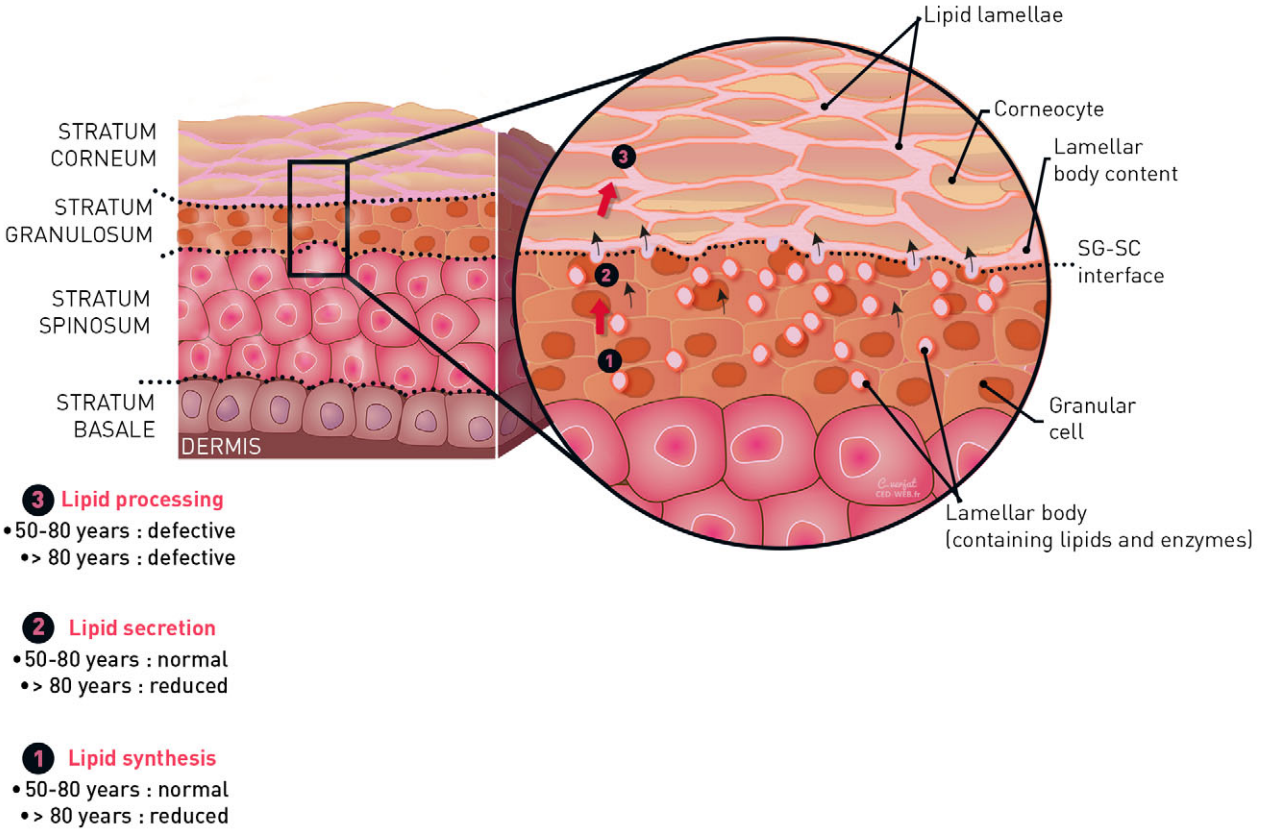

Figure 1 Epidermal barrier of older adults

In contrast to the skin's other layers, there are no changes with the stratum corneum skin thickness. However, with increasing age, the size of the corneocytes tends to increase, due to a decreased turnover, but the adhesion between corneocytes decreases. Additionally, lipid levels and hydration levels of the stratum corneum decrease, which contributes to an increased dryness and a reduced skin strength.[9,12] Adults aged between 50 and 80 years have normal lipid synthesis and secretion, but changes in lipid processing (Fig. 1). Over 80 years of age, adults also experience a reduction in the lipid synthesis and secretion. These changes result in a less effective epidermal water barrier and a reduced capacity to repair skin damage caused by contact irritants.[13]

Within the epidermis, as the skin ages, keratinocytes change shape and reduce in size and number. There is a reduced cohesion between the dermis and the epidermis, and a reduced epidermal turnover, leading to an increase in skin fragility and vulnerability to external aggressors.[14] Additionally, the density of melanocytes in the skin decreases by 20% for every 10 years of age, leading to uneven pigmentation.[9,15] This change in melanocytes distribution also affects wound healing, making wounds in older adults more susceptible to damage from ultraviolet light.[16] Changes also occur within the dermis layer of the skin: cellularity and vascularity are both reduced, and there is a decrease both in fibroblasts number and activity. From around 80 years of age, skin stiffness decreases as collagen is less produced by fibroblasts, elastin fibres start to be degraded, and collagen fibres become more disorganized.[9]

In addition to changes within the skin, surface contours also change as skin ages, with increases in furrows, wrinkles and lines.[17] The number of closed polygons (NCP), a measurement of these cutaneous microstructures, has been shown to be negatively correlated to age and can be a useful tool in evaluating the extent of skin ageing and the efficacy of anti-ageing skin treatments.[17]

The increased fragility of ageing skin also makes it more vulnerable to tearing during daily activities, particularly in individuals who are dependent on carers for transportation and daily hygiene.[18] Skin tears have been categorized into three groups: tears without loss of tissue (category 1), with a partial loss of tissue (category 2) and with a complete loss of tissue (category 3). Within categories 1 and 2, tears can be further stratified into subcategories a and b, with the skin or flap colour being not pale, dusky or darkened in categories 1a and 2a, and being pale, dusky or darkened in categories 1b and 2b. Skin care plays a key role in maintaining skin integrity and helping to prevent skin tears in older adults. Application of emollients, barrier creams and bandages to fragile skin is recommended as a preventive measure to reduce the incidence and severity of skin tears in this age group, as well as behavioural measures to avoid unnecessary knocks and bruises.[18]

Circumstantial fragile skin

External factors to the epidermis, such as exposure to ultraviolet light, lifestyle choices (e.g. smoking, alcohol consumption), chronic illnesses, pollution and age-related hormonal changes, impact the functionality of the skin. Sunlight, which accounts for up to 80% of extrinsic effects on skin ageing,[19] has two main detrimental effects on the skin: UVA rays (approximately 95% of light waves) act as an intermediary in the formation of reactive oxygen species, contributing to oxidative skin damage of proteins, lipids and DNA within the epidermis and the dermis, whereas UVB rays (5% of light waves) cause a direct photochemical action on the DNA of epidermal cells.[20] Mutations induced by exposure to UV-rays can ultimately lead to skin cancer development.[20]

Smoking also increases skin ageing, with a correlation between the number of years and packs of cigarettes smoked and the degree of skin ageing.[21] Smokers have a decreased skin elasticity, and a decreased concentration of collagen due to the downregulation of collagen synthesis.[21,22] Similarly to UV radiation, smoking also increases the production of free radicals and reactive oxygen species within the skin, contributing to further collagen degradation and weakening the structure of the skin barrier. Smoking also impacts the balance of the immune microenvironment within the skin, reducing the inflammatory and restorative responses, which delays wound healing and increases the risk of postoperative infection.[23]

Pathological fragile skin

Together with intrinsic structural changes to the skin with increasing age, changes to the immune system also impact skin barrier function, leaving the skin vulnerable to external pathogens and pathologies such as eczema, xerosis and dermatitis. Immunosenescence, the age-related decline in immune system functions, impacts the inflammatory response within the epidermis, including a reduction in the number and function of antigen-presenting Langerhans cells.[24,25] This decline in immune response reduces the skin defence against infections, and together with skin structural changes, they contribute to a delayed wound healing and an increased sensitivity to irritants.[10] Resulting skin pathologies further disrupt the balance of the epidermis and skin barrier function, contributing to 'pathological fragile skin'.[2,3,26]

Some of the most common skin pathologies in older adults are infections, dermatitis, xerosis, pruritus, tumours and pressure sores.[27] Fungal skin infections also become more common in older adults, due to a combination of intrinsic immunological and structural skin changes, but also due to the increased use of immunosuppressants, antibiotics and underlying chronic conditions such as heart, renal and liver diseases, or diabetes, which are more prevalent in older people.[28] The risk of xerosis and pruritus also increases as the skin ages. The reduction of lipids in the stratum corneum, the decreased in skin hydration and the atrophy of sweat glands all contribute to increase the skin dryness. The combination of xerosis and behavioural factors such as not applying emollients, incorrect soap/cleanser usage or taking

hot baths in the winter can further dry out the skin and contribute to pruritus.[10,14,29] Other medical problems such as diabetes, chronic liver, kidney and heart disease, cancer, and multiple drugs use also contribute to pruritus development.[29]

Dermatitis is another common condition in older adults. The weakened skin barrier makes older adults more sensitive to irritants, like cleaning products. In a study by Rubegni *et al.*,[30] over 20% of the patients attending a dermatology outpatients clinic with a dermatitis had contact dermatitis; of these, 70% of women with dermatitis of the hands had this pathology following contact with irritants related to housekeeping. While atopic dermatitis is uncommon in older adults (compared to babies),[31] incontinence-associated dermatitis (IAD), due to a prolonged exposure to stools or urine, is an increasing concern especially within long-term healthcare settings, where many patients are incontinent.[32–34] Faecal incontinence, high BMI, type 2 diabetes and 'friction and shear' problems have all been associated with an increased risk of IAD in incontinent patients.[32,33] IAD can range from inflamed skin to severe partial thickness wounds, which may become infected, resulting in other skin pathologies.[32]

As many older adults in healthcare settings have limited activity, pressure sores can develop due to long periods of pressure on the same area of the skin.[35] The overall reduction in skin thickness and fat layer, as well as the increased fragility of the capillaries in the skin, contributes to increase the risk of developing pressure sores in older adults.[36] Sores may become chronic and develop into open wounds, leading to bacterial and fungal skin infections, further weakening the barrier function of the skin.

