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Occlusion and hydration of scars: moisturizers versus silicone gels

Ignace De Decker[a,*], *Henk Hoeksema*[a,b], *Els Vanlerberghe*[a], *Anse Beeckman*[c], *Jozef Verbelen*[a], *Petra De Coninck*[a], *Marijn M. Speeckaert*[d], *Phillip Blondeel*[a,b], *Stan Monstrey*[a,b], *Karel E.Y. Claes*[a,b]

[a] *Burn Center, Ghent University Hospital, C. Heymanslaan 10, 9000 Ghent, Belgium*
[b] *Department of Plastic Surgery, Ghent University Hospital, C. Heymanslaan 10, 9000 Ghent, Belgium*
[c] *Faculty of Medicine and Health Sciences, Ghent University, C. Heymanslaan 10, 9000 Ghent, Belgium*
[d] *Department of Nephrology, Ghent University Hospital, C. Heymanslaan 10, 9000 Ghent, Belgium*

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ABSTRACT

Background: The mainstay of non-invasive scar management, consists of pressure therapy with customized pressure garments often combined with inlays, hydration by means of silicones and/or moisturizers as well as UV protection. It is generally accepted that scar dehydration resulting from impaired barrier function of the stratum corneum and expressed by raised trans epidermal water loss (TEWL) values, can lead to increased fibroblast activity and thereby hypertrophic scar formation. However, we have reached no consensus on exactly what optimal scar hydration is nor on barrier function repair: by means of silicone sheets, liquid silicone gels or moisturizers. Occlusive silicone sheets almost completely prevent TEWL and have been shown to be effective. Nevertheless, many important disadvantages due to excessive occlusion such as difficulties in applying the sheets exceeding 10–12 h, pruritus, irritation, and maceration of the skin are limiting factors for its use. To avoid these complications and to facilitate the application, liquid silicone gels were developed. Despite a reduced occlusion, various studies have shown that the effects are comparable to these of the silicone sheets. However, major limiting factors for general use are the long drying time, the shiny aspect after application, and the high cost especially when used for larger scars. Based on excellent clinical results after using three specific moisturizers for scar treatment in our patients, we wanted to investigate whether these moisturizers induce comparable occlusion and hydration compared to both each other and the widely recognized liquid silicone gels. We wanted to provide a more scientific basis for the kind of moisturizers that can be used as a full-fledged and cost-effective alternative to silicone gel.

Methods: A total of 36 healthy volunteers participated in this study. Increased TEWL was created by inducing superficial abrasions by rigorous (20x) skin stripping with Corneofix® adhesive tape in squares of 4 cm^2. Three moisturizers and a fluid silicone gel were tested:

* Correspondence to: Burn Center, Department of Plastic Surgery, Ghent University Hospital, C. Heymanslaan 10, 9000 Ghent, Belgium. E-mail address: ignace.dedecker@ugent.be (I. De Decker).

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DermaCress, Alhydran, Lipikar and BAP Scar Care silicone gel respectively. TEWL reducing capacities and both absolute (AAH) and cumulative (CAAH) absolute added hydration were assessed using a Tewameter® TM300 and a Corneometer® CM825 at different time points for up to 4 h after application.

Results: We found an immediate TEWL increase in all the zones that underwent superficial abrasions by stripping. Controls remained stable over time, relative to the ambient condition. The mean percentage reduction (MPR) in TEWL kept increasing over time with Alhydran and DermaCress, reaching a maximum effect 4 h after application. Silicone gel reached maximal MPR almost immediately after application and only declined thereafter. The silicone gel never reached the minimal MPR of Alhydran or DermaCress. Hydration capacity assessed through CAAH as measured by the Corneometer was significantly less with silicone gel compared to the moisturizers. Compared to silicone gel Lipikar provided similar occlusion and the improvement in hydration was highly significant 4 h after application.

Conclusion: Based on the results of both our previous research and this study it is clearly demonstrated that the occlusive and hydrative effect of fluid silicone gel is inferior to the moisturizers used in our center. Lipikar hydrates well but is less suitable for scar treatment due to the lack of occlusion. A well-balanced occlusion and hydration, in this study only provided by Alhydran and DermaCress, suggests that moisturizers can be used as a scar hydration therapy that replaces silicone products, is more cost-effective and has a more patient-friendly application.

1. Introduction

Hypertrophic scarring following severe soft tissue injury is common and is mainly caused by an excessive formation of connective tissue in the dermal layer after wound healing [1]. Excessive scarring results from disproportionate collagen deposition and/or degradation and can potentially lead to functional, aesthetic and psychosocial impairments that may hamper the patient's rehabilitation and ultimately reduce quality of life. [1–3]. Hypertrophic scars are frequently seen as a result of prolonged spontaneous healing in deep dermal burns or after skin grafting in full thickness burns [4,5]. Studies suggest that the incidence of hypertrophic scarring after these burns ranges from 32% to 72% and typically occurs within 1 year after wound closure [2,6–10]. Scar hypertrophy, in contrast to keloid scars, is by definition confined to the original wound. [2]. They show a rapid growth phase for up to 6 months and may gradually regress over a period of a few years [11]. Keloids persist for a longer time and usually show no spontaneous regression [11]. Regardless of the scar type, a common characteristic is a reported increase in trans epidermal water loss (TEWL) compared to normal skin [12]. Keloid scars show an even higher TEWL than hypertrophic scars [13]. The outermost layer of the epidermis, the stratum corneum (SC), forms a heterogeneous structure, consisting of corneocytes surrounded by anisotropic lipid layers, determining the permeability of the skin [14]. Damage to the SC will facilitate water evaporation, causing increased TEWL, reduced water content and therefore dehydrated skin [12,13,15]. In scars the additional problem of the loss of moisturizing structures is a potential, such as sweat and sebaceous glands responsible for the skins smoothness, which leads to dry skin [12,13,15]. The dehydration of the SC has been demonstrated to induce cytokine production by keratinocytes found in the basal layer of the epidermis, resulting in excessive scar formation through increased collagen deposition by dermal fibroblasts [16]. The therapeutic effect of scar hydration therefore essentially consists in modulation of the cytokine production by keratinocytes resulting in a down-regulation of collagen production by fibroblasts [17].

