

RESEARCH ARTICLE

A proposal for the use of new silver-seaweed-cotton fibers in the treatment of atopic dermatitis

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Abstract

Background: Atopic dermatitis (AD) is a disease with multifactorial etiology. *Staphylococcus aureus* is one of the predominant environmental factors acting on the course and intensity of the disease.

Objectives: The aims of the study were to evaluate the efficacy and safety of clothing made of cellulose fibers with seaweed enriched with silver ions in the treatment of children with AD.

Methods: A prospective, randomized and double-blinded controlled selection was done to recruit 19 children with diagnosis of AD. This sample was divided in two groups with similar demographic and clinical characteristics (the “control” group of seven children who wore placebo clothing and the “trial textile” group of 12 children who wore clothing with the new textile). The severity of AD and clinical response were assessed by the SCORAD index, the intensity of pruritus and the changes in sleep characteristics, at the start of the study and after 7 and 90 d.

Results: The SCORAD index improvement in the group with the fiber under study was statistically significant after the first 7 d of treatment ($p < 0.001$) and was reduced by about 45% after 90 d. There was also a statistically relevant reduction of the intensity of pruritus and an improvement in the sleep quality after the initial 7 d and at day 90.

Conclusion: The results showed that the textile clothing with seaweed enriched with silver ions brings a quicker improvement of the patients in the first days in opposition to the use of standard all-cotton clothes. The results also reinforce the importance of non-pharmacological measures, like clothing, in the management of patients with a diagnosis of AD.

Keywords

Atopic dermatitis, seaweed, silver ion, *Staphylococcus aureus*, textile

History

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Introduction

Atopic dermatitis (AD), a chronic relapsing inflammatory skin disease, is characterized by relapses and remissions of intensely pruritic lesions with variable location, depending on the patient age¹. The prevalence of AD is increasing in the Western societies with a significant impact on the life quality of patients and their families, and a high economic cost^{2,3}. According to the ISAAC phase III study, the prevalence of the disease in Portugal is about 9.3% and 5.2% for the age groups of 6–7 and 13–14 years, respectively². It is frequently associated with other atopic related diseases such as rhinoconjunctivitis and allergic asthma and in many case there is a family history of atopy. This skin disease has a multifactorial aetiology but the interaction with the environment seems determinant in genetically predisposed individuals⁴.

Changes in the complex interaction between the skin barrier and the innate and adaptive immune system have

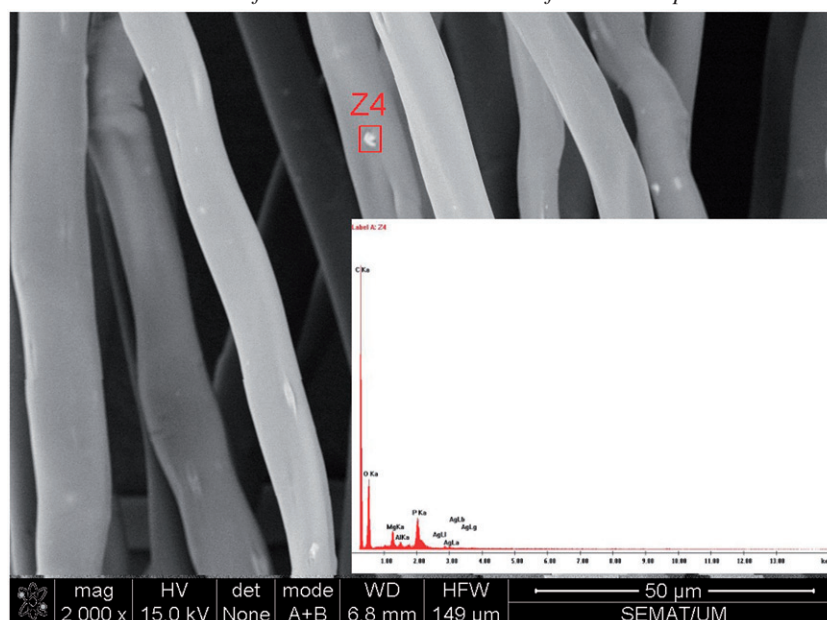
been gradually recognized and seems to affect either the development or the severity of AD⁵. Among the environmental factors that predominantly influence the course and intensity of the clinical symptoms are the infectious agents, particularly, the *Staphylococcus aureus* (SA)⁶. The SA skin colonization was observed in 80–100% of atopic patients whereas in non-atopic individuals this colonization was lower than 30%⁷. Furthermore, the degree of colonization appears to be associated to the disease severity⁸.

