

## A Randomized Double-Blind Study to Investigate the Clinical Efficacy of Adding a Non-Migrating Antimicrobial to a Special Silk Fabric in the Treatment of Atopic Dermatitis

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### Key Words

Atopic dermatitis · AEGIS AEM 5772/5 · Sericin-free silk

### Abstract

**Background:** A randomized, double-blind study designed to compare the efficacy of DermaSilk<sup>®</sup> versus a sleeve of similar structure but minus the AEM 5772/5 antimicrobial finish in the treatment of atopic dermatitis (AD). **Objective:** To evaluate the clinical effect of adding an antimicrobial finish to knitted silk garments on eczema severity and on pruritus in patients with AD. **Methods:** Thirty patients aged between 3 and 31 years (mean  $14.2 \pm 7.7$ ) were enrolled. The inclusion criterion was that the patients presented with active AD with eczematous lesions located on the arms without any sign of infection. Each participant was given a set of 4 pairs of knitted silk tubular sleeves marked with seams of different colours. Only one colour was treated with AEGIS AEM 5772/5. This information was unknown to both the clinicians and the patients/parents. At baseline (T0) and after 7 (T7), 14 (T14), 21 (T21) and 28 (T28) days, the patients were evaluated using the following methods: photographic assessment, local modified SCORAD index adapted for only the arm, and parent/patient assessment of pruritus measured with a visual analogue scale. **Results:** The mean local SCORAD index of both the DermaSilk- and the unmodified-

silk-covered arms decreased significantly between baseline (T0) and the end of study (T28). However, while the DermaSilk group showed a constant decrease each week, the unmodified-silk group showed a significant decrease only in the first 2 weeks of the study. Also the decrease in pruritus values between T0 and T28 was greater for the DermaSilk group. **Conclusions:** This study demonstrates the importance of including the AEM 5772/5 finish to the specially knitted silk for a long-term improvement of atopic eczema symptoms.

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Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by severe pruritus and relapse. It is supported by a multi-factorial aetiology, and its pathogenesis is still not completely understood. Many factors have been shown to worsen AD, including food and airborne allergies, climatic factors and chemical and physical irritants. Fabrics have been included amongst the physical irritants [1]. It is well known that fabrics such as wool can produce itch in patients with AD, and the irritation is likely to be caused by the 'spiky' nature of the fibres. Parents are often advised to use cotton clothes for their children. However, recent studies have suggested that cotton fibres when moistened may irritate and scratch

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the skin causing the deterioration of eczematous lesions in patients with AD [2]. Silk, on the other hand, has perfectly smooth fibres, and it appears not to irritate the skin. Moreover, knitted silk also helps to maintain the body temperature by reducing the excessive sweating and the moisture loss that can worsen xerosis.

The skin of patients suffering from AD is frequently found with an increased colonization of *Staphylococcus aureus* [3]. Moreover the quantity of *S. aureus* is linked to the severity of eczema [4, 5] so that topical and systemic antibacterial drugs are often used to keep the skin under control [6, 7].

The recent literature has shown the therapeutic effect of a special silk fabric in the treatment of AD. This fabric is made of knitted fibres of sericin-free silk similar to surgical suture material with antibacterial properties. Microair DermaSilk® (Alpretec – S. Donà di Piave, Venice, Italy) allows the skin to breathe and is comfortable to the wearer. It has a high capacity to absorb sweat and serous exudates (up to 30% of its weight without becoming damp). It is made up only of fibroin (the sericin, an allergenic gummy substance, is extracted during the processing of the silk threads) [8, 9]; DermaSilk also has antibacterial properties thanks to a patented permanent treatment with AEGIS AEM 5772/5, a durable antimicrobial substance active against micro-organisms including *S. aureus* [10]. It is based on the compound alkoxysilane quaternary ammonium. These combined properties suggest that DermaSilk may be an ideal fabric for patients with AD.

