

The Effect of Topical 0.1% Pomegranate Extract (*Punica Granatum*) on Trans Epidermal Water Loss (TEWL) and Skin Ph Levels in Patients with a History of Atopic Dermatitis

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ABSTRACT

Repairing the skin barrier with moisturizers is one of the five main pillars of treating atopic dermatitis. Petrolatum is considered the gold standard, but its consistency is too thick and oily making it less comfortable to use. Moisturizers containing pomegranate extract (*Punica granatum*) can be an alternative choice that is more comfortable to use. The effectiveness of this pomegranate extract can be evaluated using TEWL and pH examinations which are considered accurate indicators for changes in skin barrier conditions. Effectiveness of topical administration of 0.1% pomegranate extract in reducing TEWL and skin pH in sufferers with a history of AD. Single blind randomized clinical trial with two parallel group pre and post design. 34 sufferers with a history of AD were randomly divided into treatment groups (topical 0.1% pomegranate extract, 17 subjects) and control group (topical 100% petrolatum, 17 subjects). Moisturizer was applied twice daily to the volar area of the forearm for 4 weeks. Both groups showed a significant decrease in TEWL after 4 weeks with a TEWL delta of $-5.2 \pm 2.31 \text{g/m}^2/\text{hour}$ ($p < 0.001$) in the pomegranate extract group and $-7.0 \pm 7.95 \text{g/m}^2/\text{hour}$ ($p = 0.003$) in the petrolatum group. There was no significant difference in TEWL reduction between the two study groups. The pomegranate extract group showed a significant decrease in pH after 4 weeks with a pH delta of -0.5 ± 0.10 ($p < 0.001$), while the petrolatum group actually showed a slight increase with a pH delta of 0.0 ± 0.59 ($p = 0.6$). The pomegranate extract group showed a significantly greater decrease in pH ($p < 0.001$). Topical 0.1% pomegranate extract is as effective as 100% petrolatum in reducing TEWL, but more effective in lowering skin pH.

Keywords: *Punica granatum*, pomegranate extract, TEWL, pH, atopic dermatitis

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INTRODUCTION

Atopic dermatitis (AD) is one of the most common types of chronic inflammatory skin disease globally, (Hay et al., 2014) with a reported prevalence of 15–25% in children and 1–10% in adults. (Sánchez-Alzate & Sánchez-Torres, 2017) This chronic and recurrent disease can reduce the sufferer's quality of life and increase the financial burden due to the treatment costs that must be incurred, So it is very important to provide optimal therapy to control symptoms and prevent exacerbations that affect daily activities (Frazier & Bhardwaj, 2020).

The etiology underlying AD is multifactorial and involves internal factors in the form of atopy and mutations in the filaggrin-producing gene (FLG), accompanied by various external factors that can cause disruption of the epidermal barrier. This complex interaction between various etiological factors will cause disruption of the integrity and function of the epidermal barrier, dysregulation of the local and systemic immune system, as well as disruption and imbalance in the composition of the skin microbiome (Hrestak et al., 2022). The combination of these various mechanisms can ultimately increase transepidermal water loss (TEWL) and reduce the water content of the stratum corneum, reduce the production of natural skin moisturizing factors (NMF), trigger denaturation of various important enzymes in the stratum corneum, increase skin pH, and increase skin permeability to external antigens and pathogenic microbes. In turn, a number of these conditions can also further aggravate skin barrier damage, aggravate inflammatory conditions in the skin, and increase the dominance of pathogenic microbes on the surface of the skin, resulting in a vicious cycle that continues and further worsens the patient's skin condition over time if no action is taken. to break the chain of pathogenesis of atopic dermatitis (Rawlings & Matts, 2005).

Efforts to improve and maintain optimal function of the skin barrier are one of the five main pillars of AD management (Mathiasen et al., 2020). The use of moisturizing preparations that have occlusive, humectant and emollient effects as maintenance therapy for people with a history of AD can help improve the condition of the skin barrier and prevent recurrence (Saeki et al., 2022). especially through its effect in reducing TEWL, modifying skin pH, and improving the condition of the skin microbiome by reducing the colonization of pathogenic bacteria, especially *S. aureus*, so that it can help improve the structure and function of the skin barrier and overcome the symptoms of atopic dermatitis (Kim & Leung, 2018).