Iatrogenic fragile skin

Finally, older adults can also experience the fourth type of fragile skin, following medical interventions or medications, termed iatrogenic fragile skin. While medical interventions (e.g. surgical operations, chemical peels) can directly impact and damage the skin, this, combined with the other three types of fragile skin outlined above, makes skin in older adults particularly vulnerable to complications following medical procedures.[10] Skin thinness and loss of elasticity contribute to healing difficulties and tearing after surgical interventions. In addition, the increased risk of infection makes older adults more vulnerable to poorer outcomes from medical procedures.[37,38]

Medications can also increase skin fragility. For example, repeated application of topical steroids results in structural changes to the epidermis, increasing the risk of pathologies and vulnerability to injuries.[39,40] The use of multiple medications increases with age, with many patients taking five or more medications daily. Many dermatologists are not aware of all the medications their patients are taking, and therefore of potential interactions or impacts on skin barrier integrity.[39] The increased prevalence of multiple diseases and conditions in older adults makes gerontodermatology particularly challenging to manage. With the increase in both the proportion and overall numbers of older adults, the burden of age-related disorders will have an ever larger impact on the health sector. Understanding the mechanisms of skin ageing and the multiple pathologies linked to epidermal fragility in older adults, when considered together with confounding factors such as mobility and chronic diseases, can aid in individualizing dermatological treatments in this diverse population.

Section 2: Europe's ageing population: prevalence of dermatological conditions

Globally, the proportion of people over 60 years old is growing faster than any other age group, as the result of a lower mortality, combined with a longer longevity, and a reduced birth rate.[41,42] Within Europe, the proportion of the population aged over 60 years old is estimated to reach or exceed 30% by 2050.[42] Currently, Italy and Germany have the second and third highest

Table 1 Top ten countries or areas with the highest proportion of adults aged over 60 years in 1980, 2017 and projection for 2050. Adapted from United Nations population ageing report[43]

Rank	1980		2017		2050	
	Country/Area	Population ≥ 60 years of age (%)	Country/Area	Population ≥ 60 years of age (%)	Country/Area	Population ≥ 60 years of age (%)
1	Sweden	22.0	Japan	33.4	Japan	42.4
2	Norway	20.2	Italy	29.4	Spain	41.9
3	Channel Islands	20.1	Germany	28.0	Portugal	41.7
4	United Kingdom	20.0	Portugal	27.9	Greece	41.6
5	Denmark	19.5	Finland	27.8	Republic of Korea	41.6
6	Germany	19.3	Bulgaria	27.7	Taiwan	41.3
7	Austria	19.0	Croatia	26.8	Hong Kong	40.6
8	Belgium	18.4	Greece	26.5	Italy	40.3
9	Switzerland	18.2	Slovenia	26.3	Singapore	40.1
10	Luxembourg	17.8	Latvia	26.2	Poland	39.5

percentage of adults aged 60 years and over in the world (Table 1), whereas Spain is predicted to have the second highest proportion in the world by 2050, totalling 41.9% of the population.[43]

While population estimators generally use an aged-based cut-off of 60 years to define 'older adults', other measures often use different age thresholds (from 50–70+ years). This wide range in definitions impacts the overall characteristics of the considered population, especially in terms of activity level and average health status. For example, companies often market products to a senior population starting from 50 years of age.[44] People of this age are generally a lot more active and have less health concerns than older adults who are often included in clinical studies, where the definition is often 60 years or older. The 60–75 years age group tends to be a mixture of active, healthy adults, together with 'young senior', who are less active and suffer from more pathologies. The 75 years and older group is mainly composed of 'seniors', including a large percentage of frail and dependent individuals. Additionally, there is often a difference between physiological and psychological age (i.e. how old a person feels), based on factors such as mobility, health and independence, which contribute to whether they consider themselves to be 'senior' or not.[45] The age at which people consider themselves to be 'senior' is also increasing with time. In 2015, the mean age at which people started to feel that they belong to the senior category was 66 years, whereas in 2016 this age had increased to 69 years.[45,46] Therefore, the 'senior' population is a variable group, including active, healthy individuals, as well as bedridden patients with chronic health problems. In consequence, this population represents a real challenge to gerontodermatologists.

In dermatological terms, physiological age plays a large role in the function and integrity of the epidermis. However, lifestyle factors throughout life and as an older adult also impact epidermal integrity, such as smoking, and exposure to UV radiation.[47,48] Several studies have assessed the epidemiology of skin diseases and associated predictive factors in older adults. In a study including residents of three nursing homes in Turkey, Kilic *et al.*[49] reported that fungal infections and xerosis were the most common dermatological diseases, occurring in 49.7% and 45.3% of residents, respectively. Male gender was an associated risk factor for both conditions, while being bedridden was also a risk factor for xerosis. Dermatitis and pruritus were less prevalent in these older adults, with only 11% and 10.3% of individuals experiencing the conditions, respectively. These findings were

Table 2 Prevalence of skin disorders across dermatological studies in older adults

Study	Country/Area	Location	Number of subjects	Age	Condition and prevalence
Kilic *et al.* (2007)[49]	Turkey	Nursing homes	300	Mean: 76.4 years Range: 57–104 years	1 Fungal Infections – 49.7% 2 Xerosis – 45.3% 3 Actinic keratosis – 29.3% 4 Senile angiomas – 20.3% 5 Seborrhoeic keratosis – 11.3% 6 Eczema/dermatitis – 11.0% 7 Pruritus – 10.3%
Smith *et al.* (2002)[50]	Taiwan	Nursing homes	398	Mean: 76.2 years Range: 22–108 years	1 Fungal Infections – 61.6% 2 Xerosis – 58.3% 3 Dermatitis – 7.3% 4 Scabies – 3.3% 5 Bed sore – 1.8%
Liao *et al.* (2001)[29]	Taiwan	Outpatients hospital dermatology clinic	16 924	≥65 years	1 Dermatitis – 58.7% 2 Fungal infections – 38.0% 3 Pruritus – 14.2% 4 Benign tumours – 12.8% 5 Viral infection – 12.3%
Darjani *et al.* (2013)[52]	Iran	Hospital dermatology centre	440	≥60 years	1 Benign neoplasms – 65% 2 Erythematosquamous lesions – 35.3% 3 Precancerous lesions – 26.1% 4 Dermatitis – 16.6% 5 Pruritus – 12.3% 6 Fungal infections – 8.2%
Hahnel *et al.* (2017)[53]	Germany	Nursing homes	223	Mean: 83.6 years Range: ≥65 years	1 Xerosis – 99.1% 2 Incontinence-associated dermatitis – 35.4% 3 Pressure ulcers – 9.0% 4 Skin tears – 6.3%

Table 3 Prevalence of incontinence-associated dermatitis

Study	Country	No. included	Mean Age	Location	Prevalence
Keller *et al.* (1990)[55]	US	NA	NA	Nursing home	41%
Lyder *et al.* (1992)[56]	US	15 (Group 1, *n* = 9; Group 2, *n* = 6)	Group 1: 71 years Group 2: 82 years	Geriatric psychiatry unit	33%
Bliss *et al.* (2006)[58]	US	59 558 records	83 years	Nursing homes	5.7%
Zimmaro Bliss *et al.* (2006)[59]	US	981	79 years	Nursing homes	3.4%
Petersen *et al.* (2006)[60]	US	NA	NA	ICU unit, oncology unit, medical unit	ICU: 95% Oncology: 35% Medical: 32%
Driver *et al.* (2007)[61]	US	Phase 1: 16 Phase 2: 16	NA	ICU unit	Phase 1: 50% Phase 2: 19%
Junkin *et al.* (2008)[62]	US	2005: 198 2006: 120	NA	Hospital	2005: 54% 2006: 42.5%
Long *et al.* (2012)[57]	US	39	Median: 55 years	Long-term acute care centre	22.8%
Kottner *et al.* (2014)[32]	Austria Netherlands	3713	81.2 years	Austria: hospitals, nursing homes Netherlands: healthcare institutions	Austria: 4.3% Netherlands: 7%

ICU, intensive care unit; NA, information not available.

echoed in a similar study in a nursing home in Taiwan.[50] In this study, fungal infections and xerosis were again the most prevalent (61.6% and 58.3% of residents, respectively). Being bedridden was also found as a risk factor for fungal infection, and older age (80–90 years) was associated with an increased risk of xerosis. Regarding dermatitis, only 7.3% of residents suffered from this disease. In contrast, other studies found higher rates of dermatitis in populations of older adults. In a study evaluating the prevalence of skin diseases in 16 924 outpatients aged 65 years and older in the Dermatologic Outpatient Clinic of the National Taiwan University Hospital, dermatitis was the most prevalent condition (58.7% of patients), followed by fungal infections (38.0%) and pruritus (14.2%).[29] Similarly, in a study of dermatologists in the Netherlands, 25.7% of them reported that eczema/dermatitis was the reason for their nursing home visits.[51] The most common reason in this study was cutaneous (pre)malignancies, accounting for just over half of all visits. Fungal infections were much less common, with only 2.9% of the dermatologists stating this disease as the reason for the visit. Dermatitis was the second most common dermatological diagnosis (14.4%, after pruritus 18.9%) in patients aged 65 years and older attending a dermatological clinic in Siena.[30]

While the prevalence of skin conditions varies with the location of the study (e.g. hospital outpatient clinic versus nursing home residents), climatic variables such as humidity and sunlight exposure, or lifestyle choices,[52] the most commonly reported conditions across all the studies were the same: pruritus, dermatitis, fungal infections and benign/malignant skin tumours (Table 2).