Although the mechanism of action is not fully understood, hydration is generally considered to be the main mechanism responsible for the beneficial effects of topical products used for scar treatment. [18–20]. The retention of water in the skin is mainly dependent on the presence of natural hygroscopic agents within the corneocytes and the intercellular lipids located in the SC and, when arranged in an orderly manner, form an evaporation barrier [21]. The water gradient originating from the deeper parts of the epidermis (underlying layers of the stratum granulosum) towards the more superficial epidermal layers (SC) functions as a trigger for important keratinocyte functions, such as the production of natural moisturizing factors, and ensures the natural flow of water towards the SC [21]. Dehydration of the skin occurs when water of the SC is lost more quickly than the gradient can supply [21]. Hydration of the skin can be achieved in several ways but for the prevention and treatment of scars, silicone sheets, fluid silicone gels (FSG) and moisturizing creams are generally used [3]. Since silicone gel sheets were first used for burn scars at the Australia's Adelaide Children's Hospital in 1981 and reported by Perkins et al. in 1983 [22], silicone gel sheets (SGS) are universally considered as the first-line prophylactic and treatment option for hypertrophic scars and keloids [1,3,13]. The direct working mechanism of silicone treatment is mainly based on occlusion (Fig. 1). Occlusion creates an environment for hydration, regulating epidermal signalling that normalizes fibroblast behaviour

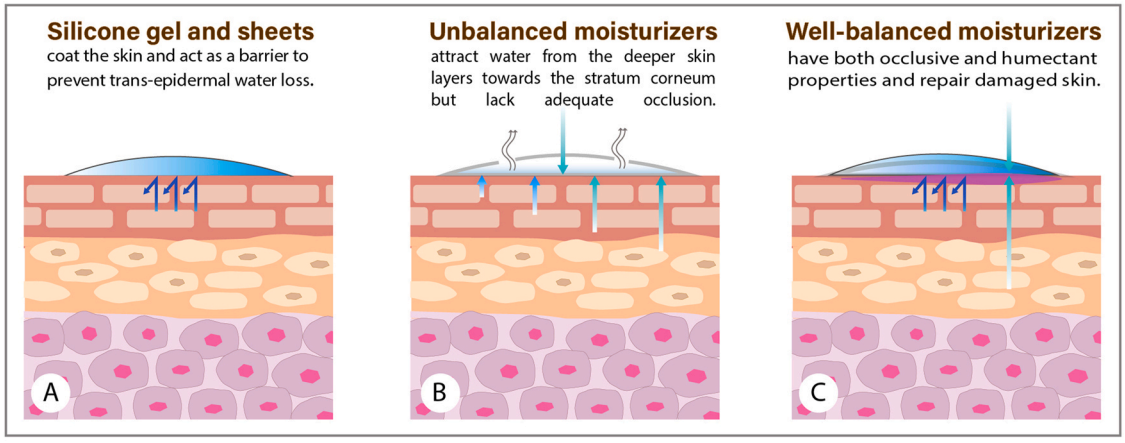

Fig. 1 – Working mechanism of (1) silicone products. (2) unbalanced moisturizers. (3) well-balanced moisturizers.

and subsequently influencing both collagen synthesis and eventual scar formation [15]. Covering a scar with a silicone product leads to the accumulation of water in the SC, resulting in hydration through the formation of a water reservoir [18,23,24]. After removal of the silicone sheets evaporation rapidly rises, therefore no true repair or long-term effect on skin barrier restoration can be expected [18,25–27]. Fluid silicone gels were designed to overcome various disadvantages associated with the use of silicone sheets such as maceration, itching, rash, bad odour and difficult attachment. [17,28–30]. They are mostly used during immediate postoperative care, on uneven and difficult areas such as joints, and on visible areas such as the face and hands [17].

Although silicone sheets and fluid silicone gels are widely used and extensively studied, research has shown that occlusion and/or hydration is also the mechanism of action of numerous moisturizing creams and silicone-free pads (inlays) that are successfully used in the treatment of hypertrophic scars [31]. This may indicate that the silicone is replaceable and that the original idea that silicone itself has intrinsic anti-scar properties is outdated [15,32–35]. Moisturizers are especially developed for skin hydration and appear in various forms such as lotions, creams, pastes and oils [13]. Besides the different dispensing formulations, the ingredients of moisturizers vary widely. Ingredients can include: water, oils, emollients, humectants, fragrances, emulsifiers and preservatives [13]. Many moisturizers incorporate vegetable oils which are rich in essential fatty acids and δ-linoleic acid, aiding in the replacement of the skin lipids [36–38]. These natural plant oils are commonly used as topical therapy worldwide, are easily accessible and are relatively inexpensive for skin care [39]. Emollients fill the spaces between partially desquamated skin flakes, making the skin more flexible and its appearance smoother while enhancing corneocyte adhesion [13,39]. Many moisturizers contain preservatives or fragrances, but these can cause allergic reactions and should therefore be avoided as much as possible [13]. Water directly hydrates the skin, but evaporates rapidly when no sufficient occlusive component is present [13,18]. Humectants, on the other hand, attract water from the deeper layers of the skin and from the environment when the humidity is high enough, supplying a long lasting effect and are thus superior for dehydrated skin such as scars, provided adequate occlusion is ensured [13,18]. Humectants however can be a double-edged sword. Hoeksema et al. [18] and Klotz et al. [12,13] stated that not all moisturizers provide adequate occlusion, on the contrary they can actually increase TEWL values when only humectant substances are incorporated, subsequently reducing the thickness of the SC while contributing to a drying function of the outer skin layer [13,18]. This is the case for unbalanced moisturizers (Fig. 1), where adequate occlusive substances are absent with an imbalance between occlusion and hydration [40]. The TEWL values will paradoxically increase by enhancing water absorption from dermis to epidermis and subsequently the increased water content will be lost to evaporation [40]. Although many different moisturizers are commercially available, a well-balanced moisturizer is capable of truly repairing the disrupted skin barrier by providing both hydrating hydrophilic and occlusive hydrophobic constituents and has essentially just three main properties: occlusive, humectant and emollient effects [39,41]. A well-balanced moisturizer provides sufficient occlusion and long-lasting hydration while repairing the lipid layer of the damaged SC (Fig. 1).

Surprisingly, the occlusive, hydrating and restorative effects of moisturizers in scar treatment have rarely been studied in depth with a lack of scientific interest in these products despite the fact that all burn patients use moisturizer, often multiple times daily [18]. Following the promising results of Hoeksema et al. [18] investigating the capacities of Alhydran, a well-balanced moisturizer, our outpatient clinic has been using this moisturizer as standard of care for the hydration of burn scars since many years. DermaCress is another moisturizer that is used in our clinic with excellent functional and aesthetic results. Both moisturizers are often used without silicone products, but in combination with polyurethane inlays providing additional pressure underneath the pressure garments. In the sporadic condition where both moisturizers elicit an allergy-like reaction in a

patient, a switch is made to Lipikar Baume AP+M, a moisturizing cream often prescribed for extremely sensitive skin. In this study these 3 different moisturizers are compared to BAP Scar Care silicone gel, which was the most occlusive of 3 silicone gels investigated in a previous comparative study [18].

This study aims to further clarify if the occlusive and hydrative properties of the moisturizers we use are comparable to the widely used fluid silicone gels and identify their potential role in the prevention and treatment of hypertrophic scarring, by making use of a standardized scar-like simulation model based on tape-stripped skin.

2. Methods

2.1. Ethics committee

This study was approved by the ethical committee of Ghent University Hospital on the 26th of May 2021 (Belgian registration number B6702021000403). Prior to enrolment, signed informed consent was obtained from each healthy volunteer.