Petrolatum is a moisturizing preparation that is considered the gold standard for initial therapy in AD sufferers because it can reduce TEWL and repair the skin barrier effectively through its role as an occlusive agent, where petrolatum with a minimum concentration of 5% is known to reduce TEWL by more than 98%. Unfortunately, the use of petrolatum is generally not preferred because it has several disadvantages, including the consistency being too thick and oily so it is less comfortable to use, and it can stick

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and leave marks on clothes. Therefore, it is necessary to consider the use of alternative moisturizers that can be beneficial in improving the skin barrier without any undesirable effects so that it can increase patient compliance in using moisturizers.

Nutraceutical ingredients in the form of pomegranate extract (*Punica granatum*) which is rich in various phytochemical compounds from the tannins, alkaloids, organic acids and flavonoids are thought to be useful for helping improve the condition of the skin barrier in sufferers with a history of AD because it can act as a humectant through its effect in increasing acid production. hyaluronic acid in the skin, as well as an emollient through the phytosterol compound content of pomegranate seed oil.¹⁶¹⁷Pomegranate extract also has other effects that can be beneficial in cases of atopic dermatitis, including anti-oxidant effects, anti-inflammatory,¹⁶and can improve the composition of the skin microbiome (Chakkalakal et al., 2022).

A panel of experts evaluating the use of pomegranate extract in skin care products found that the concentration of whole red pomegranate extract, which is commonly used in topical products and has been proven safe and effective, was 0.1%.¹⁹This study aims to evaluate the benefits of using red pomegranate extract cream with a concentration of 0.1% in improving the skin barrier in individuals with a history of AD. The use of pomegranate extract in the form of topical preparations is considered more beneficial because it can have a direct effect on the skin surface in the therapy area, reduce systemic side effects, and is considered more acceptable by patients for long-term use (Hamidi et al., 2023).

The condition of the skin barrier in AD sufferers appears to be directly proportional to the activity and severity of the disease, so changes in the condition of the skin barrier can be used to evaluate the level of success of therapy (Lee & Jamil, 2020). The condition of the skin barrier in AD is known to be closely related to TEWL and pH, where increasing TEWL will trigger an inflammatory cascade and play a role in causing a number of clinical abnormalities on the skin surface such as desquamation, reduced skin elasticity, and epidermal hyperplasia (Del Rosso & Levin, 2011). while an increase in pH can cause disruption in the production and composition of skin barrier lipids, causing damage to the skin barrier and triggering desquamation (Lynde et al., 2019). Previous research has proven that a decrease in TEWL and skin pH values is an accurate indicator for improvement in skin barrier conditions, so that TEWL examination using a tewameter and skin pH using a pH meter can be used to assess the success of therapy in AD sufferers (Akdeniz et al., 2018).

The aim of this study was to prove the effectiveness of topical administration of 0.1% pomegranate extract (*Punica granatum*) in reducing TEWL and skin pH in patients with a history of atopic dermatitis (AD). Specifically, this study aims to analyze differences in TEWL and skin pH values before and after topical administration of 0.1% pomegranate extract and 100% petrolatum, as well as comparing differences in TEWL

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and skin pH values between the two treatments in AD sufferers. The benefits of this research include expanding knowledge about the benefits of topical pomegranate extract for improving skin conditions in AD sufferers, providing evidence for clinical practice in the use of pomegranate extract as a maintenance therapy, additional information for further research regarding the use of pomegranate extract in topical formulations, and providing information to the public regarding the benefits of pomegranate extract in skin care products.