In addition to the above-mentioned skin pathologies, older adults also frequently experience skin dryness and incontinence-associated dermatitis (IAD). A study by Lichterfeld *et al.* in nursing homes and hospitals in Germany estimated that nearly half (48.8%) of the patients, who were 77 years of age on average, experienced dry skin. The occurrence of skin dryness increased with age, and comorbidities such as pruritus, oncological and musculoskeletal diseases were identified as risk factors for skin dryness.[54] In contrast, being 'skin care independent', defined as being able to wash, shower, bath or apply skin care products independently, was associated with a lower risk of skin dryness. While the prevalence of IAD outside of community-based settings is unknown, a number of studies have been performed within nursing homes and long-term care facilities. The highest prevalence (41%) was noted by Keller *et al.*[55] across nursing home residents. A study in a small group of patients in a geriatric psychiatry unit reported a prevalence of 23–25%,[56] whereas a study in a long-term acute care centre in the United States reported a similar prevalence (22.5%) among residents on admission.[57] Other studies have estimated a prevalence of between 3% and 23% in nursing home residents, and up to 95% in intensive care units (ICU) (Table 3).

Given the burden of fragile skin and skin pathologies in institutionalized older adults, as well as potential medication interactions or contraindications in older adults with chronic illnesses, dermo-cosmetics can play a critical role in restoring the natural protective barrier function of the skin. In the remaining sections of this supplement, we discuss the *in vitro*, clinical and in-daily clinical practice studies of dermo-cosmetics containing Rhealba® Oat Extract in older adults, and their impact in reducing fragile skin and skin pathologies.

Section 3: *In vitro*, clinical and in-daily clinical practice studies of dermo-cosmetic products containing Rhealba® Oat Plantlet Extract in older adults

Rhealba® Oat Plantlet Extract is a protein-free extract which contains a high concentration of saponins and flavonoids. The

flavonoids in the extract have been previously shown to impact the anti-inflammatory arachidonic acid pathway, helping to reduce inflammation within the epidermis, whereas saponins inhibit both cytokine production and stimulation of T-cell proliferation from epidermal dendritic cells.[63] The extract inhibits bacterial adhesion, reduces the incidence of secondary skin infections and helps to stimulate keratinocytes proliferation, aiding in skin hydration.[64] Products containing the Rhealba® Oat Plantlet Extract help to restore the skin barrier function, reducing fragile skin, and associated symptoms such as itching and redness. In this section, we highlight some of the recent research on the extract in older adults, and the implications for use of these products in skin care regimen.

In vitro models

Skin care protection of a dermo-cosmetic product containing Rhealba® Oat Plantlet Extract in a full-thickness skin model of fragile skin in older adults The skin establishes a multifunctional barrier between the body and its external environment. However, it becomes thinner and more fragile with age.[3,8] Older adults present a progressive loss of skin integrity and moisture that impacts their quality of life; hence, the development of specific skin care products for this age group may aid in skin ageing. To date, there are few data from *in vitro* skin models which mimic fragile skin in older adults, allowing testing of the efficacy of specific anti-ageing dermo-cosmetic products. Therefore, the aim of this study was to first develop a full-thickness skin model that presents characteristics of exposed skin in older adults following chronic ultraviolet A (UVA) radiation and then to investigate the benefits of an A-Derma skin care product containing Rhealba® Oat Plantlet Extract in protection of fragile skin in this senior skin model.

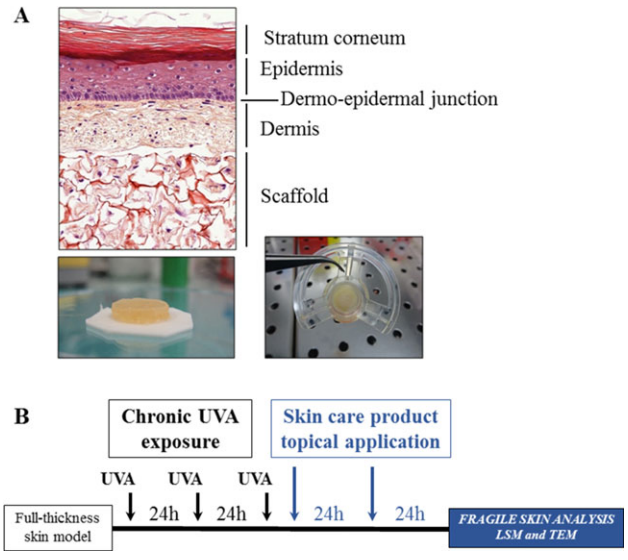

Figure 2 The full-thickness skin modelling the fragile skin model of the elderly and skin care protection by Rhealba® Oat formulation. (a) Structure of the full-thickness skin. Pictures represent the morphology of the tissue after bio-engineering reconstruction. Model is presented on its cell culture insert used to maintain the skin at the air–liquid interface. Histology of the skin is also presented after staining with hemalun eosin of paraffin sections. The three compartments of the skin are well defined as in native skin. (b) Schematic representation of the protocol for modelling the fragile skin of the elderly *in vitro* by using chronic UVA irradiation. The skin care product was topically applied after UVA exposure and fragile skin was analysed by both laser scanning microscopy (LSM) and transmission electron microscopy (TEM).

Characterization of a full-thickness skin model that mimics the fragile skin of older adults We first reconstituted a full-thickness skin model using previously reported engineering techniques.[65] Briefly, a dermal equivalent was prepared by seeding fibroblasts on top of a scaffold substrate made of chitosan-crosslinked collagen-glycosaminoglycan matrix. After culturing for 21 days, keratinocytes were seeded on the dermal substitute. After 7 days of submerged culture, skin equivalents were elevated at the air–liquid interface and cultured for further 2–4 weeks. The reconstructed skin tissue is presented in Fig. 2a and routine histology by hemalun and eosin staining revealed that the model presented the three classical layers of the skin: an epidermis presenting well-differentiated layers of keratinocytes including a *stratum corneum*, a dermo-epidermal junction (DEJ) that separates the epidermis from the dermis, which in turn was rich in fibroblasts producing extracellular matrix (ECM) and embedded in the scaffold.

To mimic the fragile skin *in vitro*, the skin model was chronically exposed to UVA, the main cause of photoaging and wrinkle formation. The skin was irradiated by using a Biosun Vilbert Lourmat device (UVA filter at 365 nm). Samples received 3 doses of 12 J/cm^2 UVA once a day and were harvested 48 h after the last UVA exposure. They were then processed to analyse the three compartments of the skin by laser scanning confocal microscopy (LSM) and transmission electron microscopy (TEM), as detailed in Houcine *et al.* and Rouvrais *et al.*, respectively.[65,66] For LSM, the fluorescent signals emitted by specific antibodies coupled to the Alexa Fluor 488® or 594® (green and red channel, respectively) were observed by using a Nikon A1$^+$ confocal microscope. Cryosections were mounted in Prolong medium with nuclear dye 4′,6-diamino-2-phenylindole (DAPI, blue channel). TEM analysis was performed by using a Hitachi HT7700 device from skin samples fixed with glutaraldehyde, embedded in epoxy resin and ultrathin sections mounted on copper grids. All experimental data were reproducible and were obtained from three independent tissue reconstructions.

The dermis is an important target of UVA radiation during the skin ageing process.[67] Therefore, the UVA-induced fragility of the dermal compartment was analysed first, with the research

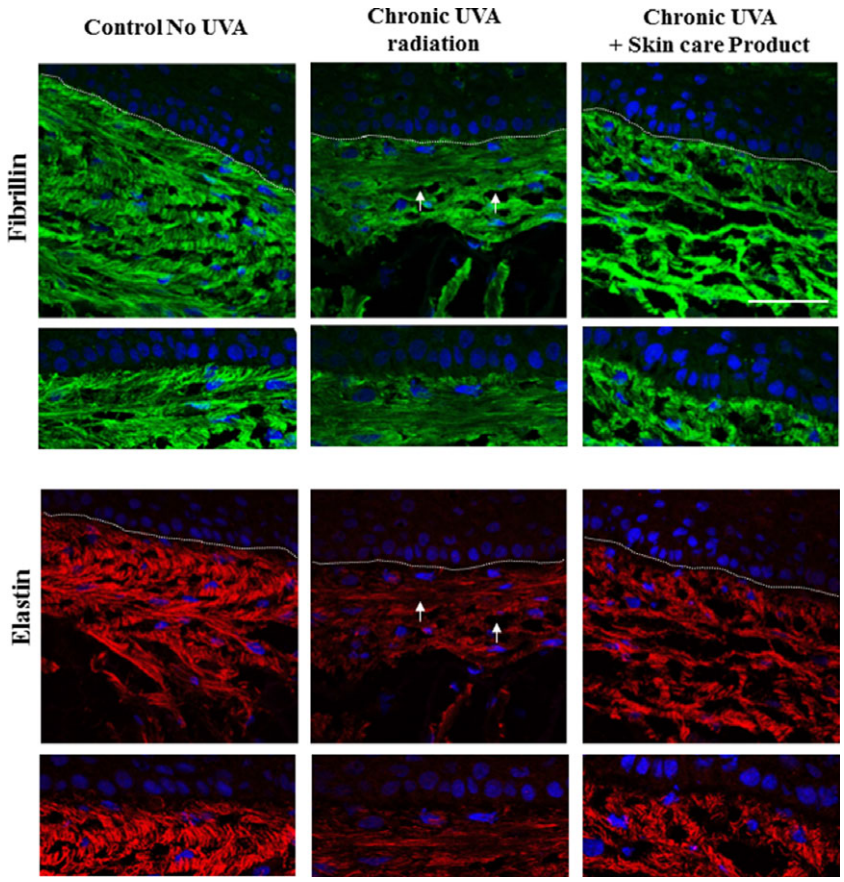

Figure 3 Skin care protection of the dermal elastic network in the full-thickness skin model of older adult fragile skin. Laser scanning confocal microscopy (LSM). Immunofluorescence staining of fibrillin (green labelling) and elastin networks (red labelling) counter-stained with DAPI (blue nuclei). Dashed line represents the dermo-epidermal junction. Arrows indicate elastic network alteration. Insert is a magnification of the DEJ area. Scale bar = 100 μm.

focussing on the cutaneous elastic system, which is deficient in older adults. Immunohistochemical assays were performed from cryosections to detect by LSM the presence of both fibrillin and elastin, major components of the elastic fibres in the dermis, in the skin model.

