

## The Effect of Topical 100% Sunflower Seed Oil (SSO) Extract on Trans Epidermal Water Loss (Tewl) and Skin PH Levels in a History of Atopic Dermatitis

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### Abstract

The skin barrier function can be disturbed in various conditions, one of which is atopic dermatitis (AD). Efforts to improve the skin barrier can be done by using various types of moisturizers. Natural oil from sunflower seed oil (SSO) can be used as "skin barrier therapy" by reducing trans epidermal water loss (TEWL) and skin pH levels. A randomized single blind clinical trial with a two parallel group pre and post design was conducted on subjects with a history of AD who were treated at the Skin and Venereology Polyclinic at Sunan Kalijaga Hospital, Demak. Samples were randomized into 2 groups to receive 100% SSO or petrolatum as a control. TEWL and pH assessments were carried out at the beginning of the study and at week 4. Bathing habits and complaints about using moisturizers were also assessed. TEWL values decreased in the SSO and petrolatum groups ( $-5.8 \pm 1.93$  vs  $-6.1 \pm 9.08$ ,  $p = 0.9$ ). The pH value in AD patients also decreased after administration of SSO extract and petrolatum ( $-0.4 \pm 0.10$  vs  $-0.2 \pm 0.75$ ,  $p = 0.2$ ). The decrease in TEWL and pH in both groups was not statistically significant. This may be related to differences in bathing habits and moisturizer use in the two groups. Most of the samples in the SSO group stated that they had no complaints regarding usage. The entire sample completed the study without any reports of allergic reactions or hypersensitivity. Administration of SSO extract was effective in reducing TEWL and pH in DA with the majority of samples stating that they had no complaints about use.

**Keywords:** sunflower seed oil, skin barrier therapy, TEWL, pH

### INTRODUCTION

The skin is the outermost layer of the body which functions as a protective barrier for various organs within it, including by limiting passive water loss, chemical absorption from the external environment, and preventing microbial infections, both physical, chemical and immunological. The skin barrier function can be disturbed in dry

skin conditions, namely a condition where the skin becomes flaky, rough, cracked and accompanied by inflammation and secondary infections. Dry skin can occur due to the influence of internal and external factors, including the aging process, environments with temperatures that are too cold or hot, air with low humidity levels, the use of skin cleansing products, and various pathological skin conditions, one of which is atopic dermatitis ( DA) (Yang et al., 2020).

Atopic dermatitis or eczema is an inflammatory condition of the skin that is chronic and residue, has a spongiotic pathological picture, is accompanied by itching, and has a predilection for certain parts of the body according to age, including the face in babies and the flexural parts of the extremities in children (Chan & Zug, 2021). Atopic dermatitis is a major health problem that affects more than 200 million people worldwide, (Langan et al., 2017) with a prevalence ranging from 2–10% in adults,<sup>8</sup> and 10–20% in children in the United States, Northern and Western Europe, Africa, Japan, Australia, and various other industrialized countries (Pratama, 2017). The International Study of Asthma and Allergies in Childhood (ISAAC) states that AD is most common in women with a female/male ratio of 1.3:1.0, (Kang, 2019) where the majority of cases show onset in childhood and then recover or continue into adulthood, and the remaining 20–25% are AD cases with onset in adulthood (Lobefaro et al., 2022). The epidemiology, incidence and prevalence of AD in Indonesia are still difficult to know with certainty. Many AD studies have been conducted, but the results can vary depending on the AD diagnostic criteria used, the characteristics of the research subjects, and the country where the research was conducted.

The diagnosis of atopic dermatitis can be made based on clinical symptoms and signs, where the Hanifin and Rajka Criteria are considered the gold standard for establishing the diagnosis of atopic dermatitis in both children and adults. The major criteria for AD include the presence of pruritus, typical morphology and distribution of lesions, recurrent chronic dermatitis, and personal or family history of atopy, while one of the most frequently encountered minor criteria is the presence of dry skin or xerosis.<sup>14</sup> This dry skin condition is associated with damage to the skin barrier, increased skin immunological activity and changes in the condition of the skin microbiota, thus playing a role in causing chronicity and increasing the risk of exacerbations.

The stratum corneum is the outermost layer of the epidermis which functions as a physical barrier and permeability barrier which is tasked with protecting the skin from mechanical disturbances, ultraviolet (UV) radiation, cold and hot temperatures, exposure to chemicals and microbes, as well as maintaining the water content in the skin.<sup>15,16</sup> Components that play a role in maintaining the function of the stratum corneum include lipids, lysozyme, and antimicrobial peptides.<sup>17</sup> Damage to the skin barrier can facilitate the penetration of microbes, allergens and irritants, which in turn will trigger an increase in skin immunological activity and changes in the skin microbiota,

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thus further aggravating the damage to the skin barrier. This damage can occur continuously until adulthood, and will cause an increase in TEWL and a decrease in skin hydration.

