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Scar management by means of occlusion and hydration: A comparative study of silicones versus a hydrating gel-cream

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ABSTRACT

Despite the worldwide use of silicones in scar management, its exact working mechanism based on a balanced occlusion and hydration, is still not completely elucidated. Moreover, it seems peculiar that silicones with completely different occlusive and hydrating properties still could provide a similar therapeutic effect.

The objective of the first part of this study was to compare the occlusive and hydrating properties of three fluid silicone gels and a hydrating gel-cream. In a second part of the study these results were compared with those of silicone gel sheets.

Tape stripped skin was used as a standardized scar like model on both forearms of 40 healthy volunteers. At specific times, trans epidermal water loss (TEWL) and the hydration state of the stratum corneum were measured and compared with intact skin and a scar-like control over a 3–4 h period.

Our study clearly demonstrated that fluid silicone gels and a hydrating gel-cream have comparable occlusive and hydrating properties while silicone gel sheets are much more occlusive, reducing TEWL values far below those of normal skin.

A well-balanced, hydrating gel-cream can provide the same occlusive and hydrating properties as fluid silicone gels, suggesting that it could eventually replace silicones in scar treatment.

1. Introduction

Perkins et al. [1] used silicone inlays in combination with pressure therapy to convey uniform pressure to any scar. After application of silicone gel sheets as the main part of the treatment in 20 patients, they were the first to introduce silicone as a possible therapy for burn scars and contractures. Since then (1983), a lot of articles have been published on the efficacy of silicone and the possible mechanisms of action.

In several randomized controlled trials (RCTs) silicones have been reported to significantly improve the following scar characteristics: elasticity [2], color [3,4], hardness [3–5], extensibility [3], height [6], smoothness [4], elevation [4], blood flow [7], volume [7], pruritus [7], redness [5], thickness [8], pliability [6,8] and pigmentation [6]. It has also been demonstrated that there is no difference between the different brands of silicone gel sheets [3,4]. These results are also supported by other (comparative) clinical trials [9–24].

Although a review article in 2006 indicated that the majority of the silicone-related studies was of suboptimal quality, due to limited sample sizes, suspicion of bias and a lack of control groups [25], still a lot of clinical trials nowadays

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recommend silicone gel sheeting as an effective method to prevent and to treat abnormal scarring.

There was a wide variety however as to the treatment period of the trials reported in the literature, ranging from 2 months to one year or more [10,15] but there was more uniformity as to the length of application on a daily basis. Most authors suggest that silicone gel sheets should be worn progressively for longer periods until at least 12 h per day are reached [2,10,11].

Although most trials indeed seem to confirm the efficacy of silicone gel sheeting, a few studies have failed to do so. Wittenberg et al. [7] found no significant difference between scar sections treated with silicone gel sheeting and the control sections. Li-Tsang et al. [26] showed that both pressure in combination with silicone gel sheeting and pressure alone are significant in reducing scar thickness. This was not the case for silicone gel sheeting alone. Steinstraesser et al. [27] came to a similar conclusion that silicone gel sheeting or silicone spray and pressure improve the Vancouver Scar Scale, but the improvement was not different from pressure alone.

Niessen et al. [28] published a clinical trial that failed to establish the prophylactic effect of silicone gel sheeting. The investigators did not provide a clear explanation but suggested that the treatment might have started too early, i.e. immediately after surgery. However, this is in contradiction with other studies reporting that an early start within days after wound closure is crucial [29,30].

As to the disadvantages of silicone therapy, the most commonly reported adverse effects of silicone gel sheeting are transient rashes, superficial maceration leading to skin breakdown [2,5,6,13,31] and skin irritation at the scar site [6,7]. These are often due to poor hygiene and resolve promptly after treatment withdrawal. Other side effects of the treatment include persistent pruritus of the scar and a foul smell underneath the sheet [32].

Silicone gel sheets can also be difficult to apply on uneven or irregular surfaces or near joints because of the increased mobility [4]. Fixation by tape is often necessary to obtain adequate skin contact and compliance can be compromised because of the appearance on exposed areas [3]. Therefore, equally effective formulations of silicone were developed to facilitate their use and acceptability [33]. A fluid and transparent silicone gel applied from a tube is currently available for use in scar management on exposed or mobile body parts and should be applied twice daily for a variable period of time [21,33].

Recent RCTs suggest that these fluid silicones are as effective as silicone gel sheeting for treatment and prevention of abnormal scarring [21,34,35]. An overall improvement in scar quality was reported [35], as well as a decrease in roughness and itchiness of scar tissue [36] and a significantly flatter, less red, more pliable and less painful scar [34]. A significant reduction in occurrence of abnormal scarring was found, which confirms that fluid silicone gel is equally effective in the prevention of abnormal scarring [34,37].

Although Perkins et al. [1] introduced the silicone-based treatment more than two decades ago and despite the multitude of research that has been published on this topic, there is still no final word on its exact mechanism of action.

Quinn [10] suggested a direct effect of low-molecular-weight silicone fluid on the skin as a possible explanation, but this is not likely to be the mechanism of action, because silicone oil alone has minimal effects on scarring and biopsies could not find any foreign body reaction in scar tissue [2,10,38]. Pressure and blood flow have also been excluded as possible mechanisms of action [10,39]. Other hypotheses are increased surface temperature [39], increased oxygen tension [29] and the creation of a static electrical field [15,40–42]. However, literature does not provide sufficient evidence to prove any of these theories.

The most popular explanation for the mechanism of action of silicones is hydration and occlusion. Quinn [10] were the first to demonstrate that the stratum corneum could accumulate water when covered with a silicone gel sheet and thus can act as a water reservoir. Although this is difficult to visualize directly, a significant increase in water loss from the stratum corneum was seen for a period of 15–20 min after removing the silicone gel [39,43].