As shown in Fig. 3, non-irradiated control skin presented a well-developed and organized fibrillin-rich microfibrillar network (oxytalan fibres). These fibres were dense in the DEJ and were connected to the underlying elastin network. In contrast, UVA impaired the cutaneous elastic network altering both fibrillin and elastin-rich fibres in the dermis. The elastic system was strongly disorganized, especially in the papillary dermis close to the DEJ. Both fibrillin and elastin-rich fibres appeared cut and shorter under the epidermis and in the dermis. The alteration of the ECM under UVA exposure was confirmed by TEM analysis.

Figure 4a shows that the dermal fibroblasts had a different morphology in response to UVA. They seemed to be retracted and diffuse in UVA-irradiated skin. Moreover, it was evident that the ECM surrounding the fibroblasts was modified and that the collagen fibres were less dense around the cells. These data show that chronic UVA exposure induced an important disruption of the elastic network and loss of density in the dermis. Thus, the UVA-exposed skin model mimicked the loss of elasticity and ECM density observed in the fragile skin of older adults.

The next step was to study the UVA-induced fragility of the DEJ. The DEJ plays a major role in skin integrity since it allows the anchorage of the epidermis on the underlying dermis.[68] The immunostaining was focused on the laminin, a main component of the DEJ that is essential to the tissue cohesion by anchoring the keratinocytes to the dermal compartment. LSM imaging shows in Fig. 5 that laminin formed a regular network along the basal layer of the epidermis.

Moreover, the papillary dermis was also positive for the laminin since this protein is produced by the dermal fibroblasts. The ultrastructural analysis allowed visualization of the DEJ, with the presence of the hemidesmosomes in the keratinocytes and their anchorage to the underlying lamina (Fig. 4b). In response to UVA, the DEJ was strongly altered. It was disorganized and presented loss of homogeneity in the lamina but also a decrease in the anchoring fibres. Overall, the DEJ was seriously damaged by the UVA, and this loss of DEJ cohesion shown in the full-thickness skin model indicates a fragile DEJ following UVA exposure, which has been described previously in elderly patients.[68]

Since fragile skin has a skin barrier defect, we also investigated the impact on the epidermis. We first focused on the claudin-1

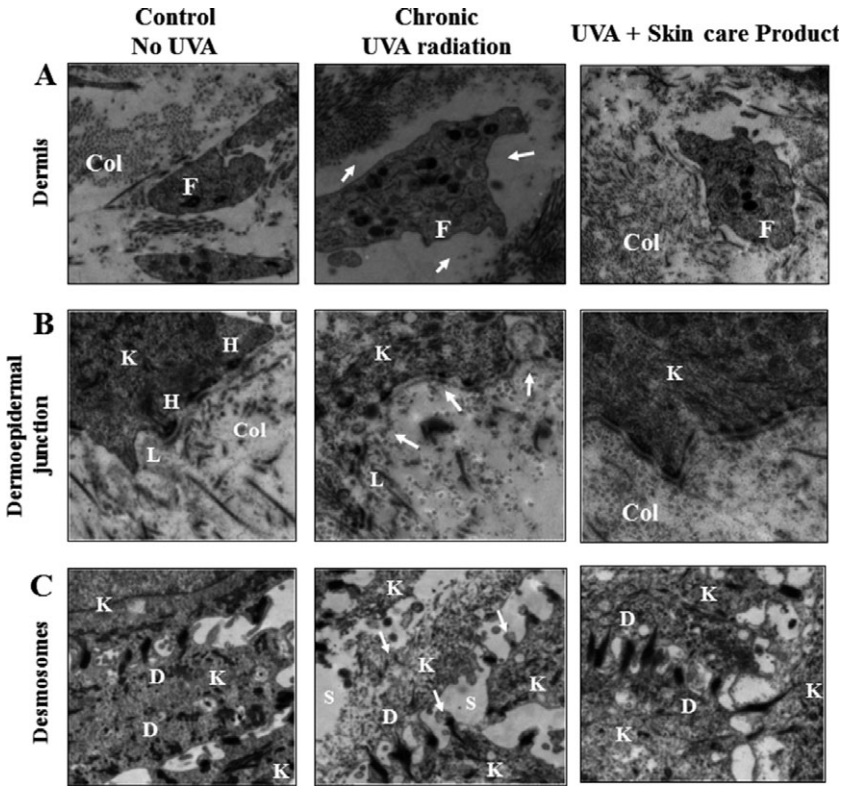

Figure 4 Skin care protection of the full-thickness skin model of older adult fragile skin analysed by transmission electron microscopy (TEM). (a) The dermis in the skin model. Ultrastructural micrographs show the density of the fibres (Col, collagen) in the dermis around fibroblasts (F). Arrows indicate ECM dermal alteration. Magnification ×3K. (b) The DEJ in the skin model. Pictures show the ultrastructure of DEJ with the presence of hemidesmosomes (H) in the basal keratinocytes (K) which are connected to the underlying lamina (L) and the dermis (Col). Arrows indicate DEJ alteration. Magnification ×3K. (c) The desmosomes in the granular layers in the skin model. Micrographs show the ultrastructure of the desmosomes (D) which link adjacent keratinocytes (K). Arrows indicate desmosomal alteration and formation of larger intercellular spaces (S). Magnification ×10K.

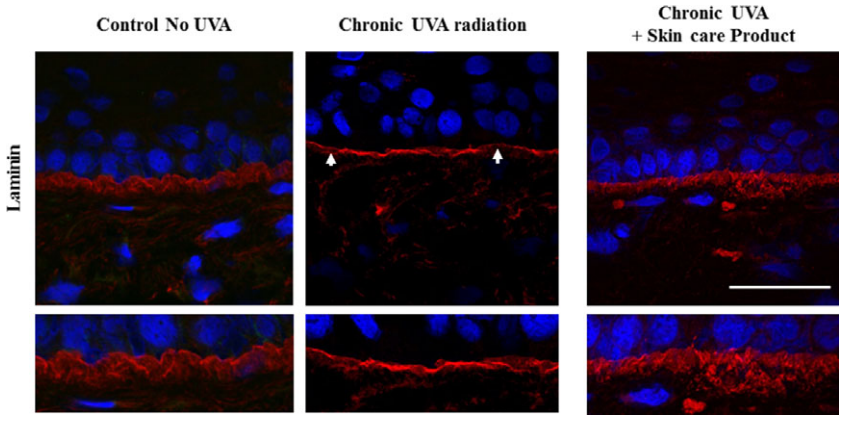

Figure 5 Skin care protection of the dermo-epidermal junction in the full-thickness skin model of older adult fragile skin. Laser scanning confocal microscopy (LSM). Immunofluorescence staining of laminin (red labelling) counter-stained with DAPI (blue nuclei). Arrows indicate DEJ alteration. Scale bar = 50 μm.

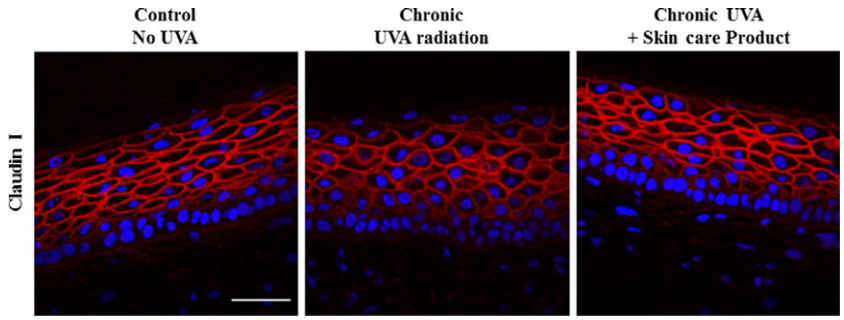

Figure 6 Skin care protection of Claudin 1 in the epidermis in the full-thickness skin model of older adult fragile skin. Laser scanning confocal microscopy (LSM). Immunofluorescence staining of Claudin I (red labelling) counter-stained with DAPI (blue nuclei). Dashed line represents the dermo-epidermal junction. Arrows indicate epidermal alteration. Scale bar = 100 μm.