2.2. Power analysis

To assess the number of participants needed, a power analysis was performed using data gathered during the previous study with Alhydran (BAP Medical, The Netherlands) as a moisturizer versus silicone sheeting and fluid silicone gels [18]. In this current study we want to assess the hydrating and occlusive properties of well-balanced moisturizers such as Alhydran or DermaCress (Cressana, Belgium) compared to fluid silicone gels. Alhydran will be compared to BAP scar care gel (BAP Medical, The Netherlands), a fluid silicone gel (superiority testing), and DermaCress to Alhydran (non-inferiority testing).

2.2.1. Superiority analysis

To assess the superiority of Alhydran compared to the reference standard of silicone gel therapy, a sample of 32 volunteers was found to be necessary to achieve 90% power, at the 5% significance level. This was based on a paired design and the normally distributed data collected from the previous study, assuming a minimal relevant clinical change of 0.10 or 10% reduction in TEWL with a standard deviation of 0.168.

2.2.2. Non-inferiority analysis

To assess the non-inferiority of DermaCress compared to Alhydran using the confidence interval approach of the mean difference TEWL reduction (95% CI constructed) on data from a paired design and also based on the data from the previous study, a sample size of 25 patients being treated with both Alhydran and DermaCress, achieves 90% power when the true difference between the means is 0 and thus assuming that both products are equal, the standard deviation is 0.073, and the non-inferiority limit is 0.05.

To enable the evaluation of both the superiority of Alhydran over BAP scar care gel as well as the non-inferiority of DermaCress over Alhydran, a minimum sample size of 32 people was needed. A standardized surplus rate of 10% to the total number of volunteers needed was applied, yielding a total sample size of 36 people.

2.3. Scar-like model

Hypertrophic scars usually show elevated TEWL values, with a wide inter-individual and intra-individual variability. When measured in the same scar, large differences due to spatial variability can be observed, making comparisons of products inaccurate. In this study we used a standardized, more reliable, and uniform scar-like model with increased TEWL similar to scar tissue, with consistent intra-individual TEWL increases and decreases. Tape-stripping was used to inflict superficial abrasions on the volar aspect of the forearms of healthy individuals. This scar-like model was previously studied by Hoeksema et al. in [18].

2.4. Research equipment

TEWL was measured by use of the Tewameter® TM 300 (Courage + Khazaka electronic GmbH, Köln, Germany). Skin hydration status was assessed by use of the Corneometer® CM 825 (Courage + Khazaka electronic GmbH, Köln, Germany). Software CK Multi Probe was used for data collection. At every timepoint, 6 values with both the Tewameter® and Corneometer® were taken and each time the mean value was calculated and recorded. Between every measurement, the probes were cleaned with a dry cloth. Between volunteers, the probes were wiped with an alcoholic swab. The temperature and humidity of the examination room was assessed continuously using an ambient condition sensor RHT 100 (Courage + Khazaka electronic GmbH, Köln, Germany).

2.5. Products and testing

Based on the experience in our burn center, 2 frequently used moisturizers with very high patient satisfaction were chosen: Alhydran, and DermaCress. Alhydran is considered the standard of care moisturizer in our burn center and DermaCress was introduced five years ago as a possible alternative. Additionally, Lipikar Baume AP+M (La Roche-Posay, France) was chosen as it is frequently prescribed for very sensitive skin or in case of irritation and/or suspected allergy.

Alhydran has been used in our center for almost 15 years with great satisfaction. Alhydran is an oil in water emulsion mainly comprised of Aloe vera Gel. It also contains high quality oils and special fatty ingredients including: mineral oil, decyl oleate, sorbitan stearate, propylene glycol, jojoba oil, and vitamins A, C, E and B12. The mechanism of action is a combination of the moisturizing effect of the Aloe vera gel with an occlusive effect provided by the special fatty ingredients of the cream [18,42].

DermaCress has been used in our center for the last five years and is highly appreciated by the patients. DermaCress is frozen watercress macerated in virgin coconut oil and improves skin hydration through both occlusion and humectant-induced water attraction because of the evening primrose, borage, and extra virgin coconut oil. DermaCress

also has antioxidants, constituents of watercress, lavender, cloves, oregano, and sage. Additionally, we have found that DermaCress is low-allergenic based on our clinical experience, with only 3 cases out of an estimated total of 250 patients treated during the last five years showing a possible allergy-like reaction, although an allergy could not be subsequently demonstrated with dermatologic patch testing.

Lipikar Baume AP+M is a hydrating moisturizer, primarily consisting of water, niacinamide, shea butter and aquae posae filiformis. Niacinamide, an amide of vitamin B_3 (niacin), has anti-pruretic, anti-inflammatory, depigmenting and photo-protective properties [43,44]. In addition, it helps to protect the lipid barrier of the skin by increasing the biosynthesis of intercellular lipids [43,44]. Shea butter contains lipids that are similar to those of the skin, thereby supporting the skin's natural lipid layers [45].

A study previously performed in our research center evaluated three different, but widely used silicone gels: Dermatix (Mylan, The Netherlands), Kelo-Cote (InTe Medical, Belgium) and BAP Scar Care silicone gel (BAP Medical, The Netherlands) [18]. Bap Scar Care gel was the newest silicone gel and proved to be the most occlusive and hydrating of the three, and thus this was chosen as a representative product for silicone gels to compare with the moisturizers in our current study. Bap Scar Care gel consists of polysiloxanes providing occlusion, it also contains Vitamin E but no hydrating ingredients are present.

2.6. *Recruitment of participants*

Young adult volunteers (20–35 years) were eligible for participation in this study. Inclusion of this age group helped to ensure comparable thickness of the skin. Exclusion criteria were: wound healing or active scarring in the region of interest, dermatologic disorders, metabolic conditions affecting the skin, or medication altering the hydration state of the SC.

All participants were asked to refrain from showering the evening prior to and the morning of the study. Additionally, coffee, soda, smoking or usage of any sort of creams or lotions were prohibited the day of the trial. Upon arrival, volunteers had to remove clothing covering the lower arms. An acclimatization period of 30 min for adjusting to room temperature and humidity was maintained. After obtaining informed consent, 4 areas of 2 by 2 cm were drawn on the volar side of both lower arms, starting at 2 cm distal from the elbow crease and spaced 2 cm apart, ensuring no product mixing during application (Fig. 2).

Sites with a prominent superficial venous network were avoided by slightly translating the areas laterally. Hair on the designated areas of some volunteers was removed with a 3 M™ surgical clipper with pivot head (3 M™, Minneapolis, United states of America).