Practically all studies since then have confirmed the importance of occlusion and hydration which are now general regarded as the mechanism of action of silicones [5,29,38,44–51]. The positive effects of hydration could be explained by a decrease in capillary activity, resulting in a decrease in collagen deposition [52]. Another suggestion was that hydration increases diffusion of soluble factors, most likely cytokines, which are important factors in cell proliferation, migration and matrix synthesis [53]. Chang et al. [48] supported the occlusion and hydration hypothesis from another point of view. Silicone could act on the epidermis through influencing its keratinocytes and thus initiate signaling cascades affecting the dermal fibroblasts and their collagen and glycosaminoglycan production [49,50]. This hypothesis has been confirmed by the in vitro observation that keratinocytes release soluble factors, presumably cytokines, which induce a decrease in collagen synthesis by fibroblasts [49,51].

All these results suggest that hydration and occlusion are responsible for the modulation of the keratinocytes which affects the skin fibroblasts and their production of excessive collagen. [54,55]. However, most of these studies are also indicating that silicone as such is not obligatory to obtain hydration and occlusion [45]. Some studies are showing equally good results with completely occlusive dressings [56] although it is generally accepted that semi-occlusive dressings are preferable to prevent over-hydration [57]. Still, Wigger-Alberti et al. [56] published a clinical trial in which they compared the effectiveness of silicone gel sheeting versus a polyurethane dressing. They found a significant reduction in the clinical signs of hypertrophic scarring, but the results of the polyurethane dressing were more pronounced and better tolerated than the silicone gel sheets.

In view of these unclarities concerning the exact role of silicone, we hypothesized that the silicone component as such may not be necessary to obtain adequate occlusion and hydration which are considered to be the most important features in silicone scar treatment. We therefore set up a prospective, open controlled, comparative trial to investigate to what degree hydration and occlusion are indeed provided with silicone gels and compared these results to the hydrating and occlusive properties of a hydrating gel-cream. Additionally,

another prospective open controlled study was performed to investigate the occlusive and hydrating properties of two thick and two thin silicone gel sheets and compare them with the results of the silicone gels and the hydrating gel-cream.

2. Materials and methods

2.1. Enrollment

A total of forty healthy volunteers were enrolled in a prospective, open controlled, comparative trial comparing silicone gel with a hydrating gel-cream (part one) and eight of these healthy volunteers were also included in a separate controlled comparative study of silicone gel sheets (part two). Enrollment began in July 2011 after the trial was approved by the local ethical committee at the Ghent University Hospital, and the trial was completed in March 2012.

2.2. Inclusion criteria

The volunteers were eligible for the study if they were eighteen years or older and had intact skin on their inner forearms. Participation was only approved after the volunteers had read and signed the informed consent.

The participants were asked not to put any hydrating creams on their forearms for at least one day before the trial and to wear something warm but not covering the forearms during the trial because all these factors could easily influence the hydration state of the stratum corneum and the applicated products.

Because hair can influence the measurements of the Corneometer CM 825® (Courage and Khazaka, Germany) [58], all excessive hair was removed from the forearm prior to the start of the trial. This was only necessary in two male participants and was done with a clipper.

To guarantee similar conditions for all included subjects, everybody stayed in the same two rooms where temperature and relative humidity were controlled (23 °C ± 0.5 °C; 36% RH ± 5% RH) for the entire duration of the study [59].

2.3. Experimental design

2.3.1. Test areas (Fig. 1)

In the first part of the prospective open controlled comparative trial, in which three silicone gels and a hydrating gel-cream were tested, two test areas were defined, one on each inner forearm of the participants. These test areas were divided into four subareas (2 cm × 2 cm), one control subarea of normal skin and one stripped only subarea (=scar-like control) and two stripped subareas for the application of each of the four test products. For the second part of the study two subareas on each inner forearm were added for application of each of the four silicone sheets. Fig. 1 is a photograph from our study, showing the different test areas.

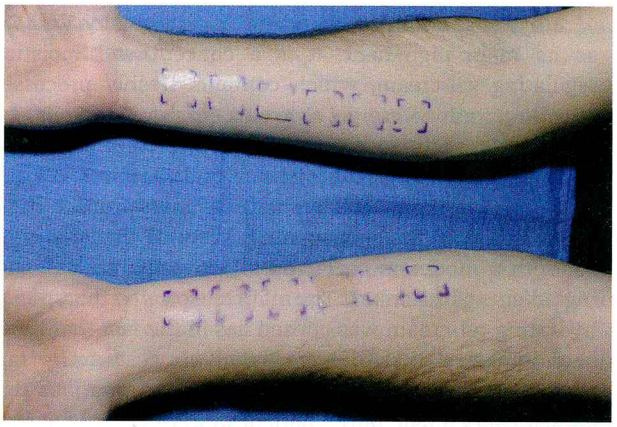

Fig. 1 – Test areas.

2.3.2. Tape stripping

Our initial plan was to perform this study in patients with abnormal scar formation after deep burns as it is generally accepted that in these scars the function of the stratum corneum is disrupted and TEWL is increased after healing and can take longer than one year to recover to basal levels [33,60–62]. However, in a small feasibility study on scars after split thickness skin grafts, we observed such a wide variety of TEWL values in different scars and even within a single scarred area, that an objective comparison of the capacity of different products to decrease TEWL would be extremely difficult. In addition, most scars did not have a surface area large enough to test four to six different products simultaneously.

Since our main goal was to study the occlusive and hydrating qualities of the test products in a standardized way, we decided to use a more uniform and reliable 'scar-like' model with a – consistently – increased TEWL and decreased hydration state of the stratum corneum. This scar-like model was created by 'tape-stripping' of the skin in healthy volunteers and was ideally suited to mimic the two main properties of abnormal scarring (increased TEWL and decreased hydration state of the stratum corneum), as described in the literature [63,64]. It was not our purpose to create an artificial scar model with a similar composition as in real scars: tape stripping is a technique (extensively used in the dermatological literature) by which the upper layer of the stratum corneum is removed in order to create a model ideally suited to investigate the occlusive and hydrating capability of each product [63].