The five pillars of AD management include educating patients and caring parents, avoiding and modifying environmental trigger factors, strengthening and maintaining optimal skin barrier function, providing anti-inflammatory therapy such as topical corticosteroids, and controlling and eliminating the itch-scratch cycle (Rubel et al., 2013). Efforts to improve the skin barrier can be done by using various types of moisturizers, for example petrolatum which acts as an occlusive ingredient so it is useful in reducing TEWL and improving the skin barrier. Petrolatum is the main moisturizer choice that is widely used in AD sufferers, and 5% petrolatum is reported to reduce TEWL by more than 98%. Unfortunately, this type of moisturizer is less comfortable to use because it is too thick and oily, thus limiting patient compliance in using the moisturizer (Kim & Leung, 2018).

The use of alternative moisturizing ingredients to improve the skin barrier without causing discomfort and adverse effects is expected to increase patient compliance in using moisturizers. Barrier repair-based therapy has recently been widely developed, especially the use of moisturizers derived from natural oils or essential oils. Natural oils can come from food ingredients such as coconut oil, olive oil, or sunflower seed oil (SSO). The "skin barrier therapy" approach, which aims to improve the condition of the skin barrier, has been proven effective (Egawa & Kabashima, 2018). Sunflower seed oil (SSO) is a natural oil that is rich in linoleic acid.<sup>23</sup>The advantages of SSO when compared to other types of moisturizers are that the ingredients are natural from plants so they reduce the irritating effect on the skin, are relatively easy to obtain and are considered cost effective, especially in low to middle income countries like Indonesia (Pratami et al., 2022). Therapeutic use of SSO can provide anti-inflammatory and antioxidant effects on the skin and also play a role in wound healing and repair of the skin barrier (Lin et al., 2017). This natural oil helps repair the skin barrier from damage by replenishing intracellular lipids, forming an occlusive layer, increasing hydration of the stratum corneum, reducing inflammation and preventing microbial invasion (Vaughn et al., 2018). The ingredient that plays a role is linoleic acid which works to increase keratinocyte proliferation and lipid synthesis. Linoleic acid is also known as an ingredient that functions as an emollient.<sup>27</sup>Emollients work by filling the gaps between desquamated corneocytes, so that the surface of the desquamated skin is smoother and reflects light well (Baumann, 2019).

The success of the skin barrier therapy method in sufferers with a history of AD can be assessed based on improvements in the condition of the skin barrier. Parameters for assessing skin barrier damage can be done by measuring trans epidermal water loss (TEWL) and pH levels in the skin. TEWL measurements are used to measure water

evaporation from the skin. The acidity level (pH) of the skin surface, although not directly assessing barrier function, is often used as a parameter because it is related to skin integrity, namely the stratum corneum, lipid production, skin permeability and the skin as a chemical barrier.

The general objective of this research is to understand the effect of administering 100% SSO extract on TEWL and skin pH in AD sufferers, while the specific objectives include determining changes in TEWL and skin pH before and after administering SSO extract and petrolatum and analyzing the differences between the two. The benefits of this research include aspects of science and technology by providing additional information regarding the role of SSO extract in reducing TEWL and increasing skin pH, health service aspects by providing insight to dermatologists regarding the use of SSO extract in AD treatment, as well as aspects of information to the public about its importance. skin care and considerations in choosing care products containing SSO extract. The authenticity of this research lies in the fact that the effect of giving SSO extract on TEWL and skin pH in adult AD sufferers has never been studied in Indonesia, although several studies related to SSO extract have been carried out previously.

Research evaluating the use of topical SSO extract therapy in adults with a history of atopic dermatitis is still rare. Only one previous study used adult subjects with a history of AD, while the majority of other studies appear to have been conducted on neonates without a history of AD and children with a history of AD. The results of a number of previous studies are still very varied, with some finding that SSO can reduce pH and TEWL, while other studies have found conflicting results. Research conducted in Indonesia regarding the use of SSO in sufferers with a history of AD also used only children aged subjects, and only assessed changes in TEWL without examining skin pH. Therefore, researchers intend to examine the effect of administering SSO extract on TEWL and skin pH in children and adults with a history of AD.

## **RESEARCH METHODS**

This research will be carried out at the Skin and Venereology Polyclinic at Sunan Kalijaga Regional Hospital, Demak after obtaining ethical approval until the sample size is met. The type of research used was a single blind randomized clinical trial with a two parallel group pre and post design. The design scheme includes treatment (P) and control (K), with measurements of TEWL and skin pH values before (PO1, KO3) and after therapy (PO2, KO4) in the treatment group (X1: topical 100% sunflower seed oil for 4 weeks; X2: topical 100% petrolatum for 4 weeks). The target population is patients with a history of atopic dermatitis who seek treatment at the Skin and Venereology Polyclinic at Sunan Kalijaga Hospital, Demak. Samples were taken based on inclusion and exclusion criteria, using the consecutive sampling method and the sample size was calculated using the formula for two parallel group pre and post-test design. Subject allocation was

carried out using block randomization, and dropout criteria included allergic reactions. The independent variables include the administration of 100% sunflower seed oil and 100% petrolatum, while the dependent variables are the TEWL value and skin pH as measured by a tewameter and pH meter. The entire process including preparation, use of test materials, evaluation, and data analysis follows strict procedures with compliance monitoring and side effect evaluation. The research protocol will receive ethical clearance, and the subject's identity will be kept confidential. The planned schedule includes preconditions, implementation, data recap, analysis and thesis examination, with a total budget of IDR 24,610,000 for research implementation.