The deficiency of the mechanisms responsible for the innate immune response, such as the reduction of antimicrobial peptides (*cathelicidins* and *defensins*)⁹, the dysfunction of toll-like receptors (TLR-2)¹⁰, and the skin barrier permeability^{4,11}, on top of the defects of adaptive immunity (Th2) are primarily responsible for the susceptibility of atopic skin to SA¹².

About 30–60% of SA strains isolated from patients with AD produce exotoxins with super-antigen properties such as the enterotoxins A, B, C, D and E, and the toxin-1 that is responsible for the toxic shock syndrome. The presence of IgE antibodies against these toxins correlates with the intensity of the skin lesions^{13,14}. In addition to the immunological effects, the cytotoxic properties of these toxins may also directly damage the skin barrier¹⁵.

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Figure 1. SEM aspect of the algae fibers showing the silver particles as bright zones that were observed by EDS.



The proteinases produced by SA can damage the corneodesmosomas¹⁶ and secretes sphingosine desacylase and glycerophospholipids that may interfere with the formation of lamellar lipids⁴.

Another aggravating factor of AD is the physical irritation caused, for example, by synthetic textiles¹⁷. Their fiber structure and dimension have a significant impact on how these fibers are tolerated by the patients¹⁸.

An approach to reduce SA colonization includes the use of biofunctional clothing. Studies with silver ion impregnated textiles in patients with AD reported a reduction of staphylococcal colonization and the formation of toxins, an improvement in the clinical parameters and reduced use of topical corticosteroids^{19,20}. The antibacterial action of silver on SA could be one important measure, both in the preventive point of view and also as a treatment adjuvant^{21,22}. The extract of brown seaweed (*Ascophyllum nodosum*), harvested from the Northern icy seas is a natural antioxidant with antibacterial activity especially against Gram-positive bacteria (*Micrococcus luteus* and SA) and anti-pruritus properties^{23–26}. In addition, these algae allow silver to attach to the cellulose fiber through connection with the carbonyl, carboxyl or hydroxyl groups.

The main objective of this study was the evaluation of the effectiveness of cellulose fiber with seaweed enriched with silver ions in the treatment of children with AD. In particular, it is envisaged the assessment of whether or not the intermittent use of this textile is adequate to prevent recurrence, and if side effects are likely to occur.

Methods

Textiles

In this study, it was assessed the use of clothing made with a new biofunctional textile (*Skintoskin textiles*®, Caldas das Taipas, Portugal) consisting of 70% cotton fibers, 20% cellulose fibers with algae extracts and 10% silver activated algal cellulose fibers (Figure 1). This textile contains about



Figure 2. Trial textile babygrow.

6000 ppm (0.6%) of silver. In this paper, this material will be referred as “trial textile”.

Similar 100% cotton clothing was prepared for the control group. The cotton fibers were woven similarly to the trial textile.

The clothes were of two types: *babygrows* for babies around 1-year-old (Figure 2) and *pyjamas* and *sockets* for older patients (Figure 3).



Figure 3. Trial textile pyjama and socks.

Patients

A sample of 19 children with a clinical diagnosis of AD was followed during 27 months (October 2008 to January 2011) in the Department of Dermatology and Venereology of the Hospital de Braga (Portugal).

The selection of the population for the study followed as inclusion criteria: age between 0 and 15 years; AD diagnosis according to the Hanifin and Rajika criteria³¹; and presence of active lesions at the recruiting occasion, regardless of their severity. Exclusion criteria included: presence of other skin diseases; history of hypersensitivity to silver; use of antibiotics and/or anti-inflammatory in the 2 weeks prior to the start or during the study. In the cases of unbearable itching or severe clinical symptoms, the use of topical emollients and mild to moderate topical corticosteroids was allowed. Body bathing and cloth washing were kept as usual, but the use of cloth softeners was disallowed.

In order to achieve the objectives of this study, it was carried out a prospective, randomized, controlled and double-blind trial. The sample was divided in two groups with similar demographic and clinical characteristics: a group of 12 children who wore the trial textile (Figure 4), and a control group of seven children who wore a placebo textile (Figure 5).

