Observer-blind randomized controlled study of a cosmetic blend of safflower, olive and other plant oils in the improvement of scar and striae appearance

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Abstract
OBJECTIVE: The normal process of skin tissue repair following injury invariably results in visual scarring. It is known that topical treatment with hydrophobic cosmetics rich in silicone and mineral oil content can improve the appearance of scars and striae. Given lifestyle preferences of many cosmetic consumers towards so-called natural treatments, the objective of this controlled randomized study was to investigate the efficacy of a plant body oil rich in oleic and linoleic acids (Bio Skin Oil®) for improving the appearance of scars and striae.

METHODS: A panel of 80 volunteers with non-hypertrophic scars (40) or stretch marks (40) not older than 3 years applied a cosmetic face and body oil for 8 weeks. Compared to an untreated scar/stretch mark region, a blinded investigator as well as volunteer assessments with given observed parameters demonstrated the efficacy of the oil under test.

RESULTS: On the Observer Scar Assessment Scale (OSAS), the mean score was reduced on the product-treated area by approximately 5% (P = 0.006). The untreated area remained unchanged. Observed effects by volunteers were more pronounced – Patient Scar Assessment Scale (PSAS) giving a reduction of approximately 20% on the treated area, and on the control untreated area a reduction of approximately 6%. The overall product effect of 14% was shown to be clearly significant (P = 0.001). All statements relating to product traits achieved higher frequencies of agreements than of non-agreements and were therefore assessed positively by the volunteers. Highest frequencies of agreements occurred in statements that the test product provides a long-lasting, soft and supple skin feeling (93%); caring effect (87%); and quick absorbance (84%). Agreement was also found for statements that the product improves the skin appearance (61%) and that scars/striae appear less pronounced (51%). Only 17% of volunteers felt the oil had no benefit to the appearance of their scars/striae.

CONCLUSIONS: The oil blend under test is effective in improving the appearance of non-keloid scars and striae. Further work is required to understand the mechanisms of how plant oil fatty acids ameliorate scar and striae appearance.

Résumé
OBJECTIF: Le processus normal de réparation des tissus cutanés suite à une blessure entraîne immanquablement des cicatrices visibles. Il est connu qu’un traitement local à base de cosmétiques hydrophobes à haute teneur en silicone et huile minérale peut améliorer l’apparence des cicatrices et des vergetures. Au vu de la préférence de nombreux utilisateurs de cosmétiques pour des produits dits naturels, l’objectif de cette étude aléatoire contrôlée était d’examiner l’efficacité d’une huile végétale pour le corps riche en acides oléiques et linoléiques (Bio Skin Oil®) dans l’amélioration de l’apparence des cicatrices et des vergetures.

MÉTHODES: Un groupe de 80 personnes volontaires présentant des cicatrices non-hypertrophiques (40) ou vergetures (40) datant de moins de 3 ans ont appliqué une huile cosmétique pour le corps et le visage pendant 8 semaines. En comparant avec une zone de vergetures/cicatrices non traitée les chercheurs travaillant à l’aveugle et les personnes volontaires ont observé des paramètres démontrant l’efficacité de l’huile pendant le test.

RÉSULTATS: Sur l’échelle OSAS (« Observer Scar Assessment Scale »), le résultat moyen a été diminué d’environ 5% (p = 0.006) sur la zone traitée par le produit. La zone non traitée est demeurée inchangée. Sur l’échelle PSAS (« Patient Scar Assessment Scale »), les effets observés par les volontaires ont été plus notables, permettant une réduction d’approximativement 20% sur la zone traitée, et une diminution de 6% sur la zone de contrôle non-traitée. Les 14% d’effet global du produit sont clairement significatifs (p = 0.001). Toutes les affirmations relatives aux caractéristiques du produit ont reçu davantage d’accords que de désaccords et ont par conséquent fait l’objet d’une évaluation positive par les volontaires. Les points d’accord ont concerné en majorité les affirmations sur le produit relatives à une sensation durable de peau souple et douce (93%), une action traitante (87%) et une absorption rapide (84%). Les avis ont également concordé sur les affirmations sur le produit relatives à l’apparence de la peau (61%) et l’atténuation des cicatrices/vergetures (51%). Seuls 17% des volontaires n’ont observé aucun changement suite à l’application de l’huile sur leurs cicatrices/vergetures.