## RESULTS AND DISCUSSION

### 5.1. Research result

In the period February 2024 to April 2024 at the Polyclinic and Venereology of Sunan Kalijaga Hospital, Demak, 34 patients with atopic dermatitis (AD) were found who were research subjects, and all subjects met the research criteria and were randomly divided into two groups: the treatment group using Extract moisturizer. Sunflower Seed Oil/SSO (n=17) and a control group that used petrolatum moisturizer (n=17) for 4 weeks. No subjects dropped out during the follow-up period, so all subjects were used for data analysis. The characteristics of the research subjects showed that the average age was  $30.9 \pm 7.44$  years, with the majority being female (67.6%). In the SSO Extract group, the mean age of the subjects was  $32.4 \pm 8.24$  years, while in the petrolatum group it was  $29.4 \pm 6.43$  years, but this difference was not statistically significant ( $p = 0.2$ ). The gender in the SSO Extract group was mostly men (52.9%), while in the petrolatum group the majority were women (88.2%), this difference was significant ( $p < 0.001$ ). The most recent education of the subjects in the SSO Extract group was high school/vocational school (47.1%), while in the petrolatum group most of them were bachelor's degrees (58.8%), but this difference was not significant ( $p = 0.1$ ). The duration of suffering from AD in the SSO Extract group averaged  $25.0 \pm 10.41$  years, longer than the petrolatum group which averaged  $20.3 \pm 6.72$  years, with a significant difference ( $p = 0.008$ ). Bathing frequency, type of bath soap, how to dry the body, and initial complaints did not show significant differences between the two groups. However, the habit of bathing in warm water was significantly different ( $p = 0.02$ ), and the history of using moisturizers showed a significant difference ( $p = 0.001$ ). There were mostly no complaints about using moisturizer in the SSO Extract group, whereas in the petrolatum group the majority experienced complaints of stickiness and oiliness. This difference was also significant ( $p < 0.001$ ).

### TEWL Value Before and After Using SSO and Petrolatum Extract Moisturizer

TEWL values before and after using SSO Extract Moisturizer and Petrolatum are shown in table 8.

**Table 8.** TEWL value before and after using moisturizer SSO and Petrolatum Extract.

TEWL value	Group		p
	Extract SSO (n=17)	Petrolatum (n=17)	
<b>Right side</b>			
Baseline	20.4±4.34; 19.5 (12.3-28.4)	20.5±7.79; 19.7 (12.2-34.1)	0.9 <sup>§</sup>
4th week	14.3±3.60; 13.2 (10.3-21.4)	14.5±3.39; 14.4 (10.3-21.4)	0.8 <sup>¥</sup>
<b>p&amp;</b>	<0.001	0.02	
<b>Delta TEWL right side</b>	-6.1±2.20; -5.8 (-10.5--2.1)	-6.0±8.30; -6.2 (-21.2-9.2)	1.0 <sup>§</sup>
<b>Left side</b>			
Baseline	21.4±5.34; 19.7 (13.2-31.0)	21.8±8.66; 19.7 (12.2-35.2)	0.9 <sup>¥</sup>
4th week	15.9±4.70; 13.4 (10.5-24.6)	15.8±4.55; 14.2 (10.5-24.6)	1.0 <sup>¥</sup>
<b>p&amp;</b>	<0.001	0.03	
<b>Delta TEWL left side</b>	-5.4±2.01; -5.0 (-9.7--1.6)	-6.1±10.08; -4.9 (-24.2-10.7)	0.8 <sup>§</sup>
<b>TEWL # average value</b>			
Baseline	20.9±4.56; 20.3 (12.8-28.1)	21.2±8.19; 19.7 (12.6-34.5)	0.9 <sup>¥</sup>
4th week	15.1±3.95; 14.2 (10.9-22.2)	15.1±3.73; 14.7 (10.9-22.2)	0.9 <sup>¥</sup>
<b>p&amp;</b>	0.1	0.06	
<b>Delta TEWL</b>	-5.8±1.93; -5.5 (-10.1--1.9)	-6.1±9.08; -5.5 (-22.7-9.7)	0.9

#Right-left side average

<sup>§</sup>Unpaired t-test

<sup>¥</sup>Mann-Whitney test

<sup>&</sup>Baseline vs week 4; Wilcoxon test

The results of the homogeneity test for TEWL value data at baseline on the right side obtained a p value <0.001, which means the data is not homogeneous, while the left side value is p = 0.01 and the average of the right and left TEWL values is p = 0.03, which means the data is not homogeneous. Based on this, data analysis for the right and left side of TEWL uses non-parametric tests, taking into account the normality of the distribution.