2.3.3. Products

The tested products were:

1. Three silicone gels
   - Dermatix® (Meda Pharmaceuticals, Belgium)
   - Kelo-Cote® (InTe Medical, Belgium)
   - BAP Scar Care® Gel (BAP Medical, Belgium)

   Kelo-Cote® and Dermatix® are two widely used silicone gels, while BAP Scar Care® Gel is a newer silicone gel which differs from the other two as it also contains Vitamin E.

   A hydrating gel-cream

   - Alhydran® (BAP Medical, Belgium)

Alhydran® is an oil in water emulsion with Aloe Vera Gel as its main ingredient. It is a concentrated moisture regulating gel-cream, which contains freshly processed pure Aruba Aloe Vera gel as well as high quality oils and ingredients such as mineral oil, decyl oleate, sorbitan stearate, propylene glycol, jojoba oil, and vitamin A, C, E and B12. The working mechanism of this product is a combination of the moisturizing effect of the Aloe Vera gel with a moderate occlusion effect of the special fatty ingredients of the cream. The main reason why this specific hydrating gel-cream was chosen lies in the fact that it has been intensively used for more than six years to hydrate scars in all our patients. Another major reason was that almost every single burns patient in our center – by far – preferred Alhydran® above any other moisturizing product.

2. Two thick silicone gel sheets (±1.3 mm)
   - Scarban® Elastic (Tricolast, Belgium)
   - BAP Scar Care S® (BAP Medical, Belgium)
3. Two thin silicone gel sheets (±0.3 mm)
   - Mepiform® (Molnlycke Health Care, Belgium)
   - BAP Scar Care T® (BAP Medical, Belgium)).

Application of the products for the first part of the study: A drop of each product, just enough to cover the area, was applied after stripping of the skin.

Twenty minutes later each area was gently dabbed once with a soft disposable tissue.

Application of the products for the second part of the study: application of the products used in the first study was the same. Silicone gel sheets were cut just to the size of the subareas (4 cm^2) and applied after stripping of the areas and measurement of TEWL.

2.3.4. *Measurements*

Tewameter TM 300® (Courage + Khazaka electronic GmbH, Germany)

The measurement of TEWL is the most important parameter for evaluating the efficiency of the skin barrier function. Many international scientific studies have demonstrated its importance in dermatological and cosmetological application [65,66]. The measurement of TEWL which allows an early determination of even the slightest damage in the skin barrier function is based on the diffusion principle in an open chamber, which is the only method to assess TEWL continuously without influencing the skin surface. The effect of air turbulences inside the probe is minimized by the small size of the probe head and the low weight of the probe has no influence on the skin surface.

According to scientific publications, the Tewameter TM300® is one of the standard devices used worldwide [67]. The hand held probe was applied stable and with minimal pressure on the skin. Special attention was paid to prevent air convection in the room by avoiding unnecessary movements and additionally we avoided to breathe out into the direction of the head of the probe, which could have influenced the results.

The TEWL calculation has been conducted using the following Tewameter settings: calculation of the average value of the last 5 measurements, automatic cessation of the measurement when reaching a standard deviation of 0.5. For this study, the measurement value has been determined as follows: The mean value of the last 5 measurements was added to the last measured value and divided by 2.

Corneometer CM825® (Courage + Khazaka electronic GmbH, Germany)

The Corneometer CM 825® has provided a well established method to determine, in a reproducible and accurate way, the hydration level of the stratum corneum. This is documented by the numerous publications in the dermatologic and cosmetologic literature in which the terms 'corneometry' and skin hydration measurements are inseparable [68].

The measuring principle of the Corneometer CM825® is based on capacitance measurement of a dielectric medium, which has the advantages that products applied to the skin only have minimal influence on the measurements. Also, the measurement depth is very small (in the first 10–20 μm of the stratum corneum). This is important because the influence of deeper skin layers (e.g. from the blood vessels) is to be avoided when investigating the epidermal hydration.

The high quality electronics of the probe provide temperature stability and exclude interference with the measurement of the base capacity and power supply fluctuations. A spring in the probe head ensures constant pressure on the skin, enabling exact, reproducible measurements which do not influence the skin.

All these advantages made the Corneometer CM 825® the most reliable instrument to determine the hydration state of the stratum corneum.

In our protocol the mean out of three measurements per subarea was used.

2.3.5. *Design*

In order to make the skin more scar-like as to the generally accepted increase in TEWL, we performed a stripping of the skin with Corneofix® F20 adhesive foil (Courage and Khazaka, Germany) which was applied to 3 of the 4 subareas of each arm. The adhesive foil was pressed firmly against the skin for five seconds, with a special tool consisting of a handle and a flat lower surface (stamp). The adhesive foil was then slowly removed from the subarea. This stripping, repeated 20 times per subarea, caused a controlled removal of the upper layer of the stratum corneum resulting in an artificial increase in TEWL, resembling real scar tissue. This procedure was always performed by the same investigator in order to obtain comparable results [66,67].

This prospective, open controlled, comparative trial consisted of a single test per volunteer, lasting about 5 h.

2.3.6. *Part one*

After an acclimatization period of 30 min, the baseline values were measured with the Tewameter TM300® and the Corneometer CM825® on every subarea, followed by the stripping of the skin on each subarea except for the unstripped control subareas. 5 min after stripping the TEWL was determined on every subarea to objectify its increase after stripping, followed by the application of the four products on their respective subarea. During the next 3 h, the TEWL was measured every hour and the water content of the stratum corneum was determined at the end of the test, after 3 h.

2.3.7. Part two

For the second part of the study the protocol remained the same except for the following small modifications: two subareas were added to each forearm test area to apply the silicone gel sheets and after 3 h, the silicone gel sheets were removed. Additionally 5 min and again 1 h after removal of the silicone gel sheets the TEWL and the water content of the stratum corneum was measured in all areas. This means that in this setting, the duration of the study was extended with 1 h compared to the first study.