CONCLUSIONS: Le mélange d’huiles testé est efficace pour améliorer l’apparence des cicatrices et des vergetures non chéloloides. Des travaux supplémentaires sont nécessaires afin de comprendre les mécanismes relatifs à l’amélioration de l’apparence des cicatrices et des vergetures grâce aux acides gras contenus dans l’huile végétale.
Introduction

Human wound healing, especially in adults, invariably leads to scarring giving rise to both functional and cosmetic imperfections. Scars appear as a different colour to the surrounding skin and can be flat, stretched, depressed or manifesting a range of symptoms including lack of scar skin pliability, inflammation, erythema and dryness. Cosmetic imperfections can be both emotionally and physically disturbing for the patient and can have consequences in some circumstances within the wider society [1]. This puts pressure on both physicians and product developers to provide treatments, which will diminish and improve scar pliability – or even ‘cure’ their scars. In addition to the visual aspect of scars in terms of colour and contour, scars can also generate pruritic sensations, which can be difficult to manage [2].

At the other end of the spectrum are striae distensae or stretch marks sometimes considered inside-out scars. They are a well-recognized, common skin condition that rarely causes significant medical problems but is often a significant source of emotional distress for those affected [3]. They arise from stretching of the dermis and appear along cleavage lines perpendicular to the direction of greatest tension in areas with the most adipose tissue [4, 5]. The classic anatomical sites affected include the abdomen and breasts for pregnancy-related striae, the outer thighs and regions in adolescent boys, and the buttocks, thighs, upper arms and breasts in adolescent girls [4, 6]. Causes of striae are not agreed on with a number of theories proposed [7–9]. Striae progress through three different stages of maturation – acute characterized by red and slightly raised striae (rubra); subacute characterized by purpuric striae; chronic characterized by hypopigmented and atrophic striae (alba) [10]. In particular, striae rubra are flattened areas of skin with a pink-red hue that may be itchy and slightly raised. Then, they are predisposed to increase in length and to acquire a darker purple colour. Over time, the striae rubra develop into striae alba that appear white, flat and depressed [11, 12].

To improve scars and stretch marks, multiple therapies are available each with their own individual success and failures. Treatment varies including topical tretinoin, moisturizers, topical oils for stretch marks sometimes considered inside-out scars. They are a well-recognized, common skin condition that rarely causes significant medical problems but is often a significant source of emotional distress for those affected [3]. They arise from stretching of the dermis and appear along cleavage lines perpendicular to the direction of greatest tension in areas with the most adipose tissue [4, 5]. The classic anatomical sites affected include the abdomen and breasts for pregnancy-related striae, the outer thighs and regions in adolescent boys, and the buttocks, thighs, upper arms and breasts in adolescent girls [4, 6]. Causes of striae are not agreed on with a number of theories proposed [7–9]. Striae progress through three different stages of maturation – acute characterized by red and slightly raised striae (rubra); subacute characterized by purpuric striae; chronic characterized by hypopigmented and atrophic striae (alba) [10]. In particular, striae rubra are flattened areas of skin with a pink-red hue that may be itchy and slightly raised. Then, they are predisposed to increase in length and to acquire a darker purple colour. Over time, the striae rubra develop into striae alba that appear white, flat and depressed [11, 12].

To improve scars and stretch marks, multiple therapies are available each with their own individual success and failures. Treatment varies including topical tretinoin, moisturizers, topical oils for improved appearance and increased skin scar pliability [13–15]. More recent treatments involve the use of lasers [16, 17].

Methods for assessing and measuring scars and striae – as well as their treatment efficacy – are now well developed. Various scar assessment scales are available, yet need to show reliability, consistency, feasible and valid at the same time. Furthermore, these scales must attach significant weight to the opinion of the patient. The Patient and Observer Scar Assessment Scale consists of two numeric scales: the Patient Scar Assessment Scale (patient scale) and the Observer Scar Assessment Scale (observer scale). The patient and observer scales have to be completed by the patient and the observer, respectively [18,19]. It has been shown that scars and striae can improve under treatment irrespective of their age within a range of up to 3 years [20]. The Mallol scale is used for striae assessment [21].