The aim of our study was to evaluate the clinical efficacy in AD of a special silk fabric, DermaSilk, compared with the same fabric without the AEGIS AEM 5772/5 antimicrobial.

## Subjects and Methods

We studied 30 patients between 3 and 31 years (mean  $14.2 \pm 7.7$ ) who were referred to our dermatology outpatient clinic between October 2006 and May 2007 (table 1). Patients were affected by AD diagnosed by the criteria according to Hanifin and Rajka [11]. Patients presenting with an active AD with eczematous lesions located on the arms and without any sign of infection were included in the study. Parents and patients over 18 years old had to give a signed informed consent. No approval was required from our ethical committee, and no conflict of interest concerning sponsorship of any kind was noted in this study. The wash-out phases for current treatment were 1 week for topical corticosteroid or antibiotics, on the body areas to be treated with silk, 2 weeks for systemic corticosteroid or antibiotics, 1 week for topical antimicrobics, 4 weeks for topical calcineurin inhibitors and 8

**Table 1.** Age and sex distribution of the enrolled patients

Age range	Patients		Males	Females
	n	%		
5–9 years	11	36.67	7	4
10–14 years	8	26.67	2	6
15–19 years	3	10	1	2
20–24 years	3	10	1	2
≥25 years	5	16.67	4	1
Total	30	100	15	15

weeks for systemic immunosuppressant therapies other than corticosteroid, investigational agents, UV light therapy or systemic antimicrobics. Patients affected by acute infections, neurological or psychiatric disorders, autoimmune disease and immune defects were also excluded. The garments used in our trial were produced and provided by Alpretec. Tubular sleeves were made up of identical-looking fabrics: (i) DermaSilk, the current, commercially available product made from knitted fibroin silk, bonded with AEGIS AEM 5772/5, and (ii) an identical product without the bonded AEGIS AEM 5772/5.

### Study Plan

We performed a single-centre, side-to-side comparison, double-blinded study. Each participant was given 4 pairs of tubular sleeves. Each pair consisted of a sleeve with a red seam and one with a green seam. One of these colours indicated that the sleeve had been treated with AEGIS AEM 5772/5 but neither the authors, parents nor patients knew which one had been coated. This information was known only to the manufacturer and sealed in an envelope. The main characteristics of these fabrics were clearly explained to the parents/patient, and they were asked to dress their arms with the sleeves all night and day, changing them once a day and washing them with a mild detergent as indicated by the manufacturer. The parents/patients were informed to use the same coloured sleeve always on the same arm, and not to cross them over. The choice of which arm to dress with the red- or green-coded sleeve was randomized and labeled on the basis of a computer-generated randomization schedule. Only moisturizing therapy with an assigned emollient cream (a fatty cream containing a mixture of 5% lactic acid and 20% propylene glycol) was permitted to be used once or more per day. The same emollient cream was the only topical therapy permitted in the other areas of the body affected by AD. A gentle non-irritating skin cleanser without antiseptics or antimicrobial products was provided.

At baseline (T0) and after 7 (T7), 14 (T14), 21 (T21) and 28 (T28) days, the patients were evaluated, always by the same investigator, with: (i) photographs, (ii) the local SCORAD index adapted for the only arm [12], and (iii) parent/patient assessment of pruritus measured with a visual analogue scale of 10 cm (value between 0 and 10).