The first set of measurements was taken following the acclimatization (time T0), (see Fig. 2). Subsequently, the stripping process to inflict superficial abrasions was initiated. Corneofix CF 20 (Courage + Khazaka electronic GmbH, Köln, Germany), a special adhesive tape of 2 by 2 cm which collects corneocytes (flakes of dead cells) was used. Arms were kept in a maximal extended position on the table with closed fists to enable a stable, even and comparable surface for Corneofix

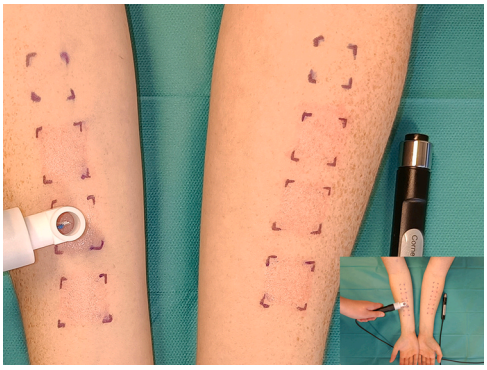

Fig. 2 – Measurements after stripping and prior to product application (T1) with the Tewameter TM300 (left) and the Corneometer CM825 (right).

application. The designated areas for the unstripped controls were the most proximal. Following the sticking of the Corneofix, extra pressure using a purpose-designed stamp was applied to ensure full and equal adhesion of the Corneofix patch to the skin. The stamp had a built-in mechanism to ensure equal pressure application with every use. The Corneofix was then slowly removed upwards using the one-sided lip, to maximize absolute traction tension. Adequate stripping could be observed by the number of corneocytes affixed to the Corneofix. This process was repeated 20 times for each stripping area and thus required 120 Corneofix strips per volunteer. A demarcated slightly moist and erythematous surface could be seen almost immediately after stripping. A waiting time of 20 min was used for induced TEWL stabilization. A second set of measurements was then taken (T1) and immediately thereafter products were applied on the different areas (see Fig. 3).

The designated areas for the unstripped and stripped controls were the first and second most proximal areas, respectively. The two designated areas situated most distal on both arms were preserved for product application. Randomization of products was obtained by creating 4

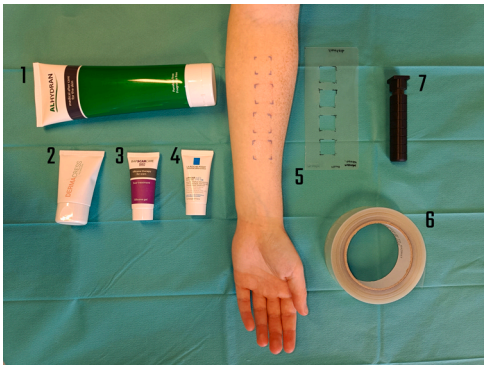

Fig. 3 – Experimental setup, after stripping, immediately prior to product application – (1) Alhydran (2) DermaCress (3) BAP Scar Care silicone gel (4) Lipikar Baume AP+M (5) Drawing template (6) Roll with Corneofix strips (7) Purpose-designed stamp for applying pressure to Corneofix strips.

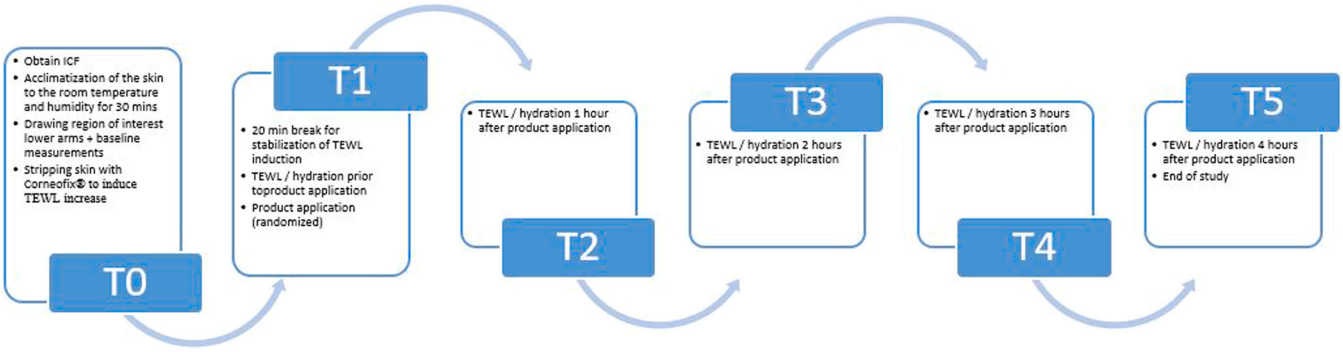

Fig. 4 – Study protocol / timeline.

groups of 6 volunteers where each group received the same 4 products, but on different locations of the volar forearms. The 6 volunteers in the same group, shared the same application location of products. The product application and sites in the last two groups of 6 volunteers was completely randomized using Research Randomizer Version 4.0. Prior to application, the clinicians' hands were disinfected and sufficient product was taken from the container for an area of 4 cm^2. The product was applied with the index finger and smeared in a smooth motion without interfering with other areas. After application, the volunteers were asked to remain still and avoid touching the test zones. Every hour after application, for up to four hours, TEWL and hydration was measured (T2, T3, T4 and T5; Fig. 4).

After completion of their follow-up, volunteers were handed samples of moisturizers and instructed to apply the given product two to three times daily until full healing and loss of erythema was achieved in all the designated areas. Additionally, UV-protection was advised to prevent discoloration.

2.7. *Statistical analysis*

Statistical analysis was performed using GraphPad Prism version 9.0.2 (San Diego, CA, USA). Normality of the data was assessed by the Shapiro–Wilk test. Data is presented as mean ± standard deviation (SD). For non-normally distributed data, pairwise comparisons between more than 2 groups were accomplished with Friedman tests. A p value < 0.05 was considered a priori to be statistically significant when using the Friedman test. When significant, post-hoc Wilcoxon signed-rank tests for pairwise comparison between 2 groups were made. An adjusted p value of < 0.0125 using the Bonferroni correction was considered a priori to be statistically significant.

3. Results

3.1. *Participants*

A total of 36 healthy volunteers were recruited for the clinical trial. Volunteers included 13 male and 23 female participants with a mean age of 21.92 (± 1.02) years. Thirty-five volunteers were of Caucasian origin and one volunteer was of brown skin colour. Six male volunteers and none of the female volunteers' forearms required shaving. One female volunteer had a small, matured burn scar on the right lower arm. The test areas were chosen outside, but adjacent to the scarred zone. No problems were reported by any volunteers during or following the study. An overview of all the objective measurements can be found in Table 1.

3.2. *Reduction in TEWL*

3.2.1. *Mean TEWL*

Mean TEWL values with use of moisturizers, silicone gel and both stripped and unstripped controls are shown in Fig. 5. Units of TEWL are expressed as grams per hour per square meter (g/h/m^2). Unstripped controls remained stable with a slight increase over time, attributable to the ambient conditions of the room. TEWL of the stripped controls increased after stripping (T1) and remained stable thereafter. TEWL of sites where the moisturizers and silicone gel were to be applied clearly increased after stripping (T1) and already 1 h after application of the products, the TEWL started to decrease considerably (T2). The mean TEWL values of DermaCress and Alhydran kept clearly decreasing further over time.