With many patients seeking topical cosmetics to help in the improvement of scars and striae, mineral oil- and silicone-based therapies have been proven effective especially for keloid scars [22] and are available with and without prescription. However, in the eyes of the consumer the use of such products does not always meet ‘lifestyle preferences’ [23], with many consumers preferring a more natural approach especially plant oils. By developing products that are of ‘natural’ origin would help to address their emotional concern in treating the scar/striae, as well as satisfying their emotional concerns as a consumer. Furthermore, lipids rich in both linoleic, oleic and linolenic acid have been shown effective from a dietary perspective in the reduction in the formation of keloid scars [24–26]. Moreover, it is well known that these lipids also play a key role in the reduction and prevention of inflammatory mediators involved in normal skin development. Animal studies have also shown these lipids to benefit wound healing and scar formation [27–30].

To ascertain the effects of these fatty acids in the cosmetic management and amelioration of non-keloid scars and striae, we conducted as described herein, a clinical in-use study on the performance of a cosmetic face and body oil formulated with Safflower and olive oils rich in both omega-6 linoleic (73%) acid and omega-9 oleic acid (84%), respectively. Methods

The study was conducted under the guidance of Good Clinical Practice (GCP).

Test products

An organic oil cosmetic product (Kneipp Bio Skin Oil®, Kneipp GmbH, Würzburg, Germany) comprising 55.9% Safflower oil (Carthamus tinctorius seed oil), 42% olive oil (Olea europea fruit oil), 2% grapefruit oil (Citrus grandis peel oil) and 0.1% tocopherol (antioxidant) was evaluated in this study.

Volunteers

Eighty volunteers (mean age 35 years), 8 male and 68 female with striae (55%) and scars (45%), were recruited onto the study. Informed consent was given, and the scar/stretch mark was assessed according to a POSAS (Patient Observer Scar Assessment Scale) by a trained evaluator – either body or face with two skin areas with comparable scars/stretch marks or one long stretch mark/scar (at least 10 cm) to enable half of the scar/stretch mark to act as the untreated control.

Participants were eligible if they were aged 18 years and above with stretch marks (Mallol score 1 to 3) due to either post-pregnancy, weight training, weight gain or adolescent growth not older than 3 years; or scars due to abrasions, cuts or surgery, on the body or face also not older than 3 years; either two comparable areas or one large area that could be appropriately allocated to test and control; stable weight for at least 2 months (less than 3% weight changes) with a willingness not to change normal eating habits during the course of the study.

Table 1 Test schedule and evaluation

| Day 1 | Day 1 to 56 | Day 57 |
|-------|-------------|--------|
| Informed Consent | X |  |
| In-/Exclusion Criteria | X |  |
| Visual Evaluation (POSAS) | X | X |
| Application of Test Product twice daily | X | X | X |
| Questionnaire |  |  |  |

The initial application of the test product was performed after the first visual assessment at the study centre.
Exclusion criteria for the study included, pregnancy/lactation, addiction, infectious diseases, participation/waiting period post-participation in similar cosmetic and/or pharmaceutical studies, hypertension, insulin-dependent diabetes, documented allergies to cosmetic products and/or ingredients, active skin disease at the test area, active systemic therapies, hypertrophic scars or keloids, pigmented lesions, tattoos, irritated skin, hairs, etc., topical medication at the test area within the 2 weeks prior to and during the study, application of leave-on cosmetics (e.g. creams, lotions, sunscreens, oily cleansing products) in the test area within the previous 7 days prior to and throughout the course of the study, avoid contact of the test area with water within the last 2 h prior to assessments and to avoid all sun exposure UV therapy and/or artificial tanning within the last 14 days prior to and during the course of the study.