RESEARCH METHODS

This research will be carried out at the Skin and Venereology Polyclinic at Demak Regional Hospital, after obtaining ethical approval until the sample size is met. The research design used a single blind randomized clinical trial method with a two parallel group pre and post design. This study included a target population of patients with a history of atopic dermatitis who were treated at the Skin and Venereology Polyclinic, Demak Hospital, with samples taken based on inclusion criteria such as age 13-45 years and willing to take part in the research, as well as exclusion criteria such as a history of hypersensitivity to pomegranate extract and skin disease other. The sample will be selected using consecutive sampling, with a total of 60 patients after taking into account the possibility of dropout of 25%. This study used block randomization for subject allocation, with code A for pomegranate extract and code B for petrolatum. Evaluation is carried out by measuring TEWL and skin pH before and after therapy using a tewameter and pH meter, as well as monitoring compliance through daily record sheets. Data analysis includes descriptive tests, normality tests, and hypothesis tests with SPSS version 25. Research ethics involves written consent from the subject and guarantees confidentiality and compensation of IDR 300,000 per patient. This research is scheduled to take place from September to May, covering all stages from preparation, implementation, to data analysis with a total budget of IDR 36,100,000.

RESEARCH RESULTS AND DISCUSSION

Research result

Recruitment of research subjects was carried out from August 2023 to April 2024, and in total there were 34 patients with a history of atopic dermatitis (AD) who met the criteria to be used as research subjects. There were 34 subjects with a history of AD who met the inclusion and exclusion criteria and agreed to be included in the study. Each subject was then randomly allocated to one of 2 research groups, namely to the treatment group or the control group. A total of 17 subjects were included in the treatment group which received topical 0.1% pomegranate extract and 17 subjects were included in the control group which received topical 100% petrolatum moisturizer, each

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for 4 weeks. During the follow-up period, no research subjects dropped out, so all research subjects could be used in the final analysis.

Characteristics of Research Subjects

General characteristics of research subjects in both research groups are shown in table 7.

Table 1. Characteristics in general, research subjects in the group received 0.1% pomegranate extract and 100% topical petrolatum.

Characteristics	Group		p
	Pomegranate extract 0.1% (n=17)	Petrolatum 100% (n=17)	
Age (years)	30.2±6.04; 31 (20-39)	29.4±6.43; 28 (19-42)	0.7§
Gender			
Man	5 (29.4%)	2 (11.8%)	0.4¶
Woman	12 (70.6%)	15 (88.2%)	
Education			
SMA/SMK	4 (23.5%)	7 (41.2%)	0.005¶
D3	8 (47.1%)	0 (0.0%)	
S1	5 (29.4%)	10 (58.8%)	

§Unpaired t-test

¶Fisher-Exact Test

Overall, the age of the research subjects ranged from 19 to 42 years (average 29.8±6.16 years), and no significant age differences were found between the pomegranate extract groups (average 30.2±6.04 years) and petrolatum (mean 29.4±6.43 years). The majority of research subjects appeared to be female, namely 27 people (79.4%). There were no significant differences in gender distribution between the pomegranate extract (29.4% men and 70.6% women) and petrolatum (11.9% men and 88.2% women) groups. However, there are significant differences in the distribution of education levels between the two research groups. The pomegranate extract group was dominated by patients with D3 graduates (47.1%), followed by S1 graduates (29.4%) and SMA/SMK (23.5%), while the petrolatum group was dominated by patients with S1 graduates (58.8%), followed by SMA/SMK (41.2%) without any D3 graduates.

The characteristics of research subjects related to AD in the two research groups are shown in table 8. There were no significant differences found between the two research groups in terms of duration of suffering from AD, frequency of bathing, type of bath soap used, habit of bathing in warm water, how to dry the body, history previous

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use of moisturizer, initial complaints before receiving treatment, and treatment history. However, all patients in the group who received topical 100% petrolatum complained of problems when using the moisturizer, namely a sticky and oily feeling in 76.5% of patients, and just a sticky feeling in the remaining 23.5% of patients. In contrast, none of the patients in the topical 0.1% pomegranate extract group reported any complaints during use.