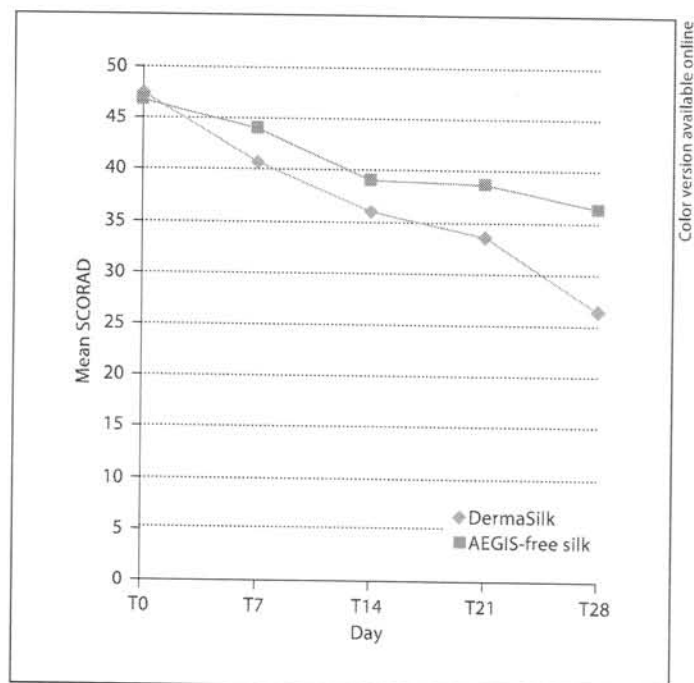
At the end of the study, the code was broken to reveal that the tubular sleeves marked with seams of green colour were DermaSilk whilst those with red seams were unmodified and did not contain the AEM 5772/5 finish.

### Statistical Analysis

Normal distribution was tested by means of the Kolmogorov-Smirnov test. Our variables being normally distributed, the Student *t* test for paired samples was used for the comparison of mean local SCORAD values in the different phases of treatment for each treatment and for the comparison of mean differences in the mean local SCORAD values between the two treatments at each time. In the tables the data are displayed as means  $\pm$  SD (standard deviation). A *p* value  $<0.05$  was considered statistically significant. Statistical analysis was carried out using the SAS V9.1 software (SAS Institute Inc., Cary, N.C., USA).