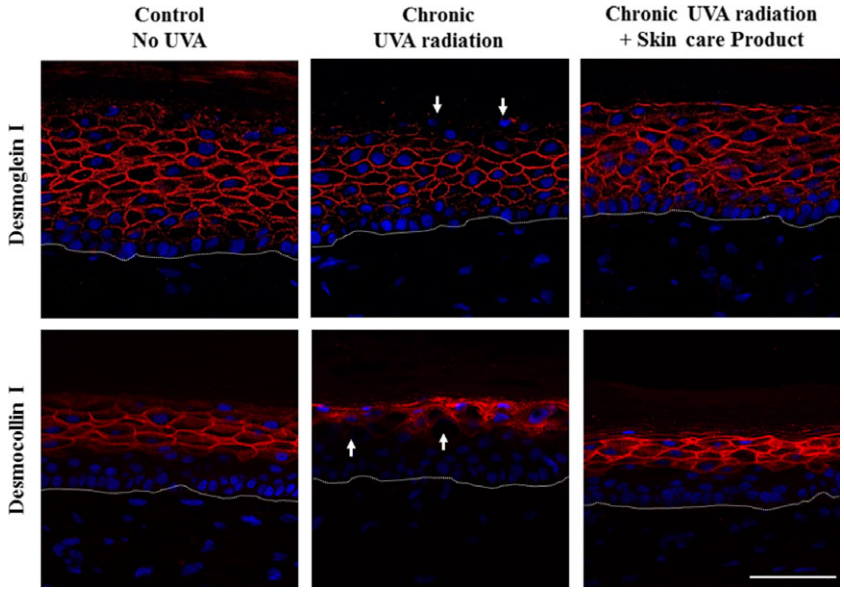

Figure 7 Skin care protection of the desmosomes in the epidermis in the full-thickness skin model of older adult fragile skin. (a) Laser scanning confocal microscopy (LSM). Immunofluorescence staining of desmoglein I and desmocollin I (red labelling) counter-stained with DAPI (blue nuclei). Dashed line represents the dermo-epidermal junction. Arrows indicate desmosomal alteration Scale bar = 100 μm.

(Cldn1) which is a component of tight junctions, a cellular structure involved in the integrity of the skin barrier.[69] Tight junctions form a belt around the keratinocytes to occlude the epidermis from the environment.[70] Jin *et al.*[71] showed that claudin-1 expression was reduced in both intrinsically aged and photo-aged human skin *in vivo*. As shown in Fig. 6, Cldn1 immunolabelling was found in all suprabasal cell layers in control skin. Its main location was observed at the cell membrane.

In response to UVA exposure, Cldn1 staining was slightly modified as evidenced by a moderate decrease in the fluorescence signal, but also a disruption of the cell membrane staining and broader localization into the keratinocyte cytoplasm. Thus, the Cldn1 expression was modified in the skin under UVA, suggesting that tight junction functionality could be affected by chronic UVA radiation. Since the desmosomes are other intracellular structures that also maintain epidermal cohesion and morphology,[69] we decided to study the expression of two specific desmosomal markers: desmocollin 1 and desmoglein 1. The desmosomal proteins were immunostained from cryosections and analysed by LSM. In Fig. 7, the results showed that the chronic UVA exposure was associated with a striking decrease in the fluorescent signal of both desmosomal markers in the epidermis, especially in the granular layers.

Ultraviolet A induced a strong disruption of the desmosomes in the skin model. The ultrastructural analyses by TEM are presented in Fig. 4c. They confirmed that the skin was clearly

affected by the UVA and harboured a desmosomal disorganization associated with the appearance of larger spaces between the adjacent granular keratinocytes. Thus, the data indicate that chronic UVA radiation induces an overall defect in the epidermal tight junctions and desmosomes, suggesting a major skin barrier alteration as observed in the fragile skin of older adults.

Skin care protection of a dermo-cosmetic product containing Rhealba® Oat Plantlet Extract in the fragile skin model We next evaluated the efficacy of a dermo-cosmetic product containing Rhealba® Oat Plantlet Extract (A-Derma Xera-Mega Confort®, Pierre Fabre Dermo-Cosmétique, Boulogne, France) to protect the skin in the full-thickness skin equivalent model exposed to chronic UVA radiation. The benefits of the skin care formulation were evaluated in the three main cutaneous compartments: the dermis, the DEJ and the epidermis. The formulation was applied onto the surface of the skin model at a dose of 5 mg/cm^2 immediately after the third UVA irradiation. A second topical application was performed 24 h later. Finally, the skin model was harvested 48 h after the last UVA exposure and received a total of 10 mg/cm^2 formulation (Fig. 2b).

After two topical applications of the skin care product on UVA-exposed full-thickness skin model, the immunostaining of fibrillin and elastin, which is shown in Fig. 3, revealed that the structure of the elastic network of irradiated and treated skin samples was partly restored and seemed identical to that of non-irradiated control samples. The fibrillin-rich fibres were denser at the DEJ and in the dermis, and both fibrillin and elastin networks appeared less fragmented. Thus, confocal microscopy analyses showed that the product containing Rhealba® Oat Plantlet Extract prevented both fibrillin and elastin degradation in response to UVA. TEM pictures in Fig. 4a suggest that the formulation treatment was associated with a better fibroblast morphology and with the presence of more ECM around the cells, including collagen fibres. Thus, a formulation containing Rhealba® Oat Plantlet Extract partly restored the elastic system of the UVA-exposed skin model.

The efficacy of the skin care product was also tested on the DEJ. The data are presented in Figs 5 and 4b. Confocal imaging confirmed that the formulation protected the DEJ from UVA-induced damage, and the laminin network was brighter and better organized following the topical application of Rhealba® Oat Plantlet Extract. The TEM analysis also showed that the hemidesmosomes were better structured and the lamina more regular. Thus, the formulation seemed to improve DEJ cohesion and therefore may help to prevent the fragility of DEJ in older adult skin.

Finally, the benefit of the product was evaluated in the epidermal compartment of the skin. As shown in Fig. 6, the claudin-1 staining was slightly increased when the product was applied, as compared to skin experiencing UVA exposure alone. Moreover, the fluorescence signal was similar to the control non-irradiated skin suggesting that the tight junction functionality could be recovered with the product. The expression of the desmosomal proteins, desmocollin 1 and desmoglein 1, was significantly restored in the Rhealba® Oat Plantlet Extract and UVA-treated skin, and the level of fluorescence was almost identical to that the control non-irradiated skin as indicated in Fig. 7. The TEM analysis of the granular layers of the epidermis is presented in Fig. 4c. It clearly shows that the ultrastructure of the desmosomes was better preserved in the presence of the formulation and that the keratinocytes were more cohesive, with less space between their cellular membranes. These data strongly support that the conclusion that the product containing Rhealba® Oat Plantlet Extract was effective in protecting the epidermis against the barrier defect induced by the chronic UVA exposure in the fragile skin model.

Conclusion Altogether, this study showed that chronic UVA radiation induced a loss of elasticity and DEJ damage associated with a skin barrier alteration, indicating that the full-thickness skin model mimicked the fragile skin of older adults in the three main cutaneous compartments. The data demonstrate that a dermo-cosmetic product containing Rhealba® Oat Plantlet Extract provides an efficient skin care protection against the chronic UVA exposure in this full-thickness skin model of older adult skin. Thus, the dermo-cosmetic product containing Rhealba® Oat Plantlet Extract might afford skin care protection and could be useful to treat the fragile skin of older adults, helping their skin age better.

Clinical and in-daily clinical practice studies

Despite the increasing proportion of older adults globally, this age group is often excluded from clinical trials. However, a number of clinical studies have evaluated the efficacy and/or tolerance of dermo-cosmetics products in this age group. A recent study by Theunis *et al.* evaluated the efficacy of a Rhealba® Oat Plantlet Extract-based emollient (A-Derma Xera-Mega Confort®, Pierre Fabre Dermo-Cosmetique, Boulogne, France) in 30 adults aged ≥60 years (average age 75.8 ± 8.3 years) with chronic xerosis and associated pruritus, who attended a dermatological clinic as outpatients in France. Nearly two-thirds of the subjects (63.3%) had suffered from pruritus for at least 5 years, 30.0% for 1–4 years and 6.7% for less than 1 year. In addition, patients suffered from five concomitant diseases (hypertension, hypothyroidism, diabetes, arthrosis for example) and had an average of 3.7 concomitant treatments. 73.3% of the subjects reported regular use of cosmetic skincare products to moisturize their skin, and 36.7% reported regularly use of cosmetic skincare products to relieve their itch. Subjects took part in the study for 4 weeks: 2 weeks with treatment and 2 weeks without treatment. All subjects were randomized 1:1 to start with either the treatment or the non-treatment phase. Pruritus improved immediately after the product application ($P < 0.0001$) and the

improvement was significantly higher during the treatment than the non-treatment phase ($P < 0.0001$), on the visual analogue scale. The product significantly reduced the intensity of pruritus from the first application and throughout the treated phase, with persistence of this effect until 4 weeks after stopping applications. Xerosis followed a similar trend and was significantly improved during the treatment phase compared to the non-treatment phase when measured by D-Squame, clinical assessment and hydration index. There were no significant differences or changes in transepidermal water loss, and the values observed throughout the study corresponded to values seen in healthy skin. While this was a relatively small open-label study, the results indicated that the emollient could provide effective relief to older adult patients experiencing chronic pruritus with moderate-to-severe xerosis and could be used as a first-line treatment.

In a separate study in France, a foaming gel containing Rhealba® Oat Plantlet Extract (A-Derma Dermalibour + Foaming Gel®, Pierre Fabre Dermo-Cosmetique, Boulogne, France) was found to be effective in the treatment of dermatological conditions and well tolerated when tested on 153 adults aged 60 years and older. A small proportion of patients received the gel as a monotherapy (5.2%), whereas the rest of the patients received the gel in combination with medicines (26.8%), another dermo-cosmetic product (25.5%) or both (42.5%). The gel was prescribed for an average of 24.5 days (standard deviation: 16.5) across a range of conditions (Table 4).