3.2.2. *Percentage reduction of TEWL*

Mean percentage reduction (MPR) in TEWL was calculated by the following formula accounting for the percentage reduction of TEWL corrected for baseline TEWL (T0) values and TEWL-induction (T1) after stripping for every individual volunteer and this consecutively for every hour after application up to 4 h (T2, T3, T4 and T5), with T1 (0% TEWL reduction) and T0 (100% TEWL reduction) as stationary values (Formula 1).

$$MPR(t) = \frac{\sum_{i=1}^{n} 1 - \frac{T(i,t) - T(i,0)}{T(i,1) - T(i,0)}}{n} * 100$$

Where:

i = i^{th} volunteer.

n = total number of volunteers (here 36).

T(i,t) = reduction of volunteer i at time t.

Table 1 – Mean and standard deviation (SD) of trans epidermal water loss (TEWL), absolute added hydration (AAH) and cumulative absolute added hydration (CAAH). A.U. = Arbitrary units; MPR = Mean Percentage Reduction.

Data overview								
	DermaCress		Alhydran		Lipikar Baume		BAP scar care silicone gel	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
MPR in TEWL % (n = 36)								
T2	27.78	45.42	32.78	33.35	26.56	29.20	29.03	39.88
T3	33.83	50.97	24.73	49.24	23.98	39.09	24.01	36.96
T4	37.42	35.17	35.05	33.34	29.91	42.55	21.90	41.77
T5	44.71	29.47	39.52	18.34	18.36	36.29	18.72	44.72
AAH A.U. (n = 36)								
T2	2.12	13.78	9.05	17.39	12.57	16.16	-3.02	16.05
T3	10.71	11.43	9.50	14.22	14.22	14.17	1.29	10.41
T4	11.25	12.39	6.78	13.77	16.44	13.91	2.85	9.02
T5	10.53	10.33	4.23	12.25	16.86	13.98	3.80	9.49
CAAH A.U. (n = 36)								
T2	2.12	13.78	9.05	17.39	12.57	16.16	-3.02	16.05
T2-T3	12.83	24.50	18.55	30.84	26.78	29.64	-1.74	24.65
T2-T4	24.08	35.60	25.33	43.98	43.22	42.49	1.12	32.66
T2-T5	34.61	44.99	29.55	55.97	60.08	55.00	4.92	40.57

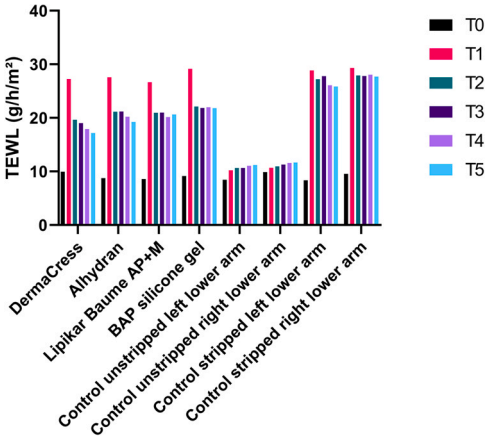

Fig. 5 – Mean TEWL values during follow-up time expressed as (g/h/m²).

MPR(t) = Mean Percentage Reduction at t hours after application.

MPR is an effect size [46] representing the magnitude of the difference in reduction in TEWL values [18] and it is a statistical measure to calculate the effect of a treatment for which the comparison with a control group is made. Here, the treatment and the control group are respectively represented by T(i,t) and T(i,1). Results are shown in Table 1.

The MPR over time provided by the moisturizers and silicone gel are illustrated in Fig. 6. Minimal TEWL reduction for DermaCress was 1-hour after application (T2) 27.78% (± 45.42). For Alhydran this was 2 h after application (T3) with a minimal value of 24.73% (± 49.24). The reduction in TEWL continued for Alhydran and DermaCress, with a maximal reductions of 39.52% (± 29.47) and 44.71% (± 18.34), respectively, measured at4-hour after application (T5). In contrast to this, the silicone gel reached a maximal reduction of 29.03% (± 39.88) at 1-hour after application (T2). From then on the MPR of the silicone gel declined over time until the minimal value of 18.72% (± 44.72) was reached. Lipikar Baume AP+M reached maximal reduction of 29.91% (± 42.55) at 3-hours after application (T4). From there, the effectiveness declined until the minimal value of 18.36% (± 36.29) 4 h after application. The longer after application, the more prominent the differences in occlusion were between the well-balanced moisturizers (Alhydran and DermaCress) versus the other products. We found no significant differences in TEWL reduction in the first 3 h after application between the different products (Table 2). At 4 h after application (T5) we found no significant differences in the reduction of TEWL between silicone gel and Lipikar Baume AP+M nor between DermaCress and Alhydran ($p > 0.0125$). However, both DermaCress and Alhydran demonstrated significantly reduced TEWL compared to both Lipikar Baume AP+M and BAP silicone gel ($p < 0.0125$).

3.3. *Hydration of the stratum corneum*

3.3.1. *Mean hydration values*

Mean hydration values are illustrated in Fig. 7. The units of the Corneometer CM 825 are arbitrary (A.U.). All mean hydration values increased over time compared to the offset value (T0). Mean hydration values of the unstripped controls increased over time due to the ambient conditions in the examination room. Mean hydration values of the stripped controls increased over time due to the latter reasoning in combination with the added hydration value of the stripping procedure. A correction for the ambient conditions and stripping procedure was done with the formula in Section 3.3.2.

3.3.2. *Absolute added hydration (AAH)*

Absolute added hydration of the different products was calculated using Formula 2, accounting for both the stripped and unstripped control values:

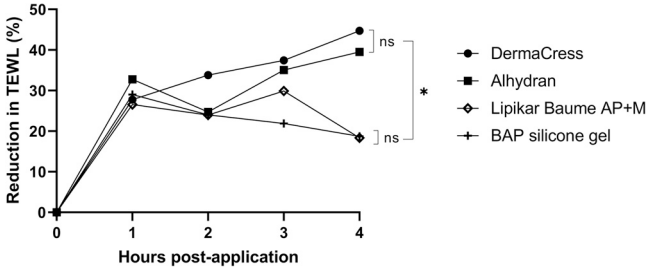

Fig. 6 – Mean Percentage Reduction (MPR) in TEWL up to 4 h after product application. No significant differences indicated with 'ns'. Significant differences indicated with '* '.

Table 2 – Mean Percentage Reduction (MPR) in Trans Epidermal Water Loss (TEWL).