Table 2. Characteristics of research subjects related to AD in the Pomegranate Extract and Petrolatum Moisturizing Group

Characteristics	Group		p
	Pomegranate extract 0.1% (n=17)	Petrolatum 100% (n=17)	
Length of suffering from AD (years)	18.1±4.15; 20.0 (10.0-25.0)	20.3±6.72; 20.0 (10.0-32.0)	0.3§
Bathing Frequency			
1X a day	2 (11.8%)	3 (17.6%)	1.0
2x a day	13 (76.5%)	12 (70.6%)	
> 2 x a day	2 (11.8%)	2 (11.8%)	
Type of Bath Soap			
Antiseptic	15 (88.2%)	11 (64.7%)	0.2
Moisturizing wash	2 (11.8%)	6 (35.3%)	
Take a warm shower			
Yes	8 (47.1%)	5 (29.4%)	0.3*
No	9 (52.9%)	12 (70.6%)	
How to dry the body			
Wiping	14 (82.4%)	15 (88.2%)	1.0
Rubbing vigorously	3 (17.6%)	2 (11.8%)	
History of Moisturizer Use			
Yes	12 (70.6%)	15 (88.2%)	0.4
Seldom	5 (29.4%)	2 (11.8%)	
Initial Complaint			
Dry	12 (70.6%)	11 (64.7%)	0.7*
Dry and Itchy	5 (29.4%)	6 (35.3%)	
Treatment History			
Topical	12 (70.6%)	11 (64.7%)	0.7*

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Topical + oral	5 (29.4%)	6 (35.3%)	
Usage Complaints			
There isn't any	17 (100%)	0 (0.0%)	<0.001
Sticky	0 (0.0%)	4 (23.5%)	
Sticky and oily	0 (0.0%)	13 (76.5%)	

[§]Unpaired t-test

[¶]Fisher-Exact Test

*Test χ^2

In table 2 it can be seen that the average duration of AD suffering from subjects in the pomegranate extract group appears to be slightly shorter than the petrolatum group (18.1±4.15 years versus 20.3±6.72 years), although this difference was not statistically significant (p=0.3).

The frequency of bathing in both research groups was mostly twice a day, namely in 76.5% of subjects in the pomegranate extract group and 70.6% in the petrolatum group. The type of bath soap used in the two research groups also appeared to be similar, namely the type of soap antiseptics containing chlorhexidine, chloroxynol, or triclosan (88.2% in the pomegranate extract group and 64.7% in the Petrolatum group). The majority of patients in both research groups did not appear to have the habit of bathing in warm water, namely 52.9% of subjects in the pomegranate extract group and 70.6% of subjects in the petrolatum group. The method of drying the body that was most widely used in both research groups was wiping, namely in 82.4% of patients in the pomegranate extract group and 88.2% of subjects in the petrolatum group.

Most patients have a history of previously used various types of moisturizing cream, both those with humectant, emollient and occlusive effects, namely in 70.6% of subjects in the pomegranate extract group and 88.2% of subjects in the petrolatum group. The initial complaint of research subjects in both research groups was mostly dry skin, namely in 70.6% of subjects in the pomegranate extract group and 64.7% of subjects in the petrolatum group. All AD sufferers who were the subjects of this study reported a history of having received previous treatment, namely topical treatment only in 70.6% of subjects in the pomegranate extract group and 64.7% of subjects in the petrolatum group, while the rest received a combination of topical and oral treatment.

TEWL Value Before and After Using Extract Moisturizer Pomegranate and Petrolatum

TEWL values before and after topical administration of 0.1% pomegranate extract and topical 100% petrolatum are shown in table 9.

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Table 3. TEWL values before and after topical administration of 0.1% pomegranate extract and 100% petrolatum.

TEWL value	Group		p
	Pomegranate extract 0.1% (n=17)	Petrolatum 100% (n=17)	
Right side			
Baseline	23.4±5.43; 24.8 (15.7-36.2)	20.5±7.85; 19.7 (12.2-34.1)	0.2\$
4th week	17.5±4.07; 16.2 (13.1-25.1)	14.3±4.17; 13.3 (7.8-20.8)	0.03\$
p&	<0.001	0.004	
Delta TEWL right side	-5.9±4.47; -5.1 (-22.6--2.5)	-6.2±7.32; -4.7 (-21.8-6.8)	0.7\$
Left side			
Baseline	21.9±4.31; 20.9 (16.7-29.0)	21.9±8.64; 19.7 (12.2-35.2)	1.0\$
4th week	17.3±5.06; 14.8 (12.5-30.2)	14.0±3.78; 12.8 (7.6-22.6)	0.04¥
p&	<0.001	0.002	
Delta TEWL left side	-4.6±2.36; -5.1 (-7.4-3.5)	-7.9±8.71; -5.0 (-23.3-6.6)	0.4¥
TEWL mean value §			
Baseline	22.6±4.27; 24.0 (16.2-28.8)	21.2±8.21; 19.7 (12.6-34.5)	0.5\$
4th week	17.4±4.34; 15.2 (12.8-25.4)	14.1±3.85; 13.6 (7.7-21.7)	0.03\$
p&	<0.001	0.003	
Delta TEWL	-5.2±2.31; -4.8 (-12.8--1.0)	-7.0±7.95; -5.0 (-21.9-6.7)	0.9¥