In table 8 it is known that the right side TEWL value at baseline in the SSO Extract Moisturizer group was 20.4±4.34 is more or less the same as in the Petrolatum moisturizer group, namely 20.5±7.79, but the results of statistical tests showed that this

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difference was not significant ( $p=0.6$ ). The right side TEWL value at week 4 in the SSO Extract Moisturizer group was  $14.3\pm 3.60$  is more or less the same as in the Petrolatum group, namely  $14.5\pm 3.39$ . The statistical test results showed that this difference was not significant ( $p=0.9$ ).

In table 8, it is known that in the SSO Extract Moisturizer group, the change in right side TEWL values from baseline to week 4 was significant ( $p<0.001$ ).

The TEWL delta of the right side of the group in the SSO Extract Moisturizing group is  $-6.1\pm 2.20$ , while in the Petrolatum moisturizer group it was  $-6.0\pm 8.30$ . This shows that in the SSO Moisturizer and Petrolatum groups there was a decrease in TEWL values which was more or less the same. The statistical test results showed that the difference in TEWL delta value was not significant ( $p=0.9$ ).

Left side TEWL value when *baseline* in the SSO Extract Moisturizer group, namely  $21.4\pm 5.34$  is more or less the same as in the Petrolatum moisturizer group, namely  $21.8\pm 8.66$ . The results of statistical tests showed that this difference was not significant ( $p=0.9$ ). The left side TEWL value at week 4 in the SSO Extract Moisturizer group was  $15.9\pm 4.70$  is more or less the same compared to the Petrolatum moisturizer group, namely  $15.8\pm 4.55$ . The results of statistical tests show that this difference is not significant ( $p=1.0$ ). In table 8 it is known that in the SSO Extract Moisturizer group the change in TEWL value on the left side from baseline to week 4 was significant ( $p<0.001$ ). In table 8 it is also known that in the Petrolatum group the change in left side TEWL values from baseline to week 4 was significant ( $p=0.003$ ).

The TEWL delta of the left side of the group in the SSO Extract Moisturizing group was  $-5.8\pm 1.93$ , while in the Petrolatum moisturizer group  $-6.1\pm 10.08$ . This shows on Both the SSO Extract Moisturizer and the Petrolatum group experienced a decrease in TEWL values, however the decrease in the Petrolatum group was greater than the SSO Extract group, but the results of statistical tests showed that this difference was not significant ( $p=0.08$ ).

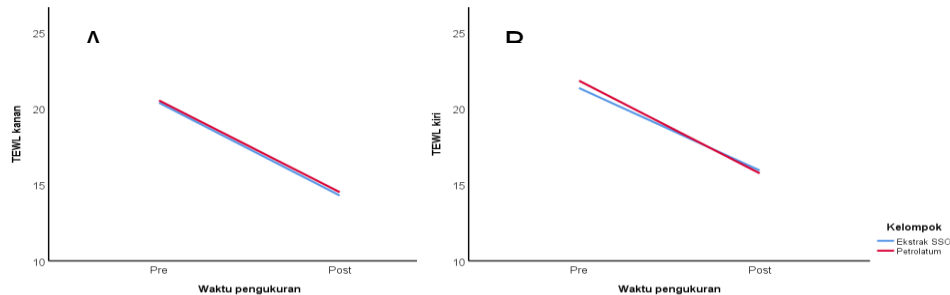
The mean value of right and left TEWL at baseline in the SSO Extract group was  $22.0\pm 7.85$  is higher than the Petrolatum moisturizer group, namely  $21.6\pm 8.19$ . The results of statistical tests showed that this difference was not significant ( $p=0.9$ ). The mean value of right and left TEWL at week 4 in the SSO Extract group was  $15.1\pm 3.95$  is more or less the same as the Petrolatum moisturizer group, which is  $15.1\pm 3.73$ . The results of statistical tests showed that this difference was not significant ( $p=0.9$ ). In table 8, it is known that in the SSO Extract Moisturizer group, the change in the right and left TEWL mean values from baseline to week 4 was not significant ( $p=0.1$ ). In the Petrolatum group, the change in mean right and left TEWL values from baseline to week 4 was also not significant ( $p=0.06$ ).

The mean delta of right and left TEWL in the SSO Extract group was  $-5.8\pm 1.93$ , while in the Petrolatum moisturizer group it was  $-6.1\pm 9.08$ . This shows that in the SSO

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Extract and Petrolatum groups there was a decrease in TEWL values, however the decrease in the Petrolatum group was greater than in the SSO Extract group, but the results of statistical tests showed that this difference was not significant ( $p=0.9$ ).

Changes in TEWL values on the right side and left side from baseline to week 4 are also shown in Figure 22.



**Figure 22.** Changes in right and left side TEWL values in the SSO Extract group and Petrolatum group. Panel A, TEWL values right side. Panel B, left side TEWL values

In Figure 22, it is known that in both research groups there was a decrease in the average TEWL value on the right and left sides. It appears that the decrease in the average TEWL value on the right and left sides in both groups was more or less the same. The delta difference in TEWL value reduction between the right and left sides is  $p=0.9$ .