MPR in TEWL statistics	
Reduction of TEWL (n = 36)	Friedman test p-value[a,b]
T2	0.488
T3	0.221
T4	0.092
T5	0.001
Reduction TEWL T5[c] (n = 36)	**Post hoc test p-value[d,e]**
DermaCress vs Alhydran	0.307
DermaCress vs Lipikar	< 0.001
DermaCress vs BAP	0.006
Alhydran vs Lipikar	0.002
Alhydran vs BAP	0.005
Lipikar vs BAP	0.932

[a] = Friedman test compares the 4 products every hour after product application
[b] = Statistical significant if $p < 0.05$
[c] = Only a significant Friedman test was followed by the correct post-hoc testing
[d] = Wilcoxon paired signed rank test was used
[e] = Significance level was adjusted by using the Bonferroni correction, statistical significant if $p \leq 0.0125$

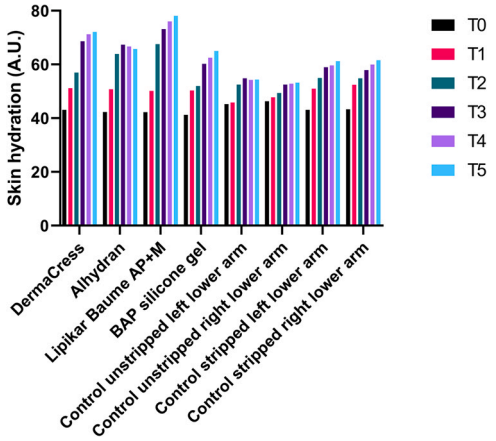

Fig. 7 – Mean hydration values as measured by the Corneometer CM825 during follow-up time.

$$AAH(t) = \frac{\sum_{i=1}^{n} [HP(i,\ t) - HSC(i,\ t)]}{n}$$

Where:

i = i[th] volunteer.

n = total number of volunteers (here 36).

HP(i,t) = hydration after application of product P of volunteer i at time t in hours.

HSC(i,t) = hydration of stripped control site of volunteer i at time t in hours.

AAH(t) = Absolute Added Hydration at t hours after application *arbitrary units [A.U.]*.

Similar to MPR, AAH is an effect size [46] representing the magnitude of the difference in hydration values [18]. Here, the treatment and the control group are respectively represented by HP and HSC. Results are shown in Table 1.

AAH of the moisturizers and silicone gel during the follow-up time is illustrated in Fig. 8 and values are presented in Table 1. Lipikar Baume AP+M provided the greatest increase in hydration of the four products during every measurement; AAH for this was maximal (16.86 ± 13.98) at 4 h after application. One hour after application all products seemed to provide an increase in hydration when compared to the offset with the exception of BAP silicone gel which actually showed a slight decrease in hydration − 3.02 (± 16.02) at T1. Bap silicone gel improved over time with a maximal value of AAH of 3.81 (± 9.49) at 4 h after application. The AAH with DermaCress improved over time with a minimal value of 2.12 (± 13.78) 1-hour after application and stabilized after 3 h after application with a maximal value of 11.25 (± 12.39). Alhydran reached a maximum value of AAH 2 h after application with 9.50 (± 14.22) and declined thereafter until a minimal value of 4.23 (± 12.25) 4 h after application. Significant differences between the moisturizers mutually and compared to BAP silicone gel are listed in Table 3.

3.3.3. *Cumulative absolute added hydration*

Cumulative absolute added hydration at time t, CAAH(t), was calculated using formula 3:

$$CAAH(t) = \frac{\sum_{i=1}^{n} 1 - \frac{HP(i,t) - HSC(i,0)}{HP(i,1) - HSC(i,0)}}{n} * 100$$

Where:

i = i[th] volunteer.

n = total number of volunteers (here 36).

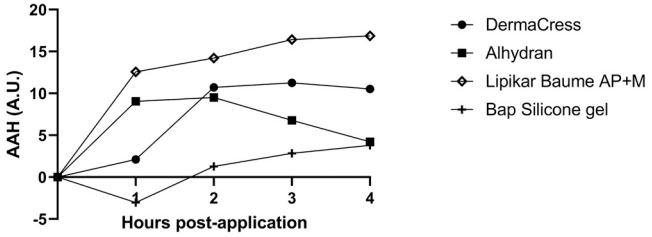

Fig. 8 – Absolute Added Hydration (AAH), expressed in arbitrary units (A.U.).

Table 3 – Absolute added hydration (AAH).

AAH statistics				
AAH (n = 36)	Friedman test p-value[a,b]			
T2	< 0.0001			
T3	< 0.0001			
T4	< 0.0001			
T5	< 0.0001			
	Post hoc test p-value[c,d]			
	AAH T2[e] (n = 36)	AAH T3[e] (n = 36)	AAH T4[e] (n = 36)	AAH T5[e] (n = 36)
DermaCress vs Alhydran	< 0.0001	0.2532	0.0002	< 0.0001
DermaCress vs Lipikar	< 0.0001	0.0847	0.0139	0.0078
DermaCress vs BAP	0.0764	< 0.0001	0.0001	0.0009
Alhydran vs Lipikar	0.1045	0.0460	< 0.0001	< 0.0001
Alhydran vs BAP	0.0003	0.0007	0.0305	0.6469
Lipikar vs BAP	< 0.0001	< 0.0001	< 0.0001	< 0.0001

[a] = Friedman test compares the 4 products every hour after product application
[b] = Statistical significant if $p < 0.05$
[c] = Wilcoxon paired signed rank test was used
[d] = Significance level was adjusted by using the Bonferroni correction, statistical significant if $p \leq 0.0125$
[e] = Only a significant Friedman test was followed by the correct post-hoc testing

HP(i,t) = hydration after application of product P of volunteer i at time t in hours.

HSC(i,t) = hydration of stripped control site of volunteer i at time t in hours.

CAAH(t') = Cumulative Absolute Added Hydration at t hours after application *arbitrary units [A.U.]*.

Similar to MPR and AAH, CAAH is an effect size [46] which represents the magnitude of the differences in hydration, but in contrast to AAH, CAAH is represented in a cumulative manner. Here, the treatment and the control group are respectively represented by HP and HSC. Results are shown in Table 1. CAAH of the different moisturizers and silicone gel are illustrated in Fig. 9. DermaCress, Alhydran, Lipikar Baume AP+M and BAP Silicone gel provided a CAAH of respectively 34.61 (± 44.99), 29.55 (± 55.97), 60.08 (± 55.00) and 4.91 (± 40.57) at 4 h after product application. At 4 h after application, DermaCress (Der), Alhydran (Al) and Lipikar Baume AP+M (Lip) showed a comparable CAAH (Der vs Al $p = 0.197$; Der vs Lip $p = 0.082$; Al vs Lip $p = 0.024$) (see Table 4). The CAAH of all moisturizers was significantly better than the CAAH of BAP Silicone gel at all times except for 1-hour after application of DermaCress, which had a higher CAAH than

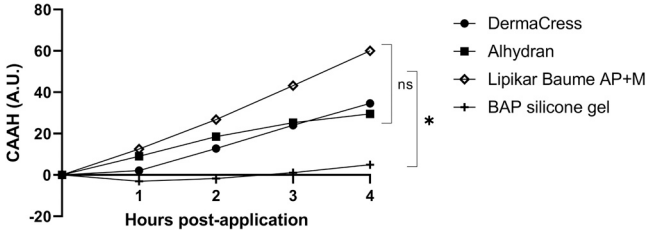

Fig. 9 – Cumulative Absolute Added Hydration (CAAH), expressed in arbitrary units (A.U.). No significant differences indicated with 'ns'. Significant differences indicated with '*'.