In total, 93.2% of doctors and 85.9% of the patients considered the product to be efficacious. Skin conditions improved for 77.7% of the patients, and the majority of patients experienced a reduction in symptoms (Fig. 8). There were no significant effects of the different therapies (monotherapy or in combination) on the results, indicating that the foaming gel is suitable for use alone or in combination with other treatments.

In a third study, conducted in 2014, the efficacy and tolerance of a drying spray containing Rhealba® Oat Extract (A-Derma Cytelium® Spray, Pierre Fabre Dermo-Cosmetique, Boulogne, France) were assessed in children, adults and older adults with oozing or exudative skin lesions. Ten subjects aged 61 years and older were included in the study, and causative pathologies in this age group were eczema ($n = 4$), mammary folds ($n = 2$), pressure ulcers ($n = 2$), wounds ($n = 1$) and zona ($n = 1$). Efficacy was assessed at baseline, and after 3 and 7 days of use (Days 3 and 7). The doctor evaluated the clinical score of exudative lesions in terms of exudate, erythema, scab and tenderness, and the subjects evaluated the pruritus, stinging, pain and burning sensations. Global tolerance was based on the presence or absence of clinical signs, and the severity of any pertinent (i.e. lasting more than 5 min with at least likely relationship to the product) clinical signs observed. A general decrease in score of clinical signs over Days 3 to 7 was seen. After 3 days of use, 70%, 87.5% and 100% of subjects had improvement in exudate, pruritus and burning sensation, respectively. This rose to 90% and 100% for exudate and pruritus by Day 7. The older adult subjects were also satisfied with the product, with most of them saying that their lesions healed quickly. The researchers concluded that the product contributed to the improvement and healing of lesions in these patients over the tested period.

Table 4 Conditions for which the foaming gel containing Rhealba® Oat Plantlet Extract was prescribed

Condition	Number (%) of patients
Eczema	27 (9.9%)
Intertrigo	17 (12.5%)
Irritant contact dermatitis	16 (11.8%)
Folliculitis	11 (8.1%)
Postcryotherapy	6 (4.4%)
Psoriasis	6 (4.4%)
Prurigo	5 (3.7%)
Pruritus	4 (2.9%)
Dermatitis	3 (2.2%)

The fourth study was an in-daily clinical practice study, conducted across eight countries. A total of 2363 patients aged 1–100 years (mean age: 47.3 ± 18.5 years) were included. Following a dermatological procedure, (e.g. peels, laser treatment, intense pulsed light, cryotherapy, injections, minor surgery), they were treated with a repairing cream containing Rhealba® Oat Plantlet Extract (A-Derma Epitheliale A.H. Duo®, Pierre Fabre Dermo-Cosmetique, Boulogne, France). The mean prescription time of the repairing cream was 18.9 ± 14.1 days, and the recommended application frequency was twice daily for 68.1% of patients. Within 5 minutes of cream application on the first day, symptoms were significantly improved ($P < 0.0001$) (Table 5). The global efficacy was assessed by the investigating dermatologists as 96.8%, and healing was significantly improved for 93% of patients.

Finally, an in-daily clinical practice study assessed the efficacy and tolerance of an emollient containing Rhealba® Oat Plantlet Extract (A-Derma Xera-Mega Confort®, Pierre Fabre Dermo-Cosmetique, Boulogne, France) in 592 adults aged 60 years and older in France. Patients were included in the study if they had dry to very dry skin (physiological, pathological or treatment-related) and the cream was prescribed as a monotherapy (71.3% of patients) or in combination with a medical treatment (27.7%) or another dermo-cosmetic treatment (1%). Patients applied the cream daily for the first 2 weeks and then switched to two or three times per week for an additional 4 weeks. Efficacy and tolerance were assessed by patient questionnaires after 2 and 6 weeks of treatment. At the end of the first 2 weeks, 99% of patients had an improvement in their skin dryness, and 98% of patients considered the product to have a good or a very good tolerability. Overall, 77% of patients had a reduction in pruritus

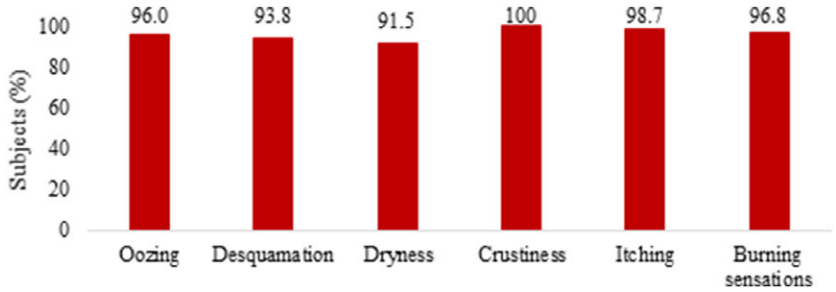

Figure 8 Percentage of subjects who reported a decrease in individual symptoms.

by the end of the treatment. Effects were seen within the first 7 days of treatment and were similar for patients using the cream as a monotherapy compared with those receiving other treatments. The best improvements in self-assessed efficacy and tolerance parameters were seen in patients who used the cream three times per day for the last 4 weeks of the treatment (Table 6).

Section 4: The use of a dermo-cosmetic product containing Rhealba® Oat Plantlet Extract on incontinence-associated dermatitis in older adults

Background

Incontinence-associated dermatitis (IAD) develops following contact with irritants such as urine and faeces, both of which reduce corneocytes cohesion and contribute to increase the fragility of the epidermis and reduce the barrier functionality (Fig. 9). Additionally, prolonged contact with moisture plays a role in the resistance to friction forces. The epidermis of patients with IAD is more likely to be damaged by shearing forces through contact with external surfaces such as bed linen or clothing.[33] Increased transepidermal water loss and penetration of the epidermis by pathogens trigger an inflammatory response and further compromise the integrity of the skin barrier, leaving it vulnerable to fungal and bacterial infections, and further damage by irritants (Fig. 9).

Incontinence-associated dermatitis is a challenge frequently encountered by dermatologists working with older adults, particularly those in long-term care settings. Approximately 26–61% of females and 11–34% of males living in community settings experience incontinence.[72] Not all incontinent individuals develop IAD; estimates range from 7% of nursing home residents with urinary incontinence, and up to 83% of incontinent patients in intensive care units.[73] IAD most frequently occurs in the diaper area and the severity is categorized based on the Ghent Global IAD classification tool, consisting of two categories according to the presence of persistent redness (category 1) and skin loss (category 2), both of which are subdivided based on the presence of clinical signs of infection. (Fig. 10).

Table 5 Reduction in clinical signs five minutes after the first application of the repairing cream

Condition	Number (%) of patients with reduction in clinical signs five minutes after application
Burning sensation	637 (35.6%)
Tingling	717 (44.1%)
Pain	606 (37.9%)
Tightness	668 (44.2%)
Pruritus	380 (56.8%)

Previous studies on dermo-cosmetics containing Rhealba® Oat Plantlet Extract have demonstrated restorative effects on skin barrier function, including reduction of itching, redness and fragility of the skin.[2,3,26,64] The Rhealba® Oat Plantlet Extract is rich in flavonoids and saponins, which have anti-inflammatories properties and stimulates keratinocytes differentiation and proliferation, aiding in barrier repair.[75] In *in vitro* trials and clinical studies, products containing the extract have demonstrated efficacy as a reparative and/or protective agent in a number of skin conditions, such as acne, atopic dermatitis, pruritus and wound healing.[2,63,64,75,76] In this recent clinical study, we investigated the efficacy and tolerance of a barrier cream containing Rhealba® Oat Plantlet Extract as a reparative and protective agent against IAD in patients aged 70 years and older with urinary and/or faecal incontinence.

Methods

Study design and participants This study was monocentric, randomized and open-trial. It was conducted between April and May 2017 in Portugal, in elderly adults suffering from incontinence. Subjects had to be 70 years or older, with any skin type, a phototype I to III, and they had to present urinary and/or faecal incontinency using diapers mainly as protection against urine. If older adults had chronic systemic treatments, they had to be stable for at least 1 month before the study start and with no changes during study period.

Any subjects already receiving medications for irritation in the diaper area were excluded from enrolment, as well as those

Table 6 Percentage of patients with improvements in self-assessed efficacy and tolerance parameters, stratified by frequency of treatment in the last 4 weeks of the study. Assessments were performed after 2 and 6 weeks. In the first 2 weeks, all patients received 1 application per day

Frequency of treatment in last 4 weeks	Assessment point	Decreased dryness	Increased skin comfort	Increased suppleness	Reduced tears	Reduced intensity of itching
2 times per week	2 weeks	85%	81%	70%	68%	67%
	6 weeks	92%	89%	84%	82%	69%
3 times per week	2 weeks	85%	86%	77%	80%	76%
	6 weeks	93%	91%	89%	87%	78%

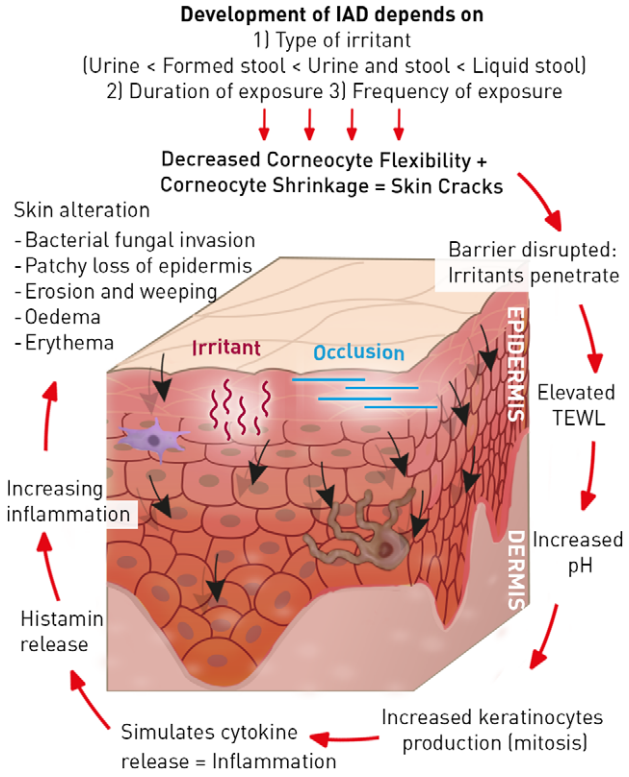

Figure 9 The development of incontinence-associated dermatitis.

with skin pathologies/treatments which may interfere with the study results, or those who had received any surgery, chemical or physical treatment on the experimental area during the previous 12 months. A topical barrier cream containing Rhealba® Oat Plantlet Extract (A-Derma Dermalibour+ Barrier cream, Pierre Fabre Dermo-Cosmetique, Boulogne, France) to be applied after each diaper change for a total of 28 days was prescribed to the included subjects.