### 5.2. pH Value Before and After Using SSO and Petrolatum Extract Moisturizer

The pH values before and after using SSO and Petrolatum Extract Moisturizer are shown in table 9.

**Table 9.** pH value before and after using moisturizer SSO and Petrolatum Extract

pH value	Group		p
	Extract SSO (n=17)	Petrolatum (n=17)	
<b>Right side</b>			
Baseline	5.5±0.54; 5.4 (4.7-6.4)	5.3±0.70; 4.9 (4.4-6.4)	0.4 <sup>§</sup>
4th week	5.1±0.58; 5.0 (4.2-6.1)	5.1±0.48; 5.0 (4.5-6.1)	0.9 <sup>§</sup>
<b>p&amp;</b>	<0.001	0.4	
<b>DeltapHright side</b>	-0.4±0.13; -0.4 (-0.6--0.1)	-0.2±0.84; -0.1 (-1.8-1.2)	0.2 <sup>§</sup>
<b>Left side</b>			
Baseline	5.5±0.49; 5.3 (4.8-6.4)	5.4±0.49; 5.3 (4.3-6.1)	0.4 <sup>§</sup>
4th week	5.1±0.52; 5.2 (4.2-6.0)	5.1±0.43; 5.2 (4.4-6.0)	1.0 <sup>§</sup>
<b>p#</b>	<0.001	0.2	



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<b>DeltapHleft side</b>	-0.4±0.19; -0.4 (-0.8-0.0)	-0.2±0.71; 0.0 (-1.7-0.8)	0.4§
<b>Average valuepH§</b>			
Baseline	5.5±0.50; 5.4 (4.8-6.4)	5.3±0.58; 5.1 (4.4-6.2)	0.4§
4th week	5.1±0.52; 5.1 (4.2-6.0)	5.1±0.42; 5.1 (4.5-6.0)	1.0§
<b>p#</b>	<0.001	0.2	
<b>DeltapH</b>	-0.4±0.10; -0.4 (-0.6--0.2)	-0.2±0.75; 0.0 (-1.7-0.9)	0.2

§Right-left side average

¥Mann-Whitney test

§Unpaired t-test

&Baseline vs week 4; Wilcoxon test

#Baseline vs week 4; Paired t-test

The results of the homogeneity test for the pH value data at the baseline on the right side obtained a value of  $p=0.7$ , on the left side a value of  $p=0.7$  and the average of the right and left Ph values was  $p=0.3$ . This shows that the pH value data when the baseline on the right side, the left side and the average right and left pH values are homogeneous. The choice of hypothesis test is also based on the normality of the pH data distribution.

In table 9 it is known that the pH value of the right side at baseline in the SSO Extract Moisturizer group, namely  $5.5 \pm 0.54$ , is higher than in the Petrolatum moisturizer group, namely  $5.3 \pm 0.70$ , but the results of statistical tests show that this difference is not significant ( $p=0.4$ ). The pH value of the right side at week 4 in the SSO Extract Moisturizer group was  $5.1 \pm 0.58$  is more or less the same as in the Petrolatum group, namely  $5.1 \pm 0.48$ . The statistical test results showed that this difference was not significant ( $p=0.9$ ). In table 9, it is known that in the SSO Extract Moisturizer group the change in the pH value of the right side from baseline to the 4th week was significant ( $p<0.001$ ), whereas in the Petrolatum group the change in the pH value of the right side from baseline to the 4th week is not significant ( $p=0.4$ ).

The delta pH of the right side of the SSO Extract Moisturizing group is  $-0.4 \pm 0.13$ , while in the Petrolatum moisturizer group it is  $-0.2 \pm 0.84$ . This shows that in the SSO Extract Moisturizer group there was a greater decrease in pH value than in the Petrolatum Moisturizer group. The results of statistical tests show that the difference in delta pH values is not significant ( $p=0.2$ ).

The left side pH value at baseline in the SSO Extract Moisturizer group was  $5.5 \pm 0.49$  is slightly higher than the Petrolatum moisturizer group which is  $5.4 \pm 0.49$ . The results of statistical tests showed that this difference was not significant ( $p=0.4$ ). The left side pH value at week 4 in the SSO Extract Moisturizer group was  $5.1 \pm 0.52$  is more or less the same as in the Petrolatum moisturizer group, namely  $5.1 \pm 0.43$ . The results of