Table 4 – Cumulative absolute added hydration (CAAH).

CAAH statistics				
CAAH (n = 36)	Friedman test p-value[a,b]			
T2	< 0.0001			
T2-T3	< 0.0001			
T2-T4	< 0.0001			
T2-T5	< 0.0001			
	Post hoc test p-value[c,d]			
	CAAH T2[e] (n = 36)	**CAAH T2-T3[e] (n = 36)**	**CAAH T2-T4[e] (n = 36)**	**CAAH T2-T5[e] (n = 36)**
DermaCress vs Alhydran	< 0.0001	0.0127	0.6247	0.1974
DermaCress vs Lipikar	< 0.0001	0.0015	0.0013	0.0825
DermaCress vs BAP	0.0764	0.0023	0.0007	0.0003
Alhydran vs Lipikar	0.1045	0.0460	0.0067	0.0239
Alhydran vs BAP	0.0003	0.0002	0.0007	0.0060
Lipikar vs BAP	< 0.0001	< 0.0001	< 0.0001	< 0.0001

[a] = Friedman test compares the 4 products every hour after product application
[b] = Statistical significant if $p < 0.05$
[c] = Wilcoxon paired signed rank test was used
[d] = Significance level was adjusted by using the Bonferroni correction, statistical significant if $p \leq 0.0125$
[e] = Only a significant Friedman test was followed by the correct post-hoc testing

BAP Silicone gel, but the comparison lacked significance (see Table 4). The CAAH of Alhydran and DermaCress was comparable at all times except for 1-hour after application in favour of Alhydran ($p < 0.0001$).

4. Discussion

The physical and psychological sequelae of burn trauma account for 10 million disability-adjusted life years lost annually, indicating the global burden of these injuries [47]. In the United States alone, over 20 billion dollars are spent yearly on the treatment and management of scars [35]. The continuous quest to improve functional and aesthetic outcomes has generated new improvements in burn care. Scar treatment has become a field of innovative clinical research, with methods which include new topical and intralesional products and drug delivery systems in combination with mechanical therapies, such as cryotherapy as well as radio- and laser therapy [35,48]. Despite the newest innovations, the pillars of scar treatment still remain robust and unchallenged: protection against UV-exposure, pressure therapy and scar hydration [49]. In this study we aimed to assess and compare the occlusive and hydrative properties of two different moisturizers, Alhydran and Dermacress, frequently used in our center, as well as Lipikar Baume AP+M, a less frequently used moisturizer, in case of allergy-like reactions. We have demonstrated their occlusive and moisturizing properties through objective measurements, and this could explain their excellent efficacy in the prevention and treatment of hypertrophic scars according to our clinical experience.

Silicone products are based on occlusion to prevent water loss and they increase hydration without adding or attracting moisture. Wang et al. [19] concluded on a cellular level that SGS is more effective at increasing the skins water content than a fluid silicone gel, probably attributable to a higher occlusion, also demonstrated in our previous study [18,19]. To achieve sufficient hydration, SGS needs to be worn for up to 12 h a day and for 12–24 months [35]. The longer SGS are in place, the longer the hydration effect will persist after removal of the sheets [18,19]. When worn for 12 h SGS will provide increased hydration for up to 80 min after removal [19]. When SGS are not well tolerated and discontinuously worn, a lesser hydration effect is achieved, not lasting longer than 15–20 min after removal [19]. When removed, water loss from the skin increases significantly [18,24]. Despite the fact that SGS has been shown to be an effective method of hydrating the skin, in some cases it is difficult to obtain sufficient contact between silicone and hypertrophic scar [50]. Wang et al. showed that SGS only effectively hydrates the skin underneath the sheet, with no to minimal lateral effects due to the absence of water diffusion to the surrounding tissue [19]. Consequently, areas with no sheet-to-scar contact will not receive the protective hydrating effect of the sheet. In the absence of pressure garments, it is difficult to achieve adequate compression and occlusion in anatomical areas such as the sternum, genital area, and joints [50]. Research has shown that a healing process occurs by lipid synthesis in response to increased TEWL [18,51]: a 1% increase of TEWL compared to normal skin, stimulates this process [18,52]. Repair of barrier function may be delayed by excessive occlusion, as achieved with SGS in a process similar to fully impermeable dressings, reducing TEWL values to nearly zero and thus ultimately impeding reparative lipid synthesis [18]. Paradoxically, hyperocclusion often lowers TEWL values far below normal values and thus decreases the responsiveness of scars [29]. The high degree of occlusion leads to frequently seen adverse events such as maceration, skin breakdown, pruritus and irritation [6,17,18,24,50,53]. Most of these issues resolve promptly after treatment cessation but treatment discontinuation can impede patient compliance [18]. In tropical climates, hyperocclusion in combination with high humidity can lead to the development of a “heat rash’ and other skin reactions, due to excessive moisture accumulating

underneath the sheet, which often leads to treatment interruption [53,54]. Not all patients tolerate SGS for more than a few hours, this is especially the case in children and patients with scars in aesthetically important and clearly visible anatomical areas such as the face and hands [50]. Build-up of SGS treatment time is advisable to prevent skin breakdown, impeding immediate adequate treatment efficacy. Gel sheeting can pick up dirt and perspiration and in combination with frequently reported lack of adherence to basic hygiene principles, it can result in increased complications [54,55]. These minor to major complications sometimes result in temporary to permanent treatment discontinuation by patients, these problems with compliance are a concern often expressed by professionals [3,24,55]. Studies by Suetake et al. and Nikkonen et al. showed that the initial effect of SGS is the induction of a mild state of hydration at the SC level [24,56]. However, it has been reported that the water-holding capacity already falls back to pre-SGS values after 1 week of treatment [24,56]. SGS alone usually fails to permanently improve the hydration of dry scars, requiring the use of topical moisturizers to maintain scar hydration for a longer period of time [24].

FSG were designed to solve problems where sheet application has proven difficult, where too much occlusion is not desirable or in warmer climates [54]. As mentioned above, the goal is to lower TEWL to values that inhibit drying of the SC and desiccation of the scar, while still stimulating lipid synthesis for encouraging skin repair. The achieved TEWL values will therefore eventually remain slightly higher compared to normal TEWL values [18]. The use of both FSG and SGS on open wounds is discouraged by official scar management guidelines, greatly limiting their applicability [3]. However, we found reports of FSG speeding up the re-epithelialization process in non-healing burn injuries and, when dry, FSG forms a protective bacteriostatic film to counter infectious complications, by reducing exposure to bacteria, antigens and irritation [3,57]. Patients sometimes complain about the gel which has a prolonged drying time, rendering patients unable to dress until it has fully dried, particularly for large scars [58]. Topical silicone gel only forms a very thin film and the use prompts the question of how effectively it remains in place when exposed to rubbing by clothing during movement [54]. Lastly, the high cost of silicone gels is an important drawback [57]. Thus, even though FSG was initially developed to counter the problems associated with SGS use, FSG has its own limitations. Various studies have demonstrated that the effects of SGS and FSG are comparable [33,59,60]. However, the recent reviews by Hsu et al. [61], Wang et al. [33] and De Decker et al. [62] stated that some of these comparative studies were highly susceptible to bias, lack intra-individual comparison, are of questionable quality, and the results need to be interpreted with caution [18,33,63–65,61,62].