A schematic overview of the design of the study is seen in Fig. 2.

2.4. Statistical analysis (only for part one)

A few basic statistical analyses were performed to facilitate working with the data and to keep the number of statistical tests to a minimum (because every test carries a margin of error). This means that we calculated the mean from the measurements in the control subareas and the stripped subareas for the TEWL and the water content of the stratum corneum, after ascertaining that there were no statistical differences between these intra-subarea and inter-subarea values.

The Friedman test was used for the comparative analysis of the data obtained in one subarea over time (t0, baseline measurement; t1, after stripping; t2, 1 h after application; t3, 2 h after application; t4, 3 h after application).

The Wilcoxon matched pairs signed ranks test was used for the comparative analysis of the data between subareas or in the same subarea to clarify the results of the Friedman test.

The statistical software used is SPSS 19.0 and the confidence level used is 95% (significance level is $p < 0.05$).

3. Results

3.1. Part 1: prospective open controlled comparative trial with silicone gels and a hydrating gel-cream

3.1.1. Trans-epidermal water loss

Forty healthy volunteers (23 females and 17 males) were included in this trial, with only one participant who failed to finish the trial because of illness. The mean age was 27 years (range, 19–61 years).

First we analyzed the data, looking at the changes in time and comparing the data with the control subarea and the stripped subarea:

The Friedman test ($p < 0.05$) for repeated measurements gave a significant decrease in TEWL, starting from t2 (=1 h after stripping), and this for all the tested products.

After comparing each applied subarea to the control subareas of normal skin, using the Wilcoxon test ($p < 0.05$), a significantly higher TEWL for each applied subarea was observed.

Compared to the control subareas of stripped skin (further called stripped subarea), the Wilcoxon test ($p < 0.05$) found a significantly lower TEWL for Alhydran® and BAP Scar Care® Gel, but not for Dermatix® and Kelo-Cote® as shown in Fig. 3.

When comparing the applied subareas with each other using the Wilcoxon Matched pairs signed rank test ($p < 0.05$) we found that Alhydran® and BAP Scar Care® Gel are equally occlusive. Both products last longer than Dermatix® and Kelo-Cote®. 1 h and 2 h after stripping no difference could be observed between the test products but 3 h after stripping the areas treated with Alhydran® and BAP Scar Care® Gel showed a significantly lower TEWL than areas treated with Dermatix® and Kelo-Cote® as shown in Table 1 and Fig. 3.

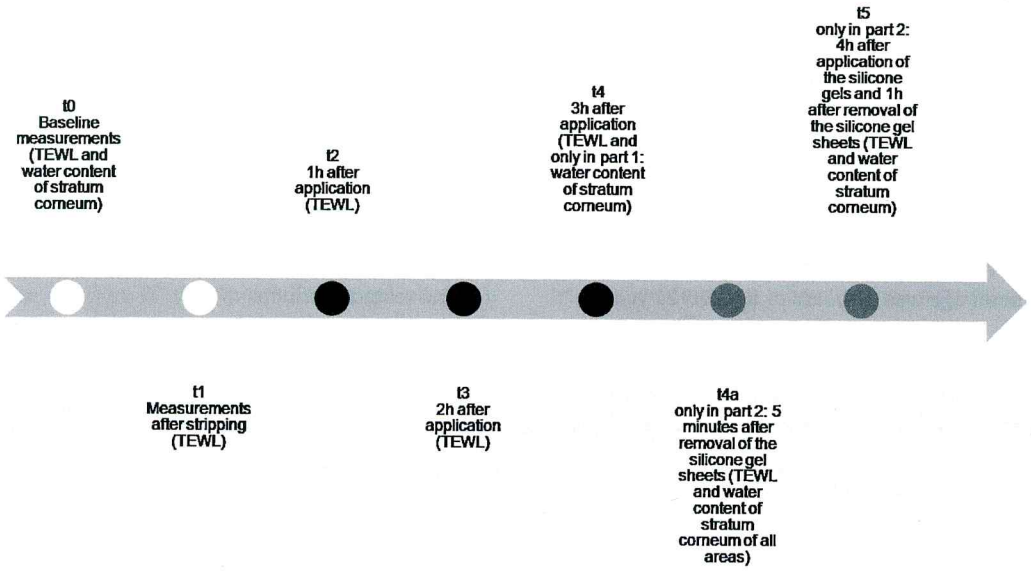

Fig. 2 – Timeline of both prospective open controlled comparative trials: white dots: without product, black dots: applied products, gray dots: silicone gel sheets removed, silicone gels and hydrating gel-cream remained untouched.