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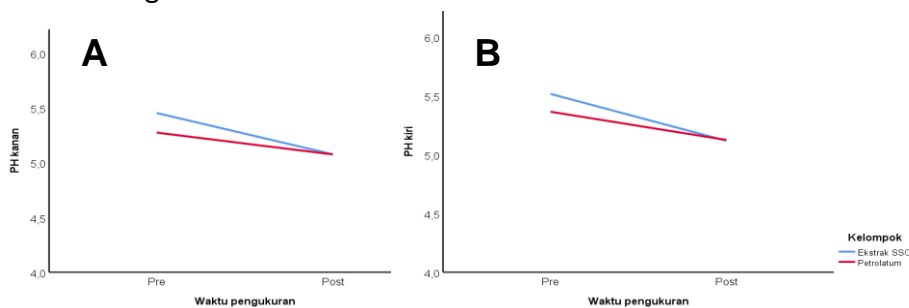
statistical tests show that this difference is not significant ( $p=1.0$ ). In table 9 it is known that in the SSO Extract Moisturizer group the change in left side pH value from baseline to the 4th week was significant ( $p<0.001$ ), whereas in the Petrolatum group the change in left side pH value from baseline to the 4th week is not significant ( $p=0.2$ ).

The delta pH of the left side of the group in the SSO Extract Moisturizing group is  $-0.4\pm 0.19$ , while in the Petrolatum moisturizer group it was  $-0.2\pm 0.71$ . This shows that in the SSO Extract Moisturizer there was a decrease in the pH value, whereas in both studies there was a decrease in the Ph value. The results of statistical tests show that this difference is not significant ( $p=0.2$ ).

The mean value of right and left pH at baseline in the SSO Extract group was  $5.5\pm 0.50$  is higher than the Petrolatum moisturizer group, namely  $5.3\pm 0.58$ . The results of statistical tests showed that this difference was not significant ( $p=0.4$ ). The mean right and left pH value at week 4 in the SSO Extract group was  $5.1\pm 0.52$  is more or less the same as in the Petrolatum moisturizer group, namely  $5.1\pm 0.42$ . The results of statistical tests show that this difference is not significant ( $p=1.0$ ). In table 9, it is known that in the SSO Extract Moisturizer group the change in the right and left pH mean values from baseline to the 4th week was significant ( $p<0.001$ ), whereas in the Petrolatum group the change in the left side pH value from baseline to the 4th week -4 is not significant ( $p=0.2$ ).

The average delta pH of the right and left groups in the SSO Extract group was  $-0.4\pm 0.10$ , while the Petrolatum moisturizer group is  $-0.2\pm 0.75$ . This shows that in both groups there was a decrease in the mean pH value on the right and left sides, however the decrease in the SSO group was greater than in the Petrolatum group, however the results of statistical tests showed that this difference was not significant ( $p=2$ ).

Changes in pH values on the right and left sides from baseline to week 4 are also shown in Figure 24.



**Figure 24.** Changes in pH values on the right and left sides in the SSO Extract group and the Petrolatum group. Panel A, Right side pH values. Panel B, Left side pH values

In Figure 24, it can be seen that the pH values on the right and left sides in the SSO and Petrolatum Extract groups saw a decrease in the average pH value, but it appears that in the SSO Extract group the decrease was greater than in the Petrolatum group. The statistical test results showed that the decrease in the mean pH value in the SSO Extract group was significant ( $p<0.001$ ) while in the Petrolatum group it was not

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significant ( $p=0.2$ ).

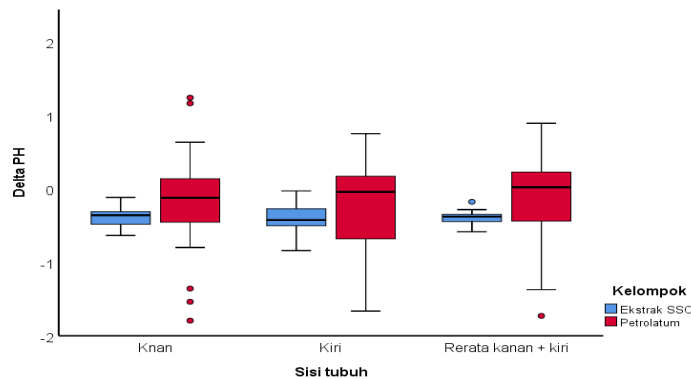
The mean changes in pH values on the right and left sides in the SSO Extract group and the Petrolatum group are shown in Figure 25.



**Figure 25.** Changes in mean pH values on the right and left sides in the SSO Extract group and the Petrolatum group

In Figure 25, it can be seen that the change in the right and left mean pH values in the SSO group is more or less the same as the petrolatum group.

Comparison of the delta pH values on the right side, left side and the average pH value on the right and left sides in the SSO Extract group and the Petrolatum group is shown in Figure 26.



**Figure 26.** Box-plot diagram of delta pH values on the right side, left side and average pH values on the right and left sides in the SSO group and Petrolatum

Figure 26 shows the median delta pH value on the right side, left side and the mean pH value on the right and left sides in the SSO Extract group is more negative than in the Petrolatum group. This shows that the decline in the SSO Extract group was greater compared to the Petrolatum group. The statistical test results also showed that the difference in the right side delta value between the SSO Extract and Petrolatum groups was not significant ( $p=0.2$ ), the difference in the left side delta value between the SSO Extract and Petrolatum groups was also not significant ( $p=0.4$ ) and the difference in the mean pH values on the right and left sides between the SSO Extract

and Petrolatum groups was also not significant ( $p=0.4$ ).