As shown in a previous study, a well-balanced moisturizer like Alhydran is able to considerably reduce TEWL levels [18,42]. The mean TEWL values of the control sites in the current study are comparable to those of Hoeksema et al. [18]. However, the TEWL values of the tape-stripped sites are much higher in the current study, we attribute this to the increased pressure used in applying the Corneofix® compared to the previous study. We have demonstrated that DermaCress provides a similar level of occlusion and hydration compared to Alhydran. The occlusive capacities of Lipikar Baume AP+M are much less prominent than those of the well-balanced moisturizers. The hydration provided by Lipikar Baume AP+M, however, was the highest of all the tested products. The combination of the attraction of moisture to the epidermal layer and the lack of adequate occlusion illustrates the 'double-edged sword' principle of humectants in unbalanced moisturizers. Paradoxically, this increase in epidermal water content can lead to dehydration and worsening of the scar [40]. However it is possible that moisturizers such as Lipikar Baume AP+M which lack adequate occlusion, provide improved protection against dehydration over time due to stimulation of barrier repair by inducing lipid synthesis in combination with an excellent dermatological tolerance [43,44,66].

Moisturizers do not induce the degree of hyperocclusion, nor do they lead to the associated adverse events frequently seen when using SGS [6,17,18,24,50,53]. In contrast to both FSG and SGS, moisturizers can be used easily on all closed areas in between residual defects and are therefore ideal for early scar treatment, if hydration therapy in combination with adequate pressure is desirable [3,42]. Additionally, they do not require treatment build-up and are easy to apply. Moisturizers can be successfully used in hot and cold climates without increasing adverse events such as skin reactions as seen with SG and SGS in hot climates [13,38,40]. Importantly, the use of moisturizers decreases itching, a feature frequently reported by patients [13]. This study shows that usage of moisturizers provides both a higher and longer effect in terms of hydration and occlusion compared to FSG. It can therefore be assumed that moisturizers such as Alhydran and DermaCress require less frequent applications compared to FSG. Many vegetable oils possess compounds with specific antimicrobial, antioxidant, anti-inflammatory and anti-itch properties making them an excellent method to counter xerotic and inflammatory conditions associated with disrupted skin barrier functions [39]. The excellent clinical results obtained with Alhydran and DermaCress has been attributed to the incorporation of these natural oils to replenish intracellular lipids, create an occlusive seal, improve skin hydration, decrease inflammation and reduce microbial contamination [39]. Alhydran and Dermacress both contain high quality natural vegetable oils: *Simmondsia chinensis* (jojoba oil) and *Cocos nucifera* (coconut oil) respectively [18,39]. Jojoba oil is the closest match to natural human sebum, has equal occlusive properties compared to both almond and mineral oil, is especially resistant to degradation due to its unique fatty alcohol esters and has already been found effective in various conditions with disrupted skin barrier [18,39,42,67,68]. Coconut oil has been shown to be as effective as mineral oil in improving hydration and increasing skin lipids, to have antimicrobial properties, e.g. against Staphylococcus aureus, and to be beneficial in skin disorders such as atopic dermatitis and skin xerosis [39,69–71]. Both Alhydran and DermaCress are easy to apply, do not require a prolonged drying time and can provide increased patient comfort in terms of pressure garment dressing and undressing. Compared to SGS, these moisturizers do not require special hygienic techniques and are not limited to a maximum usage,

therefore improving patient compliance. Silicone products do decrease TEWL values and thus contribute in the prevention and treatment of dehydrated skin. However they do not provide adequate barrier restoration nor the skin repair seen when using well-balanced moisturizers. These provide penetration of physiological lipids into damaged skin, positively influencing skin barrier recovery, which counters the dry skin that result from loss of moisturizing structures [38]. Finally, and importantly, silicone products have a high cost, which can be a potential reason for treatment discontinuation and lack of therapy compliance, especially when used for large areas [57]. Due to the longer duration of action of well-balanced moisturizers compared to silicone products, fewer applications are required, and a minimum amount of moisturizing product can be used, contributing to the cost-effectiveness of moisturizers.

The prophylactic and curative scar management effects of fluid silicone gels have been demonstrated in multiple studies [57,63,72–75]. This study clearly shows that the occlusive and moisturizing effect of liquid silicone gel is less than that of the moisturizing creams used in our center. Therefore it can be assumed that moisturizers are a potentially equal or even more cost effective method of moisturizing scars compared to SG and even SGS. Although well balanced moisturizers can be expensive, but this is relative compared to the cost of silicone products which is considerably higher [6,61].

4.1. *Limitations*

The mechanism of action of the Corneometer, is based on electrical conductivity. This might present a minor limitation to the measurement of hydration. due to variations in ion concentrations present e.g. sodium chloride (NaCl) when transpiring [76]. Additionally, its penetration depth is limited to about 40 µm [76]. However, it remains an objective and sensitive instrument for water content measurements in burn scars [77]. Further research on the mechanisms of moisturizers in the prevention and treatment of hypertrophic scars is encouraged, including techniques for visualizing water diffusion and to study their effects on a cellular level.

5. Conclusion

Well-balanced moisturizers such as Alhydran and DermaCress consist of a range of bio-active ingredients. Moisturizers can be used on scars adjacent to open wounds without interfering with the healing process. Well-balanced moisturizers have a long-lasting occlusive effect that increases hours after application and is superior to that of fluid silicone gel. The presence of humectants provides a mechanism of hydration which is absent in silicone treatment. The true restoration of skin barrier function, that is seen with moisturizers, by supplying essential skin lipids, which is lacking in silicone products, and restores moisturizing structures in scarred tissue. In conclusion, moisturizers that provide adequate occlusion and hydration have clear benefits over silicone treatment, they improve patient compliance and are potentially a more cost-effective alternative. Further studies are warranted on their mechanisms of action at a cellular level.

Ethics approval and consent to participate

The Ethical Review Committee of Ghent University Hospital approved this prospective study (Belgian registration number B6702021000403).

Consent for publication

All included volunteers and authors of this study gave consent for publication.

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Authors' contributions

All authors have made substantial contribution to:

The conception and design of the study: IDD, HH, EV, PB, SM, KC. Acquisition of data: IDD, HH, EV, AB, SM. Analysis and interpretation of data: IDD, HH, JV, MS, SM, KC. Drafting the article: IDD, HH, EV, AB, JV, MS, PB, SM, KC. Revising the article critically for important intellectual content: IDD, HH, EV, AB, JV, PDC, MS, PB, SM, KC. Final approval of the version to be submitted: IDD, HH, EV, AB, JV, PDC, MS, PB, SM, KC.

Data Availability

All data are presented in the main manuscript.

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Authors' information (optional)

Not applicable.

Declarations of interest

None.

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