Study design

After hospital ethics committee approval, the study included a period of observation of the population during

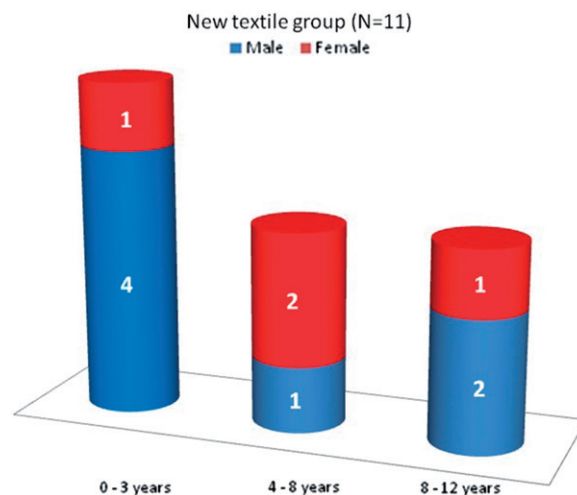


Figure 4. Trial textile group population.

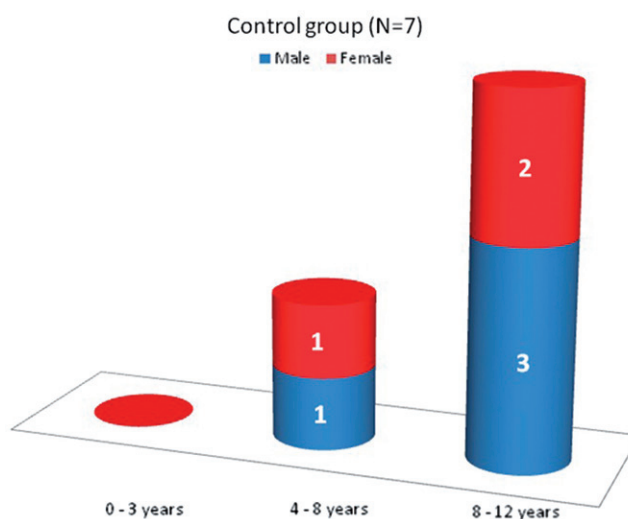


Figure 5. Control group population.

3 months (90 d). The parents were informed of the purpose and expectations of the study and a written consent was obtained. The patients were distributed randomly in two groups, one to wear clothing made with the new cotton fiber with seaweed and silver ions, and the other wearing standard 100% cotton equivalent clothes. These clothes were indistinguishable by the look and feel. Clothes made with the fiber under study and the placebo were provided by manufacturer and randomly distributed by a different element from that who made the clinical assessment.

At the start of the study, day 0 (D0), the demographic and clinical data were gathered. These included a dermatological examination and the evaluation of the disease severity using the SCORAD index (Disease Severity Score of AD), the intensity of pruritus and the record of the sleep disturbances by the same medical doctor in all clinical evaluations, as done in other studies²⁸. The SCORAD index was used for assessing the AD severity and the clinical response to the textiles in the study^{32,33}; the disease was classified as mild if SCORAD < 15, moderate if SCORAD: 15–40, and severe if SCORAD > 40²⁷. The intensity of itching and the sleep disturbances were also recorded for assessing the efficacy of treatment, using a visual analogue scale from

Table 1. The demographic and clinical characteristics of the population at the start of the study.

	Trial textile group	Control group	Total
Population size	11	7	18
Personal history of atopy	27.3%	42.9%	33.3%
Allergic rhinoconjunctivitis	0%	28.6%	11.1%
Asthma	27.3%	14.3%	22.2%
Familial history of atopy	45.5%	42.9%	44.4%
Atopic dermatitis	9.1%	14.3%	11.1%
Allergic rhinoconjunctivitis	18.2%	14.3%	16.7%
Asthma	18.2%	14.3%	16.7%

0 (lowest) to 10 points (highest). From D0 the clothes were used continuously (24 h/d).

At day 7 (D7) the results of the treatment were assessed by the same indicators used in the initial examination (SCORAD index, intensity of itching and changes in sleep). The need for any additional AD treatment (topical and/or systemic) was recorded. After D7, the intermittent use of clothing started, only overnight, until the end of the study (D90). The test ended with the final clinical evaluation of the whole population.