Product application

In a randomized application – at home twice daily for 8 weeks by each volunteer – scar/stretch marks of volunteers were treated with a neutrally packed and coded test product (B) and an untreated area served as a control (A). Volunteers were instructed on how to use each product by the study centre for the first application (Day 1). The first product application was performed under the guidance of a technician with following applications performed by volunteers at home. A summary of the test schedule is given in Table I.

Measurements

Day 1: The scar/stretch mark was assessed according to the POSAS by a trained evaluator.

Day 1 to 57: Volunteers used the test product, and the last product application was performed at least 10 to 16 h before the evaluation.

Day 57: The scar/stretch mark was assessed according to the POSAS by a trained evaluator and volunteers completed a questionnaire. Remaining test products were returned to the study center, which were reweighed at the end of the study and the amount of product used recorded.

A deviation of ±2 days was accepted for the final evaluation, as no substantial influence on the outcome of the study was expected.

Patient and Observer Scar Assessment Scale (POSAS)
The Patient and Observer Scar Assessment Scale consists of two scales: the Observer Scar Assessment Scale (OSAS) and the Patient Scar Assessment Scale (PSAS). Both scales contain six observations that are scored numerically (see below). Each of the six observations of both scales has a 10-step score with 1 indicating normal skin and 10 indicating the worst scar/sensation.

The total score for each of the both scales consists of adding the scores of the six items (range, 6–60). The lowest score, 6, reflects normal skin, whereas the highest score, 60, reflects the worst scar.

OSAS
Vascularity: Presence of vessels in striae/scar tissue assessed by the amount of redness, tested by the amount of blood return after blanching with a piece of Plexiglas. The scale ranges from normal pale (Score 1) to pink, red and purple (Score 10).

PSAS
Pigmentation: Brownish coloration of the striae/scar by pigment (melanin); apply Plexiglas to the skin with moderate pressure to eliminate the effect of vascularity.

Thickness: Average distance between the subcuticular–dermal border and the epidermal surface of the striae/scar.

Relief: The extent to which surface irregularities are present (preferably compared with adjacent normal skin).

Pliability: The extent to which surface irregularities are present (preferably compared with adjacent normal skin).

Surface Area: Surface area of the striae/scar in relation to the original wound area.

Scale: 1 = Normal skin to 10 = Worst striae/scar.

A Plexiglas tool was used to evaluate vascularity and pigmentation, because it was sometimes difficult to distinguish between the items vascularity and pigmentation. The observer used a 10 × 4 cm piece of 3-mm-thick Plexiglas. The vascularity was assessed by pressing the Plexiglas on the scar and the surrounding skin and, while releasing it, looking at the capillary refill. To assess pigmentation, the scar was blanched using the Plexiglas to eliminate the effect of vascularity.

PSAS

Pain: Are the striae/scars painful?

Itching: Is the striae/scar itching?

Scale: 1 = No, not at all up to 10 = Yes, very much

Colour: (pigmentation and vascularity): Is the colour of the striae/scar different from the colour of your normal skin?

Pliability: Is the stiffness of the striae/scar different from your normal skin?

Thickness: Is the thickness of the striae/scar different from your normal skin?

Relief: Are the striae/scar more irregular than your normal skin?

Scale: 1 = No, as normal skin up to 10 = Yes, very different

Mallol score
(Inclusion Criteria – Subjects with Striae)

The suitability of subjects with stretch marks to be included in the study was evaluated by a trained evaluator on Day 1 of the study according to the Mallol score. Subjects with a Mallol score between 1 and 3 were included into the study.

0 = no striae
1 = few and thin striae
2 = Many thin striae or a few thick striae
3 = Many thick striae

Questionnaire

Product traits were assessed by the subjects after the use period using different scores.

Statistical analysis

A significance level of 0.05 (alpha) was chosen for statistical analysis. Given the explorative character of the study, no adjustment for multiplicity was performed. Pairwise comparison of treatment codes was performed on differences to baseline separately for total scores of OSAS and PSAS using paired t-test. Further pairwise comparisons of assessment times by treatment code were conducted for total scores of OSAS and PSAS with paired t-test. Derandomization was performed by merging data to the
randomization list using a unique identifier variable (e.g. randomization number, proDERM identification number).