Measurement of diaper rash The diaper rash grading scale (Table 7) was used to stratify subjects at enrolment into two groups: subjects with a diaper rash score of 1.5 were included in Group 1 (for evaluation of the reparative effect) and subjects with a score of 0 were included in Group 2 (for evaluation of the preventive effect).

Physical and functional signs Clinical evaluation of physical (redness/erythema, swelling/oedema, desquamation, dryness, vesicles and papules) and functional (burning sensation, warm sensation, itching/pruritus, tightness and stinging/prickling) signs was performed by the same investigators for all subjects. Signs were assessed by a dermatologist and a gynaecologist on Day 1, before and immediately (10–30 mins) after application of the product, and on Days 8 and 29 of the study. For each sign, intensity was reported on a 5-point scale, ranging from none (0) to severe (4). The location, duration and frequency were also recorded. Adverse events (AEs) and serious AEs (SAEs) were recorded throughout the study and assessed by the investigators in terms of causal association with the product (very likely/likely, not clearly attributable/unlikely, excluded).

Global tolerance The overall global tolerance was assessed by a dermatologist who considered all the individual signs and reactions, and their characteristics. Global tolerance was scored as either: excellent, very good, good, moderate or bad.

Efficacy Efficacy was assessed by measurement of the modified diaper rash grading scale (Table 7), mexameter measurements of erythema, on Days 1, 8 and 29, and subject questionnaires. The erythema measurement was made using a mexameter MX18 (Courage – Khazaka Electronic GmBH, Koln, Germany) with a 5 mm probe. The amount of light (wavelength 568–660 nm) absorbed by the skin was calculated by measurements of emitted versus reflected light and was recorded as arbitrary units, with higher values indicating more erythema. A questionnaire was also provided to all subjects at the end of the study to evaluate subjective efficacy and cosmetic qualities.

Statistical analysis Comparative analyses of Day 29 against Day 8, Day 1 postapplication and Day 1 baseline were performed using student t-tests, Wilcoxon Rank Signed Test or Mann-Whitney using SPSS 20 (IBM).

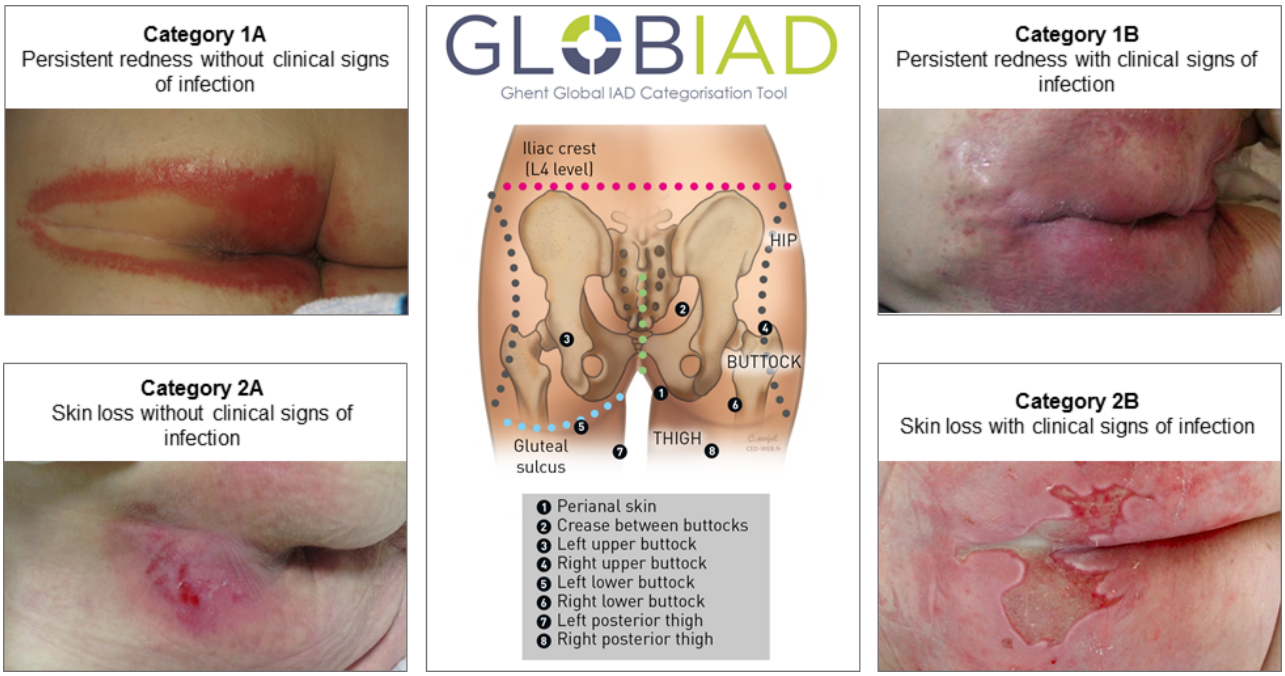

Figure 10 Categorization of IAD. Photographs reproduced with permission from Beeckman et al.[74]

Table 7 Diaper rash grading score.[77]

Skin condition global score	Integrity ulceration	Integrity scaling	Rash papules	Rash oedema	Redness Spotty	Redness continuous
0	–	–	–	–	–	–
0.5	–	Dryness only	–	–	Very slight	Very slight
1	–	Slight	–	–	Slight	Slight
1.5	–	Moderate	Very slight	Very slight	Moderate	Moderate
2	–	Severe	Slight	Slight	Moderate severe	Moderate severe
2.5	Slight	–	Moderate	Moderate	Severe	Severe
3	Moderate	–	Moderate severe	Moderate severe	–	–
3.5	Moderate severe	–	Severe	Severe	–	–
4	Severe	–	–	–	–	–
Percent coverage	<10	<10	<10	<10	<10	<10
	10–50	10–50	10–50	10–50	10–50	10–50
	>50	>50	>50	>50	>50	>50

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Results

A total of 42 subjects aged 70 to 96 years were enrolled in the study. Twenty-one subjects were included in each group. Across groups, 76.2% (n = 32) were female, and 23.8% (n = 10) were male. The mean age was 82.7 years and all subjects completed the study.

Tolerance No worsening of physical or functional signs were reported for any of the subjects at any of the timepoints postbaseline, and no AEs or SAEs were reported during the study. Therefore, the overall product tolerance was graded as excellent.

Efficacy – diaper rash scores The reparative effect of the cream was evaluated using the data from Group 1. A statistically significant decrease ($P < 0.001$) in mean diaper rash grading score on Days 8 and 29 of the study was observed, with a drop of 50.8%

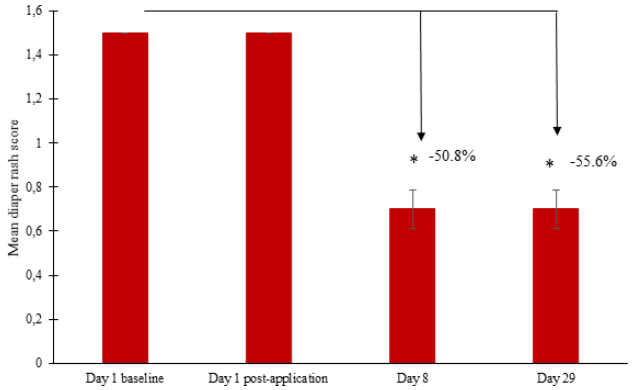

Figure 11 Change in mean diaper rash score during the study, Group 1 (Diaper rash score = 1.5) (*Statistically significant $P < 0.001$).