Statistical analysis

The statistical analysis was performed with the program SPSS 18.0® (IBM®, Armonk, NY). The study data were expressed as mean $\pm$ standard deviation and categorical variables were indicated in prevalence. The *chi-square* test corrected for sample size was used to analyze the characteristics of the sample and the Student's *t* test was used for comparison between groups. A confidence interval of 95% ($p < 0.05$) was defined as representing statistical significance.

Results

Population characteristics

The demographic and clinical characteristics of the population at the start of this study are presented in Table 1. This population was randomly split into a group of 12 patients who used the trial textile clothing and a control group of seven. In the first group, one patient did not complete the study.

The population was predominantly constituted of male patients (61%) and had a mean age of 7 years. One third of this population had personal history of concomitant atopic diseases. The high prevalence of asthma (22%) in the general population must be highlighted. Also more than 40% of the patients had a family history of atopy.

The statistical analysis of the population characteristics after the medical examination at the beginning of the study (Table 2) showed that all children had AD with moderate to severe activity, (for an average SCORAD index of 43 points). Relevant complaints of itching and sleep disturbances lead to an average of 7.3 and 5.0 points of a 10 point-scale, respectively. With the exception of the age, there were no statistically significant differences between the group wearing the trial textile and the control group.

Table 2. Clinical characteristics of the population.

	Trial textile group	Control group	Total
Pruritus intensity	7.3 $\pm$ 1.4	7.3 $\pm$ 1.4	73 $\pm$ 1.4
Sleep disturbances	5.2 $\pm$ 2.3	4.7 $\pm$ 2.4	5.0 $\pm$ 2.3
SCORAD index	43.8 $\pm$ 12.1	41.5 $\pm$ 11.6	42.9 $\pm$ 11.6

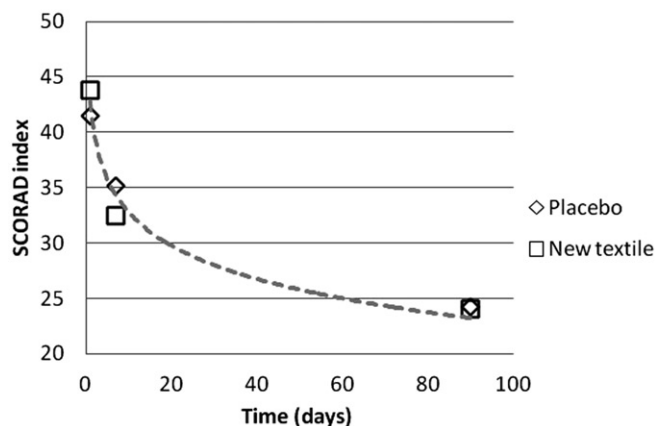


Figure 6. Evolution of the mean SCORAD index in the group wearing the trial textile and in the group wearing the placebo.

AD severity and treatment efficacy

SCORAD index

According to the SCORAD index, the severity of AD decreased almost 20 absolute points in the group using the fiber under study (Figure 6). For an initial SCORAD index average of 43.8 ± 12 points, this group reached a mean index of 24.0 ± 12.5 points after 90 d of treatment, i.e. a reduction of about 45% in the intensity of AD.

The improvement in the SCORAD index in the trial textile group was statistically significant within the first 7 d of treatment (32.5 ± 11.1 points, $p < 0.001$) and at day 90, when the clothing with the fiber under study was used only at night ($p = 0.001$). This evidence confirms the effectiveness of intermittent use (at night) of the garment.

The control group using 100% cotton clothing also obtained a statistically significant reduction ($p = 0.014$) of about 42% on its average SCORAD index (41.5 ± 11.6 points at D0 versus 24.2 ± 12.5 points at D90).

It should be noted that the observed difference in mean SCORAD index between both groups after 90 d of treatment didn't achieve statistical significance ($p = 0.97$).

Pruritus intensity

Evaluation of pruritus intensity using a visual analogue scale showed that new textile was effective in rapid relief of this symptom (Figure 7).

The average initial intensity of itching of 7.3 ± 1.4 points fell about 70% to 2.3 ± 1.3 points after 90 d of treatment. This important symptom improvement in the trial textile group had statistical significance at 7 d ($p < 0.001$) and at 90 d of treatment ($p < 0.001$).