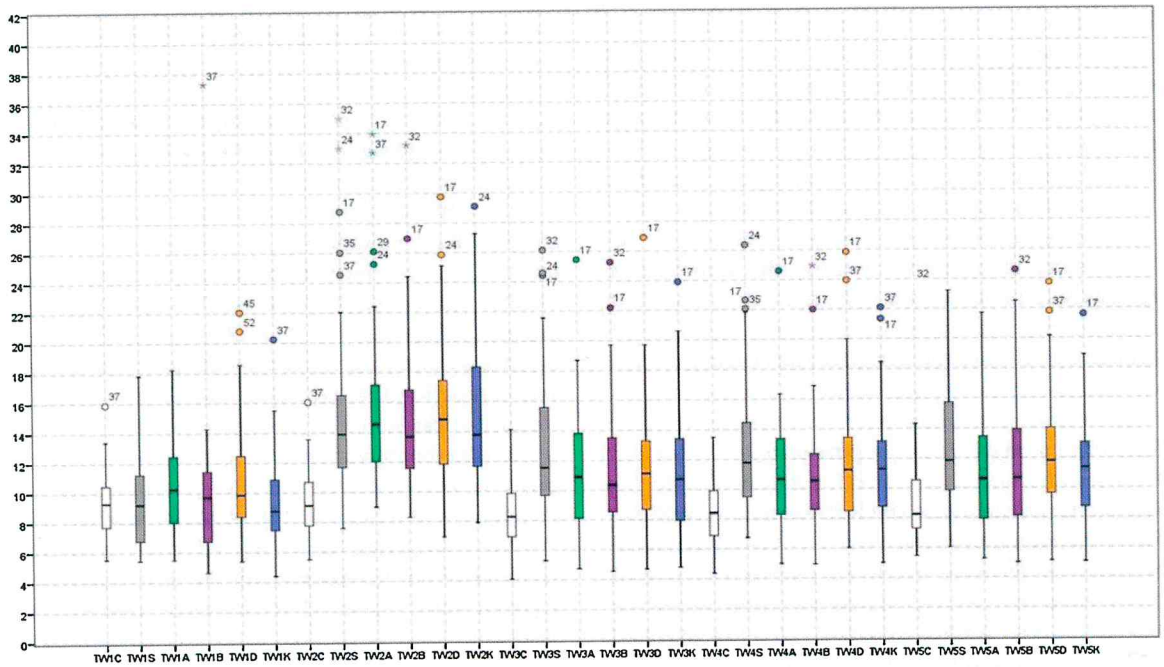

Fig. 3 – Overview TEWL (TW) part one: control (C, white), stripped (S, gray), Alhydran (A, green), BAP Scar Care Gel (B, violet), Dermatix (D, orange), Kelo-Cote (K, blue) subarea; 1 = t0 → 5 = t4.

3.1.2. *Hydration state of stratum corneum*

Fig. 4 gives a schematic presentation of the results of the hydration state of the stratum corneum for the tested products.

Using the Friedman test ($p < 0.05$) for repeated measurements, we observed that Kelo-Cote® was the only product unable to increase the water content of the stratum corneum compared to the baseline measurement before application of the product.

We also compared the applied subareas with each other using the Wilcoxon Matched pairs signed rank test ($p < 0.05$).

We observed that Alhydran® and BAP Scar Care® Gel are equally increasing the water content of the stratum corneum. Dermatix® and Kelo-Cote® are also increasing the water content, but significantly less than Alhydran® and BAP Scar Care® Gel as shown in Table 2 and Fig. 4.

3.2. *Part 2: prospective open controlled comparative trial with silicone gel sheets*

Eight healthy volunteers (5 females and 3 males) were included in this trial (these volunteers also participated in the first part of the trial). The mean age was 22 years of age (20–24 years).

This trial was set up to investigate the occlusive and hydrating properties of two thick silicone gel sheets (Scarban® Elastic and BAP Scar Care S®) and two thin silicone gel sheets (Mepiform® and BAP Scar Care T®) and to compare them with the results of the first part of the study. Baseline measurements of TEWL and water content were measured. TEWL was also measured after stripping just before application of the products. Further TEWL was measured during application and 5 min and 1 h after removal of the sheets. Water content was measured for the second time 1 h after removal of the sheets.

To illustrate the trends in TEWL and water content for the silicone gel sheets and to compare these trends with the data of the silicone gels and hydrating gel-cream from the first study, the following graphics were designed. These graphics make it possible to interpret the results of the prospective open controlled comparative trial of silicone gels and a hydrating gel-cream (part one) in a wider context.

3.2.1. *Trans-epidermal water loss*

Fig. 5 gives a schematic presentation of the results of the TEWL for the tested products.

Table 1 – Results part one – TEWL.

	BAP Scar Care® Gel	Dermatix®	Kelo-Cote®
Alhydran®	Not significantly different	Not significantly different in t2 and t3 Significantly lower in t4	Not significantly different in t2 and t3 Significantly lower in t4
BAP Scar Care® Gel	x	Not significantly different in t2 and t3 Significantly lower in t4	Not significantly different in t2 and t3 Significantly lower in t4
Dermatix®	x	x	Not significantly different
Kelo-Cote®	x	x	x

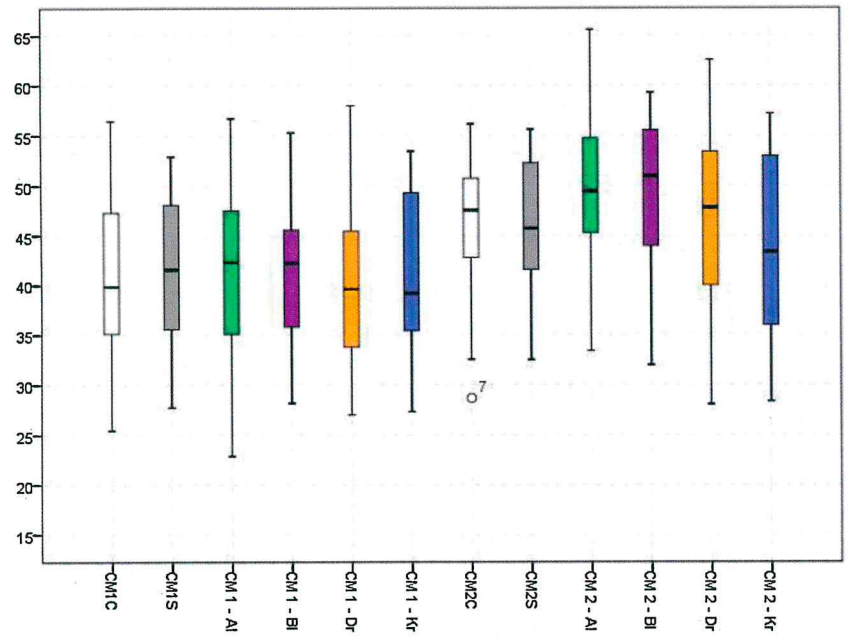

Fig. 4 – Overview hydration state of stratum corneum (CM) part one: control (C, white), stripping (S, gray), Alhydran (A, green), BAP Scar Care Gel (B, violet), Dermatix (D, orange), Kelo-Cote (K, blue); 1 = t0 → 2 = t4.

decreases gradually.

After application of the silicone gels and the hydrating gel-cream, we see the same trends as in the prospective open controlled comparative trial above.