Adverse reactions
An adverse event which the investigator classified as having a causal relationship to the test material of at least ‘possible’ (i.e. possible, probable) was defined as an adverse reaction (AR). All adverse reactions (excluding those parameters being scored as part of the protocol) were documented in the study records.

Results
Of the 80 volunteers recruited onto the study, 76 (eight male, 68 female – mean age 35.3 ± 12.0 years (mean ± standard deviation)) completed with four exclusions for protocol violations. Two volunteers missed the final visit at the study site. This was classified as major protocol deviation. The amount of product used by another two volunteers was deemed too insufficient. This was also classified as major protocol deviation. All data obtained from these four volunteers were excluded from statistical analysis. There were no adverse reactions (ARs) recorded.

Two skin areas were selected at study commencement with comparable scars or stretch marks on the face or on the body. Application of the product was performed over a period of 8 weeks twice daily to one of the stretch mark/scar; the other one was left untreated. Alternatively, a single and sufficiently long stretch mark/scar was chosen, so that half of it could be left untreated; 45% of subjects included in the study had scars; the other 55% had stretch marks with a Mallol score between 1 and 3.

Table II presents mean values for total scores of OSAS and PSAS by treatment and measurement time points, the mean differences to baseline for total scores and the results for the comparison of treatments and time points. Visual evaluation of POSAS was performed at baseline before the treatment and after 8 weeks of treatment.

The comparison of assessment times showed a significantly lower mean score for the test oil (B) on Day 57 compared to baseline (Day 1) for OSAS as well as for PSAS. For the untreated control area (A), a significantly lower mean score for PSAS was detected by the subjects on Day 57 compared to baseline while only a slight and not significant decrease was found for OSAS by the trained rater. The comparison of treatments showed a significantly higher decrease in the mean PSAS for the treatment oil (B) compared to the control oil (A).

| Parameter | Time   | Treatment A | Treatment B | Comparison of Treatments -values | Treatment A | Treatment B |
|-----------|--------|-------------|-------------|----------------------------------|-------------|-------------|
| OSAS      | Day 1  | 18.7        | 18.5        |                                  |             |             |
|           | Day 57 | 18.2        | 17.6        | 0.5                 –0.9               | 0.210**     |             |
| PSAS      | Day 1  | 19.9        | 21.0        |                                  |             |             |
|           | Day 57 | 19.9        | 16.9        | –1.3                –4.0               | 0.040*      | –0.001*     |

n.s. = not significant; * = significant

| Question                                                                 | Disagreement | Undecided | Agreement |
|--------------------------------------------------------------------------|--------------|-----------|-----------|
| 1. The test product is quickly absorbed.                                 | 8            | 4         | 64        | 84.2      |
| 2. The test product let my scars/stretch marks appear less pronounced.    | 13           | 24        | 39        | 51.3      |
| 3. The test product leaves my skin smooth.                                | 2            | 15        | 59        | 77.6      |
| 4. The test product provides a long-lasting, soft and supple skin feeling.| 2            | 3         | 71        | 93.4      |
| 5. The test product has an intensive care effect.                         | 2            | 8         | 66        | 86.8      |
| 6. The test product improves my skin appearance.                         | 7            | 23        | 46        | 60.5      |
| 7. Overall, I like the test product very much.                           | 8            | 8         | 60        | 78.9      |

Disagreement: Includes the answers for ‘fully disagree’ and ‘rather disagree’; Agreement: Includes the answers ‘rather agree’ and ‘fully agree’.

Table III Subjects’ questionnaire – frequencies of disagreements, agreements and undecided responses (n = 76)
compared to untreated. No significant difference between the treatments was found regarding OSAS.

On the final day of the study period, volunteers completed a questionnaire addressing product traits using a 5-point scale and the results are summarized in Table III. All statements achieved higher frequencies of agreements than of non-agreements (disagreements and undecided answers) and were therefore assessed positively by the volunteers.

Highest frequencies of agreements occurred in statements that the test product provides a long-lasting, soft and supple skin feeling (93%); its caring effect (87%) and its quick absorbance (84%). Agreement was also found for the statements that the product improves the skin appearance (61%) and that scars/stretch marks appear less pronounced (51%). While approximately 30% of volunteers were undecided on the effect of scar/striae improvement, only 17% expressed negativity.