The control group also achieved an improvement of about 60% in the intensity of pruritus (7.3 ± 1.4 versus 2.9 ± 1.8

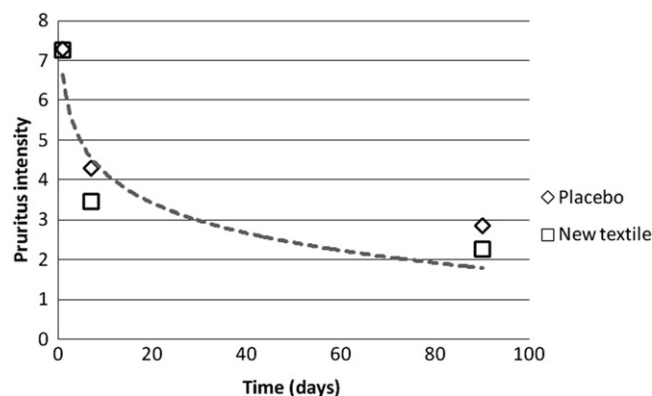


Figure 7. Mean intensity of pruritus in group wearing the trial textile and in the group wearing the placebo.

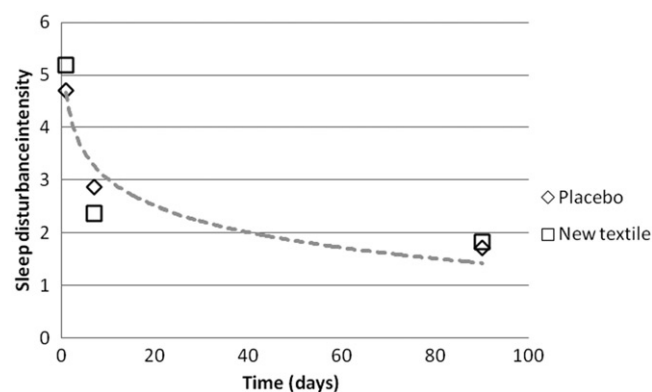


Figure 8. Average severity of sleep disturbances in group wearing the trial textile and in the group wearing the placebo.

points), which was statistically significant ($p = 0.004$). The difference in the mean intensity of pruritus in the two groups after the end of the study was not statistically significant ($p = 0.43$).

Severity of sleep changes

The influence of AD in the quality of the sleep of the patients is a common major complaint. The effect of wearing the new textile was assessed with a visual analogue scale.

The group that wore the fiber under study reached an overall improvement of quality of sleep of about 65% (mean score on sleep disorder fell from 5.2 ± 2.3 to 1.8 ± 1.5 points at the end of study) similar to the placebo group (4.7 ± 2.4 points at baseline versus 1.7 ± 1.7 points at the end of study) (Figure 8). Once again, this positive evolution of symptoms was statistically significant at the end of 7 d of continuous use ($p = 0.002$), as well as at the end of 90 d of night-time use of this fiber ($p = 0.001$). Nevertheless, in the short term, the use of the new textile conferred an impressive reduction of complaints of 54% in opposition to the 34% in the placebo group. This finding is considered as statistically significant ($p < 0.045$). There were no significant differences between the results of the two groups at the end of the study ($p = 0.90$).

Side effects of the trial textile

There were no side effects reported such as irritation, allergic contact dermatitis or contact urticary. Also, the patients did not complain about the comfort of wearing clothing.

Need for corticosteroid use

In the course of this investigation, one patient only in the new textile group and four in the control group required mild to moderate topical corticosteroids treatment after D7, during 3 and 6 d, respectively. No other treatment was used during the 3-month observation.

Discussion

The textile's properties and its interaction with the skin was the object of several studies^{18,21,22,26–28}. The use of silver in Dermatology and particularly in AD is gaining an increasing relevance^{20,22}.

The antibacterial mechanism of silver is not yet well understood, but it appears that this effect is caused by the interaction between the positively charged silver ions and the microorganism cells. In this process, silver seems to cause the detachment of the cytoplasmic membrane of the bacterial cell wall and the inhibition of DNA replication³⁰; it is reported as being effective against Gram-positive and Gram-negative bacteria as well as against fungi, as the *Candida* genus²⁶.