For the silicone gel sheets we observed that the two thick silicone gel sheets are most occlusive while applied and then the thin silicone gel sheets. After removal of the silicone gel sheets the TEWL increases rapidly to comparable values of silicone gels and the hydrating gel-cream.

3.2.2. *Hydration of stratum corneum*

Fig. 6 gives a schematic presentation of the results of the hydration state of the stratum corneum for the tested products.

This graphic illustrates the changes in water content over the duration of the study. 3 h after application of the products the water content is clearly higher compared to the control subarea and the baseline measurements. The thick silicone gel sheets give the highest water contents 3 h after application. The water content of the thin silicone gel sheets is comparable to the water contents of the silicone gels and the are comparable.

4. Discussion

Over the years, silicones in various forms with various properties have become a first-line prophylaxis and treatment option for abnormal scars. Despite its universal acceptance and its worldwide use, several questions or even doubts regarding the role of silicone in scar management still remain.

Already the literature does not seem to provide an unequivocal answer to the first and most basic question: does silicone really work? While the majority of publications have reported good to excellent results with silicones, several other studies demonstrated only minor improvements [14] or even no effect at all [28,32]. Still, the effectiveness of silicones in the treatment of hypertrophic and keloid scars has remained unchallenged and even the excellent review of O'Brien and Pandit [25], which clearly reported about the low level of evidence of silicones, has not influenced the world wide use of silicones.

Table 2 – Results part one – hydration state of stratum corneum.

	BAP Scar Care® Gel	Dermatix®	Kelo-Cote®
Alhydran®	Not significantly different	Not significantly different	Significantly higher
BAP Scar Care® Gel	x	Significantly higher	Significantly higher
Dermatix®	x	x	Not significantly different
Kelo-Cote®	x	x	x

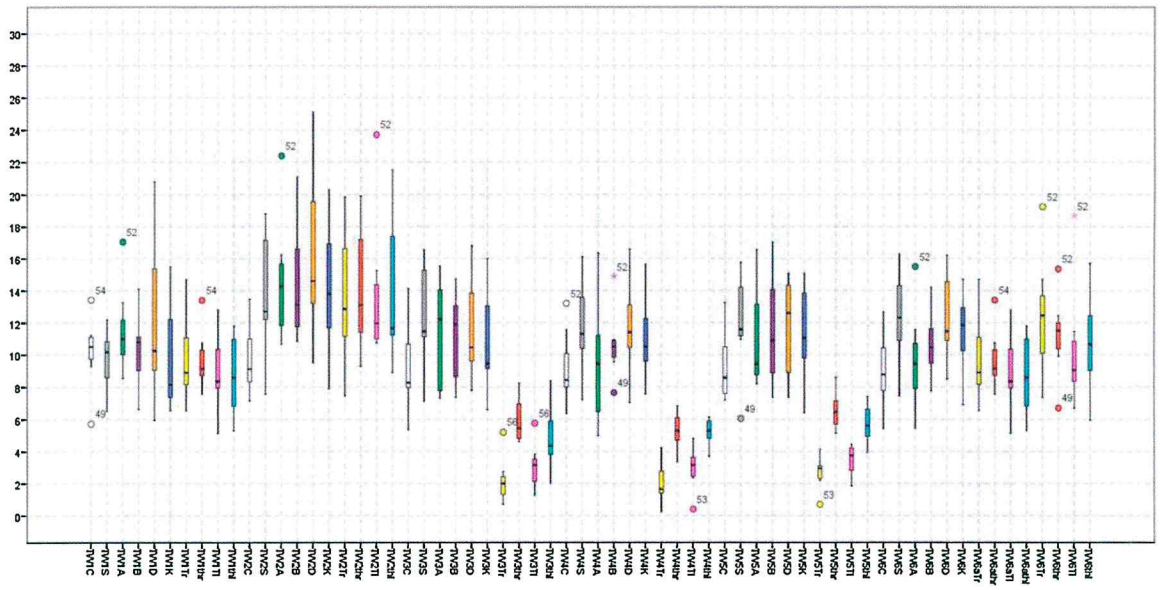

Fig. 5 – Overview TEWL (TW) part two: control (C, white), Stripped (S, gray), Alhydran (A, green), BAP Scar Care Gel (B, violet), Dermatix (D, orange), Kelo-Cote (K, blue), Scarban Elastic (yellow), BAP Scar Care T (red), BAP Scar Care S (pink), Mepiform (light blue) subarea; 1 = t0 → 6 = t5 (6a = t4a).

A second unanswered question concerns the similarities and the differences of the wide variety of products which belong to this group of 'silicones'. Indeed, although different silicone products such as silicone cushions, silicone patches, thick and thin silicone gel sheets, creams containing silicone oil, silicone sprays and fluid silicone gels are generally considered to be 'equally' effective in scar treatment, there is only limited evidence in the literature to support this [25,33]. The use of silicone products is mainly based on silicone gel sheets, but is also focusing more and more on fluid silicone gels. Several studies have demonstrated similar results in the treatment of scars with silicone gel sheets compared to fluid silicone gels, making silicone gel applied from a tube a more or less accepted method of scar treatment nowadays [20,35–37].