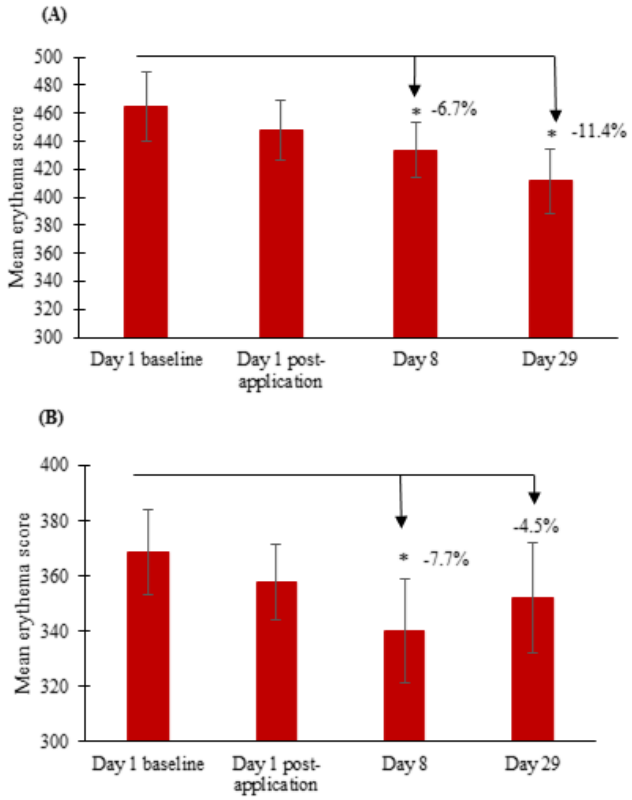

Figure 12 Change in erythema, as measured by mexameter, during the study, (a) Group 1 (Diaper rash score = 1.5) and (b) Group 2 (Diaper rash score = 0 at inclusion). (*Statistically significant $P < 0.05$).

and 55.6% compared with Day 1 baseline score for Days 8 and 29, respectively (Fig. 11).

The protective effect of the cream was evaluated using data from Group 2. No changes were observed in mean diaper rash score in this group during the study, i.e. the diaper rash score remained at 0 throughout the study for all subjects in Group 2.

Efficacy – erythema mexameter measurements Erythema index also decreased for Group 1 during the study (Fig. 12). Significant differences ($P < 0.05$) from baseline were observed on Days 8 (6.7% reduction) and 29 (11.4% reduction). In Group 2, no significant differences were observed in Group 2 after 28 days of treatment, with erythema scores of 368.6, 357.8, 340.2 and 352.0, on Day 1 baseline, Day 1 postapplication, Day 8 and Day 29, respectively (Fig. 12). A significant difference was observed on Day 8, with a 7.7% decrease in erythema index score compared with Day 1 ($P < 0.05$).

Efficacy – patient self-assessment Across both groups, 92.9% of subjects had a positive evaluation of the product (score of 5 or above) after 28 days of use, with a mean score of 7.8 out of 10 across all the questions posed at the end of the questionnaire.

Discussion and conclusions

In this small-scale study, the use of a dermo-cosmetic containing Rhealba® Oat Plantlet Extract had a reparative effect on IAD, with a significant reduction in diaper rash after 8 and 28 days of treatment. The dermo-cosmetic also had a protective effect in incontinent patients who had no IAD at the start of the study, as none of these patients developed IAD symptoms during the study period. The product was excellently tolerated in terms of physical signs, functional signs and adverse reactions, and overall, patients had a positive view of its effects.

A structured skin care regimen is important for the prevention and treatment of IAD. A review by Gray *et al.*[78] recommended daily cleansing and moisturizing of perineal skin, and routine application of a barrier product to minimize the contact between urine/stool and the skin and prevent IAD development. Similarly, Beele *et al.*[33] recommended gentle cleansing, without soap, the use of barrier and moisturizing creams to rehydrate the skin and reduce contact with irritants, and treatment of IAD, differing dependent on the severity outlined in Fig. 10. Barrier creams have demonstrated effectiveness in maintaining skin hydration[79] and providing protection against skin barrier damage caused by irritants.[80,81] By restoring the disrupted skin barrier, barrier creams, such as the one tested in the current study, can break the cycle of epidermal damage in incontinent patients and allow healing of the skin and reduction in IAD.[78] The hydrating properties of barrier creams prevent skin cracks from forming, which reduces the risk of irritants penetrating the skin. Additionally, they provide a protective layer between the skin and irritant, further reducing the detrimental impact of the irritant. While the ultimate goal for IAD treatment is reducing or eliminating the underlying incontinence issues, this may not be realistic for some frail or critically ill patients.[34] Therefore, dermo-cosmetic products which reduce or prevent IAD

development can be a key tool for managing the condition in these patients.

Overall, the use of a dermo-cosmetic containing Rhealba® Oat plantlet extract demonstrated a reparative effect in subjects experiencing IAD, with excellent tolerability and no reported adverse events. The lack of change in diaper rash score in the group without IAD at the start of the study also indicates that the dermo-cosmetic provided a protective effect against development of IAD in these individuals. Although this was a small-scale study, the results indicate the potential benefits of use of this type of dermo-cosmetic product in incontinent older adults.

Section 5: The role of healthcare professionals in the prevention and management of fragile skin in older adults

Dermatologists

Ageing is a time-dependent phenomenon resulting in specific changes to the appearance and function of the human skin, following intrinsic (genetic) and extrinsic factors (environment, sun exposure, artificial UV, smoking, pollution).[14]

Dermatologists play a key role in the management of fragile skin in older adults, as they can diagnose the pathology as soon as possible, and prescribe the appropriate treatment. Modifications in the dermis and the epidermis lead to some pathologies, such as dryness, which is one of the most commonly reported skin conditions in older adults.[82] Due to this xerosis, itching or pruritus occurs, leading to secondary lesions (excoriations), allowing allergens and pathogens to easily penetrate the skin. This alteration of the skin increases the risk of irritant and allergic contact dermatitis, and even incontinence-associated dermatitis depending on the causative agents, as the skin reactivity to irritants tends to decrease with age since the skin becomes more fragile.[83]

The appearance and function of human skin alter dramatically with ageing, resulting in higher rates of severe xerosis and other skin complaints. The stratum corneum fulfils the biomechanical barrier function of the skin and is adversely transformed with age, which is why atopic dermatitis can also occur in older adults. Indeed, this pathology is not only a paediatric disease appearing in infancy or childhood, but can last during the young adult life and the geriatric phase (elderly). Even if the prevalence of atopic dermatitis is lower in older adults than in children and young adults, the skin manifestations are similar, with chronic eczematous dermatitis on the face and neck, lichenification with or without pruriginous papules and nodules. However, lichenification around the unaffected folds of the elbows and knees is common. Atopic dermatitis in older adults can be a geriatric onset, or a geriatric recurrence following childhood atopic dermatitis, or the continuation of adult atopic dermatitis.

The difficulty with atopic dermatitis in older adults resides in the diagnosis. Older people have pruritic skin disorders due to age-related changes in skin barrier function, immunosenescence and changes in neurological and psychological functions,[84] coexisting with other pathologies which can induce itchy conditions, and complicate the diagnosis of atopic dermatitis. In addition, clinical signs of geriatric atopic dermatitis are more variable than those in other age groups, due to individual differences following the ageing. The solution is to diagnose by excluding pruritic skin conditions under laboratory examinations and/or allergic skin tests.[85]

Transepidermal water loss (TEWL), which is considered to be one of the best measures of skin barrier function,[86] is not increased in older adults, which may aid in distinguishing fragile dry skin caused by ageing to that caused by skin pathologies per se.[87]

In order to improve the state of their skin, and other than medicinal treatments, older adults should avoid fragrance soaps, irritating chemicals and hot water to reduce pruritus and xerosis for example.[85] Daily skin care is of particular importance to older adults, and managing the balance between skin cleanliness and increasing skin hydration is a significant factor to consider in personal hygiene regimens.[88] However, older adults need to be educated not to use some products that can be an irritant to their skin, but to use specific products for their needs and pathologies.

Geriatrician

Older adults can be categorized into three categories: robust, frail and dependent based on different geriatric criteria (gait speed, hand grip strength, fatigue, disability, weight loss, quality of life).[89] Older adults are at an increased risk of suffering from multiple pathologies, like diabetes, cardiovascular diseases and cancers, in addition to skin changes and disorders. As comorbidity and polypharmacy increase, the risk of dependency (i.e. frailty) also increases. As a result of being frail, older adults take less care of themselves, reducing their hygiene and use of care products.

The polypharmacy associated with comorbidity increases with age and can have many negative consequences. Taking multiple medications is associated with an increased risk of adverse drug events or drug-interactions due to a modification in pharmacokinetics and pharmacodynamics in the older adult population.[90] Corticoids, statin, diuretic and cancer therapy have potentially cutaneous side effects and can lead to skin dryness, which amplify the fragility of the skin. Thus, care of older people is a real challenge for medical professionals as it requires a perfect knowledge of all the mechanisms of the ageing process.

While careful consideration should be given to the interactions between medications, and the impact on adherence of multiple treatment regimens,[39] current evidences suggest that low-irritant cleansing products and moisturizers provide substantial benefits in daily skin care regimens for older adults.[82] Dermo-cosmetics aimed at preventing the development of common but uncomfortable skin conditions, such as incontinence-associated

dermatitis and xerosis, and maintaining the natural protective function of the skin barrier in order to improve the quality of life of older adults, and can help to reduce the impact of their pathologies and treatments.[27,82,88]

Conclusion

Age-related changes in the structure of the skin contribute to increasingly fragile skin in older adults, making this age group particularly vulnerable to skin pathologies such as dermatitis and infections. This increased fragility, together with other confounding factors, such as incontinence, frailty and the use of multiple medications, presents a unique challenge to dermatologists and geriatricians. Products containing Rhealba® Oat Plantlet Extract have demonstrated protective and restorative roles in older adults across a range of skin conditions including xerosis, skin lesions, skin tears, wound healing and incontinence-associated dermatitis; and *in vitro* full-thickness skin models have also demonstrated a protective effect of a product containing Rhealba® Oat Plantlet Extract against chronic UVA exposure in ageing skin. With the growing populations of older adults worldwide, combined with increased longevity, skin care regimens focused on this age group will become increasingly important for dermatologists and geriatricians alike. Dermo-cosmetics can assist in the prevention or treatment of skin pathologies in older adults, improving quality of life and restoring the natural barrier function of the skin.

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