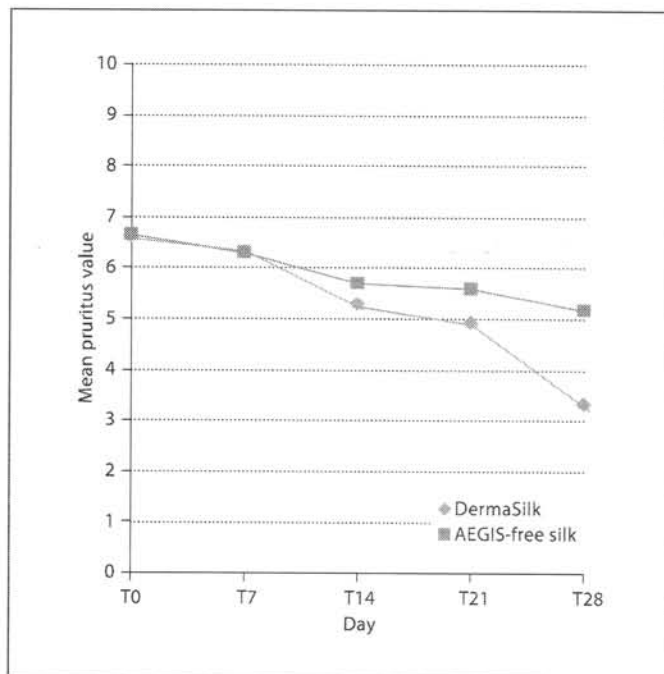
### Results

Four atopic patients withdrew from the study due to the excessive distance from our centre or other personal reasons. The other 26 patients completed the study, following the instructions regarding the continuous use of the silk sleeves. No local side effects relating to the use of the textile such as irritant or allergic contact dermatitis, contact urticaria or exacerbation of the eczema were observed. At baseline the mean local SCORAD indexes of the arms were comparable (47.35 DermaSilk-covered arm and 46.68 unmodified-silk-covered arm; *p* = 0.61). The mean local SCORAD index of the DermaSilk-covered arm decreased significantly between baseline (T0) and T7 (mean  $7.18 \pm 11.8$ ; *p* = 0.0029), T7 and T14 (mean  $4.86 \pm 7.2$ ; *p* = 0.0023), T14 and T21 (mean  $4.57 \pm 8.4$ ; *p* = 0.021), and T21 and T28 (mean  $5.09 \pm 6.9$ ; *p* = 0.002). The total decrease in the mean local SCORAD index between T0 and T28 was remarkably significant (mean  $21.03 \pm 16.7$ ; *p*  $< 0.0001$ ). Also the mean local SCORAD index of the unmodified-silk-covered arm decreased significantly between baseline and T7 (mean  $3.40 \pm 6.46$ ; *p* = 0.008), and T7 and T14 (mean  $4.9 \pm 7.8$ ; *p* = 0.004). However, between T14–T21 and T21–T28, the decrease in the mean local SCORAD index was not significant (*p* = 0.13 and *p* = 0.87, respectively). Taken over the entire 28 days, the reduction of the mean local SCORAD index was still statistically significant (mean  $10.98 \pm 11.9$ ; *p*  $< 0.0001$ ; fig. 1). The comparison between the two groups showed that while the difference is not statistically significant during the first 2 weeks, at T21 and T28 the mean local SCORAD index of DermaSilk is statistically better than that of unmodified silk (*p* = 0.02 and *p*  $\leq 0.0001$ , respectively); also the difference of the mean local SCORAD between the two arms for the whole period of the study was statistically significant (mean  $10.05 \pm 9.22$ ; *p*  $< 0.0001$ ).



**Fig. 1.** DermaSilk showed a statistically significant and constant decrease in the mean local SCORAD index during the 4 weeks of the study. The decrease in the mean local SCORAD index of the AEGIS-free-silk-covered arm was statistically significant between baseline and T28 (mean 10.98; *p*  $< 0.0001$ ) but the results compared to DermaSilk were lower (mean 21.03; *p*  $< 0.0001$ ) and not constant (the decrease in the mean local SCORAD index is statistically significant only during the first 2 weeks).

Similarly, at baseline the mean values of the pruritus of the arms were comparable (6.56 for the arm where DermaSilk was applied and 6.63 for the arm where unmodified silk was used; *p* = 0.64). The mean value of pruritus of the DermaSilk-covered arm did not show a significant decrease between baseline and T7 (mean  $0.31 \pm 1.1$ ; *p* = 0.17). The decrease became statistically significant between T7 and T14 (mean  $1 \pm 2$ ; *p* = 0.018), T14 and T21 (mean  $0.54 \pm 1.1$ ; *p* = 0.030), and T21 and T28 (mean  $1.39 \pm 1.2$ ; *p*  $< 0.0001$ ). The total decrease in pruritus values of DermaSilk tubular sleeves between T0 and T28 was remarkably significant (mean  $3.30 \pm 2.1$ ; *p*  $< 0.0001$ ). The decrease in pruritus values of the unmodified-silk-covered arm was statistically significant between T0 and T7 (mean  $0.41 \pm 0.9$ ; *p* = 0.025), T7 and T14 (mean  $0.30 \pm 0.6$ ; *p* = 0.017), T14 and T21 (mean  $0.31 \pm 0.7$ ; *p* = 0.049) but not between T21 and T28 (mean  $0.30 \pm 0.8$ ; *p* = 0.08). However, the total decrease in pruritus between T0 and T28 was statistically significant



**Fig. 2.** The decrease in the mean pruritus value between baseline and T28 is statistically significant for both fabrics but it is greater for DermaSilk (mean 3.30;  $p < 0.0001$ ) than the AEGIS-free silk (mean 1.42;  $p < 0.0001$ ). Furthermore, while DermaSilk shows a greater decrease in the mean pruritus value mostly in the last 3 weeks, for the AEGIS-free silk the decrease is statistically significant from the start to the end of the study.