A third remaining question concerns the working mechanism of silicone: what exactly is the role of occlusion and

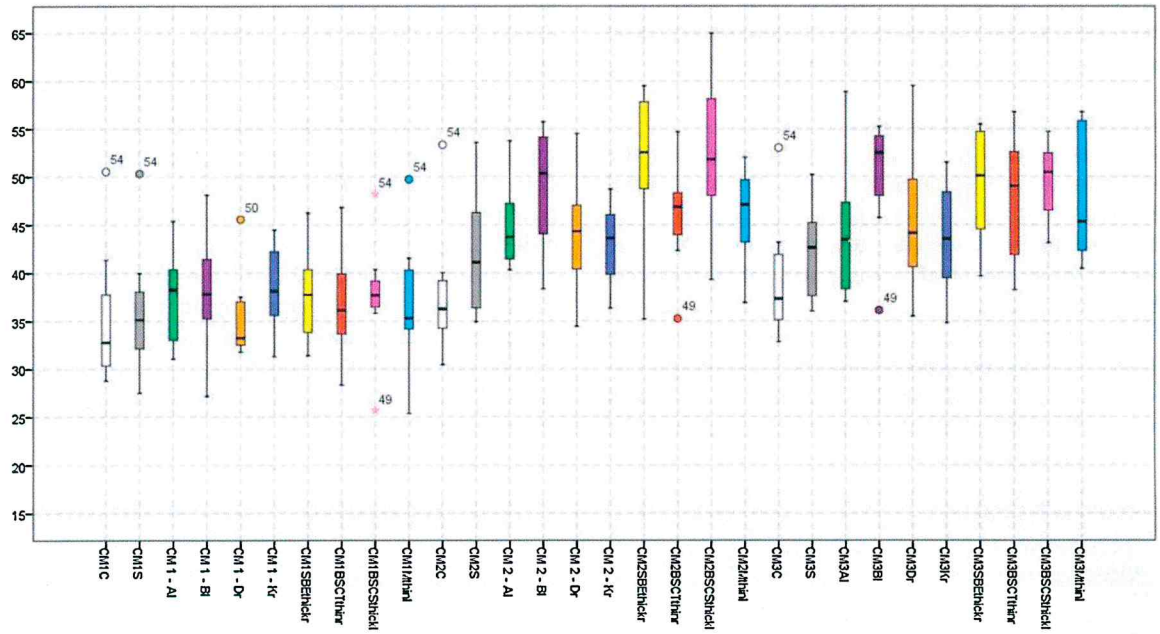

Fig. 6 – Overview hydration state of stratum corneum (CM) part two Control (C, white), Stripping (S, gray), Alhydran (A, green), BAP Scar Care Gel (B, violet), Dermatix (D, orange), Kelo-Cote (K, blue), Scarban Elastic (yellow), BAP Scare Care T (red), BAP Scar Care S (pink), Mepiform (light blue); 1 = t0 → 2 = t4 → 3 = t5.

hydration which are nowadays universally considered as the two most important features to explain the beneficial effects of silicone on scar tissue [38].

Indeed, it has been shown that after healing of a deep dermal or full-thickness wound the function of the stratum corneum remains disrupted, resulting in an increased TEWL in hypertrophic scars and keloids. Silicone has been shown in many studies to improve abnormal scar formation by decreasing TEWL [10,29]. However, the wide variety of TEWL values reported in the literature (and also noticed in the scars of our feasibility study) questions if silicone therapy is equally effective for these different kinds of abnormal scars [61,62].

Still, reliable research has shown that adequate hydration of the stratum corneum is an effective method to prevent or treat hypertrophic scars or keloids. With regards to hydration, Suetake et al. [46] in 2000 concluded that the semi-occlusive nature of silicone gel sheeting improves scars by providing adequate but not excessive hydration. With these data in mind it seems only reasonable to question the fact that silicone products with a wide range of occlusiveness can be equally effective and can all provide this so called adequate or balanced hydration [69]. Indeed, what precise degree of occlusion and hydration is exactly required to have a therapeutic effect and above what level exactly is it becoming 'excessive'?

This lack of a clear definition for the required degree of occlusiveness and hydration as well as the variable outcomes in a lot of studies regarding different silicone products [45,48], led us to hypothesize that silicone as such might not be obligatory to obtain these therapeutic effects on scar tissue. Indeed it seems only logical to suppose that if occlusion (and hydration) are the main features of the mechanism of action, then also another (semi)-occlusive and hydrating agent without silicone might have similar or even better effects on scar tissue. In order to test our hypothesis, we set up a prospective, open controlled clinical trial to compare the degree of occlusion and hydration of silicones with those of a hydrating gel-cream which has been used enthusiastically by all our burns patients for many years.

As previously demonstrated, the barrier function of the skin, and changes of that barrier function, can be evaluated by measuring the TEWL with the Tewameter TM300®, so the measurements were done before, during and after application of the different products. Similarly the hydration state of the stratum corneum was measured with the Corneometer CM825®, before application and 3 h after application of the products. In the second part of the study the hydration state was also measured after 4 h.

With these standardized measurements both the barrier function and the water content of the stratum corneum can be expressed in exact numbers, therefore we were able to investigate to what degree occlusion and hydration were provided by the fluid silicone gels, by the hydrating gel-cream and by the silicone gel sheets.

In the first part of the study we investigated whether or not three fluid silicone gels have the expected hydrating and occlusive properties as reported previously in many studies [38], and if the hydrating gel-cream possesses occlusive and hydrating properties comparable to those of the silicone gels, which could support our hypothesis that the silicone component is indeed not necessary in scar management.

For the occlusive component, the results demonstrated that all four products did have an occlusive effect, since they all reduced the TEWL compared to the baseline measurement on their subarea (after stripping).

BAP Scar Care® Gel (silicone gel) and Alhydran® (hydrating gel-cream) are more occlusive because they reduced the TEWL significantly, whereas Dermatix® and Kelo-Cote® failed to create a 'significant' difference. None of the products could decrease the TEWL enough to reach the normal skin values of the unstripped control subarea, but the graphic in Fig. 1 shows that the difference was minimal.

Further comparison of the different products also demonstrated that Alhydran® and BAP Scar Care® Gel also seem to last longer than Dermatix® and Kelo-Cote®, since the first two products resulted in a significantly lower TEWL than the last 2, 3 h after application.

As for the hydration component, our results clearly demonstrated that two out of three silicone gels, BAP Scar Care Gel and Dermatix® and the hydrating gel cream Alhydran® increased the hydration state of the stratum corneum significantly.

We observed that BAP Scar Care® Gel created a significantly higher increase in hydration than Dermatix® and Kelo-Cote® and that Alhydran® creates a significantly higher increase in hydration than Kelo-Cote®.