## Discussion

The gender of the research subjects in the SSO extract group was mostly men, namely 52.9%, while in the petrolatum group the majority were women, namely 88.2%. Based on research, AD in pediatric patients is not related to gender, but research in adults has provided mixed results. The International Study of Asthma and Allergies in Childhood (ISAAC) confirmed that AD in children is more often found in female patients, with a ratio of female/male sufferers of 1.3:1.0. There are fewer studies of AD in adults. Adult-onset AD has been shown to occur more frequently among women in two large studies from the UK. This study also does not explain gender differences and their relationship with AD.

The SSO extract group had a longer duration of suffering from DA, namely  $25.0 \pm 10.41$  years, while in the petrolatum group it was  $20.3 \pm 6.72$ . The results of statistical tests show that this difference is significant ( $p=0.008$ ). There have been no studies that directly compare the duration of AD patients and data regarding the relationship between disease duration and onset and disease prognosis is currently still limited. One study has shown an association between disease duration and prognosis. Research by Abuabara et al. stated that intermittent and chronic AD require appropriate management, and many studies have focused only on "reactive" approaches, including treatment of disease flares or periods of acute exacerbation of AD. Recent guidelines emphasize the importance of a "proactive" approach with continued use of topical corticosteroids (1-2 times/week) or topical calcineurin inhibitors (2-3 times/week) after stabilization of previously involved skin disease to reduce subsequent flares or recurrences.

Several aspects of AD management are patient education as well as avoiding and modifying environmental triggers/lifestyle modifications. Educational material for patients includes the frequency of bathing, the type of soap used, and the temperature of the water when bathing. The frequency of bathing in the SSO Extract Moisturizer Group was mostly once a day, namely 41.2%, while in the Petrolatum Group, most of it was twice a day, namely 70.6%. The results of statistical tests show that this difference is not significant ( $p=0.05$ ). Most of the types of bath soap in both research groups were antiseptic soap, namely 64.7% each. The results of statistical tests show that this difference is not significant ( $p=1.0$ ). The majority of the SSO Extract Group had the habit of bathing in warm water, namely 70.6%, while in the Petrolatum group the majority, namely 70.6%, did not have the habit of bathing in warm water. The results of statistical tests show that this difference is significant ( $p=0.02$ ).

AD management guidelines in Indonesia recommend bathing frequency 1-2 times a day. A higher frequency will cause the skin to be exposed to water more

often.<sup>5,6</sup> Longer and more frequent exposure to water causes disruption of the intercellular lipid lamellae of the stratum corneum, causing corneocytes to enlarge and water to collect in the intercellular space. Exposure to water also causes changes in the morphology of the stratum corneum so that it becomes easier for irritants or extrinsic allergens to enter the stratum corneum, resulting in an environment that supports excess bacterial growth.

The effect of bathing water temperature on skin barrier damage has been proven in various studies. A study in Spain showed that hands exposed to hot water when washing hands experienced an increase in TEWL (25.75 to 58.58 g/m<sup>2</sup>/hour). This suggests that high-temperature water promotes water mass transfer from the stratum corneum to the environment as well as changing the morphology of the stratum corneum and increasing hydration in a dose-dependent manner, thereby facilitating the penetration of extrinsic irritants or allergens and providing a suitable environment for bacterial overgrowth (Herrero-Fernandez et al., 2022).

The AD Diagnosis and Management Guide recommends bathing 1-2x a day with lukewarm water (temperature 36-37°C), using soap that contains moisturizers, and avoiding antiseptic soap. Research has also proven that the type of soap used can be related to the quality of the skin barrier. The use of antiseptic soap is associated with changes in skin microbial richness and is not superior to soap containing moisturizers.<sup>5,6</sup> Skin contains diverse communities of microorganisms, and changes in these communities can influence the effectiveness of skin as a barrier against infectious organisms or injury. Yu et al's research shows that the use of antibacterial soap results in changes in the skin microbiome, which can last for at least 2 weeks and can have long-term impacts on the skin microbiome if applied continuously. The use of soap and detergent on the skin also increases the skin's pH, thereby increasing the activity of endogenous proteases, causing further damage to the epidermal skin barrier (Yu et al., 2018).

Most of the history of using moisturizers in the SSO Extract Moisturizer Group was rarely using moisturizers, namely 64.7%, while in the Petrolatum group, most of them had a history of using moisturizers, namely 88.2%. The results of statistical tests show that this difference is significant ( $p=0.001$ ). Education regarding the use of moisturizers is also an important aspect in the pillars of AD management, namely to apply moisturizer immediately within 3 minutes after bathing, 2-3 times a day or more often. The frequency of moisturizer use is related to the amount of moisturizer applied, because it is recommended to give a very sufficient amount, namely 100-200 g/week in children and 200-300 g/week in adults.