(mean  $1.42 \pm 1.4$ ;  $p < 0.0001$ ; fig. 2). The comparison between the two groups showed that while the difference is not statistically significant during the first weeks, at T14, T21 and T28 the mean value of pruritus of DermaSilk is statistically better than that of unmodified silk ( $p = 0.03$ ,  $p = 0.01$  and  $p \leq 0.0001$ , respectively); also the difference of the mean value of pruritus between the two arms for the whole period of the study was statistically significant (mean  $1.88 \pm 1.7$ ;  $p < 0.0001$ ).

## Discussion

The development of a new textile (DermaSilk), a sericin-free silk designed to help prevent bacterial colonization with *S. aureus*, represents a promising path in the treatment and maintenance of AD. Senti et al. [13] observed no significant difference between DermaSilk-treated and corticosteroid-treated skin and suggested that this special textile would probably have an efficacy simi-

lar to a modern class III topical corticosteroid applied daily for a week. Koller et al. [14] compared three different tube fabrics: DermaSilk, sericin-free silk fabric without AEGIS AEM 5772/5 and cotton. A significant reduction of the mean local SCORAD index of the DermaSilk-covered arm was observed in comparison with cotton- and AEGIS-free-silk-covered arms. Although AEGIS AEM 5772/5 has antibacterial properties in vitro [10], recent studies performed by Ricci et al. [15, 16] were unable to demonstrate antimicrobial activity in vivo, though demonstrating superior efficacy in AD compared with cotton. Ricci et al. [15] considered a quantitative microbiological improvement significant if the number of colony-forming units of *S. aureus* per square centimetre was reduced at least to half of the baseline value; they observed a reduction of *S. aureus* colonies, but it was not significant. They suggested that the lack of efficacy in vivo was due to the strong adhesion of AEGIS AEM 5772/5 to the fibres preventing in this way its penetration into the skin and sufficient contact with bacteria to kill them. Therefore the improvement of AD with DermaSilk should be due to its protective barrier function preventing external bacterial overinfection and reducing the contact with clothes. In our study a significant improvement of the mean local SCORAD index was observed for both DermaSilk- and AEGIS-free-silk-covered arms but the improvement was statistically greater for DermaSilk than unmodified free silk (mean  $10.05 \pm 9.22$ ;  $p < 0.0001$ ). Furthermore, while DermaSilk showed a statistically significant decrease in the mean local SCORAD index that was constant during the study, the unmodified silk showed a statistically significant decrease in the mean local SCORAD index only for the first 2 weeks (T0–T7 and T7–T14). In addition, the decrease in the pruritus value was statistically significant for the DermaSilk- and unmodified-silk-covered arms but it was greater for DermaSilk than unmodified silk (mean  $1.88 \pm 1.7$ ;  $p < 0.0001$ ).

Our study confirms the importance of the textile's use for subjects affected by AD. Whilst a significant improvement in the severity of AD and pruritus was observed with both fabrics, DermaSilk produced a constant and statistically significant improvement in eczema severity during the whole period of the study, and it was greater than that of unmodified silk. Also a significant but not constant improvement of the pruritus score was observed with DermaSilk.

In our opinion, the significant improvements of the local SCORAD index and pruritus value observed both with DermaSilk and unmodified silk are probably due to the barrier effect of the dressed silk tubular sleeves but



the greater improvement with DermaSilk is relative to the slight, even if not significant, reduction of *S. aureus* colonies induced by AEGIS AEM 5772/5, as demonstrated in previous studies [15].

In conclusion, DermaSilk has been shown to be more effective in the treatment of AD than cotton and unmodified silk, as demonstrated in previous studies. Fur-

thermore DermaSilk in our study appears to be able to reduce pruritus in AD more effectively than unmodified silk.

This innovative combination of specially engineered knitted, sericin-free silk plus a non-migrating antimicrobial represents a significant step forward in the use of silk as a therapeutic agent in the management of AD.

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