Since a hydrating gel-cream demonstrated an equally or even better occlusive and hydrating effect on scar-like tissue when compared to silicone gels, the results of this comparative study confirmed our hypothesis that silicone might not be the sole nor an essential component for the hydration and occlusion of scars and thus for scar management.

In view of these results, the complete lack of attention or scientific interest in the role of moisturizers in scar management is very surprising since most patients with scars, and probably all burns patients with widespread hypertrophic scars, do apply some kind of moisturizer on a daily basis or even several times a day. We were not able to find any explanation why in comparative studies investigating the beneficial effect of silicones, the additional effect of these hydrating creams has never been taken into account. However, our study shows that it could make a major difference.

Mustoe [33] in 2008 mentioned that few studies have investigated the effects of moisturizers on abnormal scars and that no effects on scar elevation or erythema are reported. He concluded that these findings support the hypothesis that normalization of the skin barrier function and not simply hydration of the stratum corneum may be the important component of the mechanism of action of silicone therapy in reducing abnormal scarring. But from the dermatological literature it is known that moisturizers can have multiple components, including occlusive ingredients and humectants, and therefore could be equally effective in this normalization of the skin barrier function [70–72]. The occlusive ingredients (oily substances) will impede water loss and the humectants (glycerin, propylene glycol, etc.) are compounds that attract water from the dermis into the stratum corneum. Moisturizers that contain only humectants will draw water into the stratum

corneum but will not prevent the hydrated stratum corneum from losing its increased water content. For the treatment of scars with a defective barrier this is an important issue as the use of moisturizers with only humectants will contribute to a drying function of the outer layer of the skin and should be avoided [73].

It has also been reported that a scar attempts to heal itself by synthesizing lipids and that the skin responds to an increase in TEWL by up regulating epidermal lipid synthesis [74]. Experiments have shown that increasing TEWL by only 1% can stimulate lipid synthesis and therefore repair of barrier function [75]. A possible explanation for the 'subjective' excellent results as experienced in our burns patients with hypertrophic scarring using the hydrating gel-cream could therefore be explained by a reduction of the TEWL values to values just above these of normal skin and the increase of hydration as shown in our study.

As for the second part of the study with silicone gel sheets, all the products, silicone gels, hydrating gel-cream and silicone gel sheets decrease the TEWL over time, compared to the baseline measurements in their subarea. Compared to the intact control subarea, the silicone gels and the hydrating gel-cream cannot decrease their TEWL to values identical to normal skin. In contrast to silicone gels and the hydrating gel-cream, silicone gel sheets decrease the TEWL to values significantly lower than the intact control subarea, at least before removal of the sheet. Later on, their TEWL values quickly rise to comparable and even higher levels than the control subarea.

When comparing the different silicone gel sheets, we notice that the thick silicone gel sheets, (Scarban® Elastic and BAP Scar Care S®) reduce the TEWL significantly more than the thin ones, (BAP Scar Care T® and Mepiform®) and that, after removal of the sheets the results become comparable to each other.

It is clear that the gel sheets are the most occlusive of the tested products during their application, but after removal of the sheets the results become comparable to the gels and hydrating gel-cream in less than an hour, in some cases even in less than 5 min (Scarban® Elastic, BAP Scar Care T®).

The hydration state of the stratum corneum is increased by all the products compared to the baseline measurements in their subarea. Compared to the stripped subarea the thick silicone gel sheets are the only ones which could increase the hydration state of the stratum corneum over the 4 h. The thin silicone gel sheets, the Alhydran® gel-cream and BAP Scar Care® Gel showed an increase in one of the measurements (after 3 h or after 4 h) and Dermatix® and Kelo-Cote® could not evoke an increase in hydration state at all compared to the stripped subarea. Compared to the control subarea, all the products showed an increase in hydration, except for Kelo-Cote®.

When comparing the silicone gel sheets to each other, the thick silicone gel sheets are clearly the most hydrating, followed by the thin silicone gel sheets.

Our second study showed that silicone sheets will decrease the TEWL to values far below (thick sheets) or just below (thin sheets) the TEWL values of normal skin and that hydration of the skin was substantially increased. Due to these high levels of occlusion, repair of the barrier function might be delayed similar to completely impermeable dressings that have been shown to reduce the TEWL to zero and therefore preventing the start of reparative lipid synthesis [71]. In scar management these thick sheets will increase the water content of the skin to sometimes unacceptable levels of over-hydration [46] and therefore maceration of the fragile skin is frequently observed.

5. Conclusion

In this comparative study we have evaluated the role of silicone in the treatment of scars by specifically investigating *occlusion and hydration*, the two most likely features in the mechanism of action of silicones in scar management. Through objective measurement of TEWL and hydration state of the stratum corneum, we have demonstrated that a well-balanced, hydrating gel-cream can provide the same occlusive and hydrating properties as fluid silicone gels, which supports our hypothesis that the silicone component as such may not be essential in scar treatment.

An additional comparative study with the three fluid silicone gels, the hydrating gel-cream and four silicone gel sheets showed that the silicone gel sheets significantly reduce the TEWL to much lower values than the normal skin while applied, but that the results rapidly become comparable after removing the sheets. We believe this high degree of occlusion might explain the frequently encountered adverse events associated with the use of silicone gel sheets like maceration, skin breakdown and irritation, which do not occur during or after fluid silicone gel treatment or treatment with a hydrating gel cream.

If indeed, as reported in numerous articles, a 'balanced' degree of occlusion and hydration is essential to bring the TEWL back to values slightly above the level of normal skin, both fluid silicone gels and a hydrating gel-cream can have a similar therapeutic effect.

Future research on semi-occlusive and hydrating agents is required to confirm whether or not moisturizing agents may be equally effective as silicones in scar management and therefore be preferred above expensive, sticky silicone gels and impractical, too occlusive and sometimes overhydrating silicone sheets.

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