Compared to an untreated scar/stretch mark region, a blinded investigator as well as volunteer assessments with given observed parameters demonstrated the efficacy of the oil under test. On the Observer Scar Assessment Scale (OSAS), the mean score was reduced on the product-treated area by approximately 5% (P = 0.006) while the untreated area remained unchanged. However, the effect seen by volunteers was even more pronounced. In the Patient Scar Assessment Scale (PSAS), a reduction of approximately 20% was found on the treated area while on the control untreated area the reduction was only approximately 6%. The resulting overall product effect of 14% was clearly significant (P = 0.001).

Discussion

Cosmetic treatments for scars can be varied and mainly focus on the use of massage oils or moisturizers with a high oil content. While the trend today is for more natural products – with the likes of mineral oil and silicones deemed too ‘chemical’ – the need to find natural alternatives is in demand. Oils rich in linoleic acid and other polyunsaturated fatty acids have been reported to be effective in scar management. The mechanisms by which these fatty acids function are thought to range from changes in collagen organization to inhibition of post-inflammatory mediators (TNFa) and PPARs [31–34]. Furthermore, it is assumed that by adding to the pool of free fatty acids in the epidermis, these fatty acids serve in the normalization of stratum corneum integrity and development [35]. However, given the lack of solid published human data, more work in this field is required.

The objective of the study was to investigate the efficacy of a body and face oil (Bio Skin Oil®) in improving the appearance of non-keloid scars and striae compared to an untreated control site. At the beginning as well as at the end of the study period after 8 weeks of treatment, a visual evaluation according to the Patient and Observer Scar Assessment Scale (POSAS) for scars and stretch marks was performed.

The POSAS consists of the determination of the Observer Scar Assessment Scale (OSAS) by a trained evaluator and the Patient Scar Assessment Scale (PSAS) by the subjects themselves. The lower the total score for OSAS and PSAS, the better the appearance of the scars/stretch marks. Additionally, the subjects assessed product traits and efficacy by a questionnaire at the end of the study. These scar assessment scales are suitable in the case of this study as they have shown that the evaluation is consistent, reliable, feasible and valid. Furthermore, from a cosmetic viewpoint, given that scars and striae carry a weighted emotional response in a volunteer, it is important to be able to include their opinions. In addition, given that the product under test is a cosmetic, and while the opinion of the volunteers need to compare favourably with any expert and/or instrumental observations, volunteer opinions can outweigh any clinical significance.

Evaluation of the OSAS showed a significant decrease in the total OSAS score for scars/stretch marks treated for 8 weeks with the Bio Skin Oil in comparison with baseline evaluations. This effect, however, was not found to be significant for those untreated areas demonstrating the robust rating quality of the professional grader. However, a significant decrease in the total score was found for PSAS after 8 weeks of usage of the Bio Skin Oil® and for those untreated areas. Such a shift of score level is often observed in ratings of laypersons. However, the difference between treated and untreated at the end of the study is the relevant parameter. This comparison of treatments showed a significantly higher improvement of the total PSAS score on the area treated with the test oil compared to the untreated area after 8 weeks of product use.

The product traits were evaluated positively in the volunteer questionnaire; all seven statements achieved a higher frequency of agreements than of non-agreements. In this case, the Bio Skin Oil® demonstrated efficacy in helping to improve the appearance of scars and striae. Although 51% of the volunteers stated that the test product made the scars/stretch marks appear less pronounced with only 17% considering no difference, the remaining 30% were significantly undecided. These types of findings whereby some volunteers doubt or do not even see an effect can be typical of many cosmetic studies, and need to be taken into consideration especially when developing product claims.

Conclusion

Summarizing the outcomes of the study, it has been shown that Bio Skin Oil® is effective in improving the appearance of non-keloid scars and striae. Further work is required to understand the mechanisms of how plant oil fatty acids ameliorate scar and striae appearance.

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Plant oils for the treatment of striae

S. Bielfeldt et al.

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