Some studies revealed that children using clothing impregnated with silver achieved a statistically significant improvement in their symptoms^{20,21} and evidenced that the reduction of SA colonization was parallel to the improvement of eczema severity²².

The adequate textile protection is also useful by reducing the exposure to exogenous aggravating factors such trauma, UV radiation, water, detergents, sweat and temperature changes. However, textiles can, in turn, act as powerful irritants depending on their material and texture. So far, cotton clothing has been the most recommended in patients with AD; clothing enriched with silver ions further to being resistant to thermal and mechanical action and being less irritant, maintain body temperature, prevent the loss of transepidermal water and has been acquiring biologically active properties^{28,29}.

This study followed 18 children with AD randomized in two groups, one with a new cellulosic fiber with seaweed and silver ions and the other with a 100% cotton textiles, indistinguishable in look and feel, over 3 months.

Based on a population with moderate to severe AD, this trial showed significant improvements in the major index of objective evaluation of AD, the SCORAD index after using the trial textile. With regard to subjective complaints, the fiber with seaweed and silver ions proved to be extremely active in reducing the itching and changes in the usual pattern of sleep.

Starting from a population with an initial SCORAD mean of 43.8 ± 12.1 points, this group had at day 90 a statistically significant reduction of about 45% of the intensity of AD ($p = 0.001$).

With regard to subjective complaints, the fiber with seaweed and silver ions proved to be active in reducing the pruritus and changes in the usual pattern of sleep with a statistically significant decrease of about 70% ($p < 0.001$) and 65% ($p = 0.001$), respectively, at the end of the trial.

The beneficial effect of the new textile on the pruritus alleviation is even more relevant because it may indirectly

contribute to the overall effectiveness of the fiber under study, as the itchiness is a well-established risk factor for colonization by SA and its toxins that increase the likelihood of trauma to the skin barrier.

This quick effect of wearing the new textile may be considered important in the treatment of pediatric patients with AD, for whom the importance of sleep on quality of life is essential.

The observed results in the SCORAD index, the itching intensity and sleep disturbances between D7 and D90 showed, with statistical significance, that the nocturnal use can be sufficient to control AD, after an initial period of continuous use. This possibility of wearing the new fiber clothes intermittently without loss of efficacy makes it an even more valuable therapeutic strategy for reducing the associated costs, reducing the risk of possible cumulative side effects and increasing the adhesion to the therapy.

Furthermore, the absence of side effects during the follow-up should be highlighted since this was one of the initial concerns in the project.

The results at the end of the 3 month study showed that the patients who used the new textile had only a marginal improvement in the various criteria of AD severity to those who used 100% cotton textiles, with the differences not achieving statistically significant. However, the textile protection against external aggravating factors, including interruption of the itching-injury vicious cycle, and the more frequent use of anti-inflammatory therapy may have contributed to enhance the clinical improvement in the placebo group wearing 100% cotton fibers. In spite of the limitations of the study, with a relatively small population size and limited duration of follow-up, it was demonstrated that the cellulose fiber with seaweed and enriched with silver ions was able to rapid improvement in the condition of the patients after the initial 7 d of treatment and reduce the clinical severity of a period of 3 months without side effects. These findings must be considered important points in favor of this textile alternative of cellulose fiber with seaweed enriched with silver ions.

On the other hand, these new textiles with antibacterial properties may offer the advantage of increasing the clinical efficacy of corticosteroids or other anti-inflammatory therapies and reduce possible side effects of them.

These results reinforce the importance of non-pharmacological measures, like clothing, in the management of patients with a diagnosis of AD.

Conclusions

AD is a chronic disease with high psycho-social impact for patients and their families. Given the complex pathophysiology of AD, it is essential a multi-branched approach designed to the protection and repair of skin barrier, the reduction of microbial colonization and immune regulation in order to achieve a greater therapeutic efficacy and improvements in quality of life of these patients.

It was observed quicker improvement after the first 7 d of continuous use of the fiber with seaweed enriched with silver ions and its use only overnight can be adequate to get a good

outcome at the end of the 3 month period of treatment without significant side effects.

This study concluded that clothes with seaweed enriched with silver ions can be considered effective, safe and applicable as bioactive textiles as, at least, adjunctive treatment of AD.

Declaration of interest

The authors report no declarations of interest.

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