The majority of complaints about using moisturizer during the research in the SSO Extract Moisturizer Group, namely 70.6%, were no complaints, while the majority of the Petrolatum group, namely 76.5%, were complaints of stickiness and oiliness. The results

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of statistical tests show that this difference is significant ( $p < 0.001$ ). The ideal moisturizer for AD therapy includes a moisturizer that effectively hydrates the stratum corneum, reduces and prevents TEWL, and is also elegant and cosmetically acceptable. Petrolatum is an occlusive moisturizer that has a high viscosity, so its use causes an oily feeling, while the SSO extract moisturizer is more acceptable to the subjects.

TEWL values in AD patients decreased after administration of SSO extract and petrolatum compared to before treatment, but this was not statistically significant. This is shown by the delta TEWL mean value in the SSO extract moisturizer group being  $-5.8 \pm 1.93$ , which is smaller than the petrolatum group which is  $-6.1 \pm 9.08$  with a significance value of  $p = 0.9$ . This shows that the TEWL value decreased after administration of SSO Extract Moisturizer and Petrolatum, with a greater decrease in petrolatum but not statistically significant. This finding is not in accordance with the hypothesis, with a greater reduction in SSO extract moisturizer. This discrepancy may be due to differences in characteristics between subjects. Most of the subjects in the SSO extract moisturizer group rarely used moisturizer, namely 64.7%, while in the Petrolatum group most of them had a history of using moisturizer, namely 88.2%. This may influence patient habits and compliance in using SSO.

SSO extract can be used as a moisturizer because it can work as an emollient against the skin barrier. This is caused by the linoleic acid content in SSO, which is also known as an ingredient that functions as an emollient type of moisturizer. Emollients are a type of moisturizer that can affect skin physiology and pathology, and works by filling the gaps between desquamated corneocytes and increasing cohesion between cells, so that the skin surface will become smoother and can reflect light well.

The decrease in TEWL in this study is in accordance with previous research by Summers et al., in their study comparing the effectiveness of emollient therapy with SSO on the baby's skin barrier, 3 times a day for 14 days, followed by use 2 times a day until the 28th day. Its use for more than 5 weeks resulted in a decrease in TEWL and consistently high relative humidity between 80-95%.<sup>35</sup> Another study by Cooke et al also showed a decrease in TEWL values after giving SSO compared to those who did not receive moisturizer. The SCH value in the SSO group was also higher than the group that did not receive moisturizer (Cooke et al., 2016).

The pH value in AD patients decreased after administration of SSO extract and petrolatum compared to before treatment, but this was not statistically significant. This is indicated by the delta mean pH value in the SSO extract moisturizer group being  $-0.4 \pm 0.10$ , which is greater than the petrolatum group worth  $-0.2 \pm 0.75$  with a significance value of  $p = 0.2$ . This shows that the pH value decreased after administering SSO Extract Moisturizer and Petrolatum, with a greater decrease in SSO extract moisturizer but not statistically significant. These findings are in accordance with the hypothesis, with a greater pH reduction value in the SSO extract moisturizer, although

the results are not statistically significant.

The improvement in pH in this study is in accordance with previous research by Cooke et al, which showed that administering SSO reduced TEWL values, increased SCH hydration and increased skin pH. Research by Miska et al. also showed something similar but in neonate subjects. The study showed that administering SSO extract could increase the rate of skin pH reduction (maintaining skin pH) during the first week of life, which could be demonstrated by faster acid mantle development. Sunflower seed oil in neonates provides protection by reducing pH more rapidly because the acidic environment in the skin is needed for lipid metabolism, formation of bilayer structure, desquamation, bacterial homeostasis, skin colonization and inhibition of pathogenic bacteria. Reducing pH by administering SSO has a good impact on barrier normalization.<sup>147</sup>

### **Research Limitations**

1. The treatment was given in a short period of time, namely 4 weeks, so this study did not assess the efficacy or safety profile of SSO extract moisturizer in the long term.
2. All research subjects were adult patients with a history of AD and not active lesions

## CONCLUSION

Based on the results of this study, it can be concluded that the trans epidermal water loss (TEWL) value decreased after administering 100% sunflower seed oil (SSO) extract to atopic dermatitis sufferers compared to before treatment. A similar decrease also occurred after topical administration of 100% petrolatum. However, TEWL values in atopic dermatitis sufferers did not show a significant difference between topical administration of 100% SSO extract and 100% petrolatum. In addition, the skin pH value decreased after administering 100% SSO extract and topical 100% petrolatum, with the skin pH being lower after administering 100% SSO extract compared to topical 100% petrolatum. Both types of treatment, both SSO extract and petrolatum, are effective in improving skin barrier function related to decreasing TEWL and pH in atopic dermatitis sufferers, with the majority of SSO extract users experiencing no complaints. Based on the results of this study, it is recommended that treatment be carried out over a longer period of time than 4 weeks to evaluate the long-term efficacy and safety of SSO extract. Additionally, study subjects should include adult patients with active lesions of atopic dermatitis, and interventional agents should include a variety of moisturizers containing humectants, emollients, and occlusives.

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