§Right-left side average

¥Mann-Whitney test

§Unpaired t-test

&Baseline vs week 4; Wilcoxon test

The average TEWL value in the pomegranate extract group appeared to have decreased significantly after 4 weeks ($p < 0.001$), namely from 22.6 ± 4.27 g/m²/hour at the start of the study, to 17.4 ± 4.34 g/m²/hour at the end of the study period (a decrease of -5.2 ± 2.31 g/m²/hour). The petrolatum group also showed a significant decrease in the average TEWL value ($p = 0.003$), namely from 21.2 ± 8.21 g/m²/hour at the start of the

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study, to 14.1 ± 3.85 g/m²/hour at the end of the study period (a decrease of -7.0 ± 7.95 g/m²/hour).

There was no difference in the average initial TEWL value and final results were significant between the two study groups ($p=0.5$ and $p=0.03$), although the petrolatum group generally showed a lower mean TEWL value than the pomegranate extract group, both at the start of the study and after 4 weeks. The petrolatum group also showed a greater reduction in TEWL than the pomegranate extract group, although this difference was not statistically significant ($p=0.9$).

Changes in TEWL values in the volar part of the right and left arms in both research groups are shown in Figure 1.

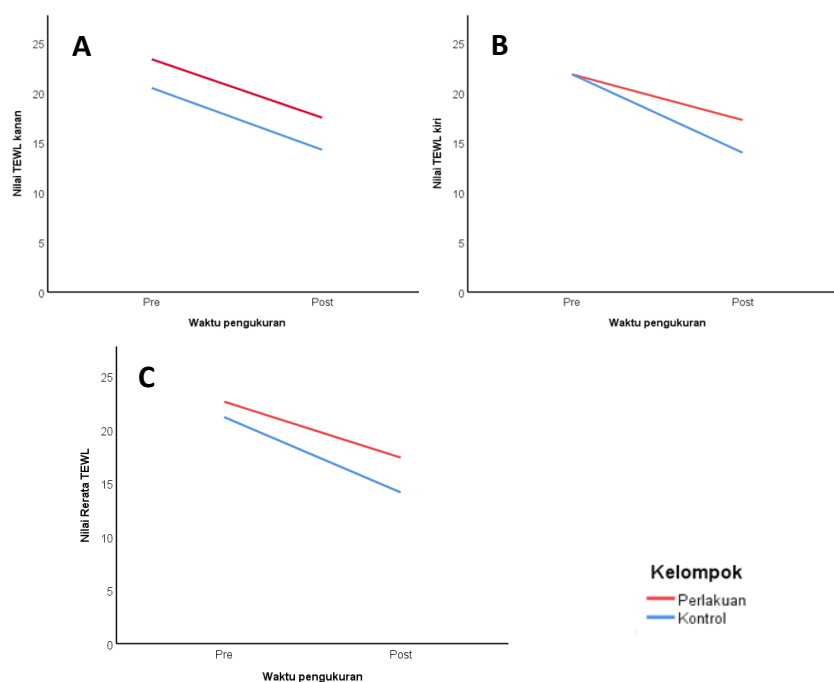


Figure 1. Graph of changes in TEWL values in the volar part of the right (A) and left (B) arm in the treatment group (topical 0.1% pomegranate extract) and control (topical 100% petrolatum), as well as the overall average change in TEWL values (C) in treatment and control groups.

The graph in Figure 1 shows a trend of decreasing TEWL values in the treatment and control groups, both in the volar part of the right arm, left arm, and overall.

The magnitude of the change in TEWL values (delta TEWL) in the volar part of the right and left arms and overall, in the two research groups is shown in Figure 21.

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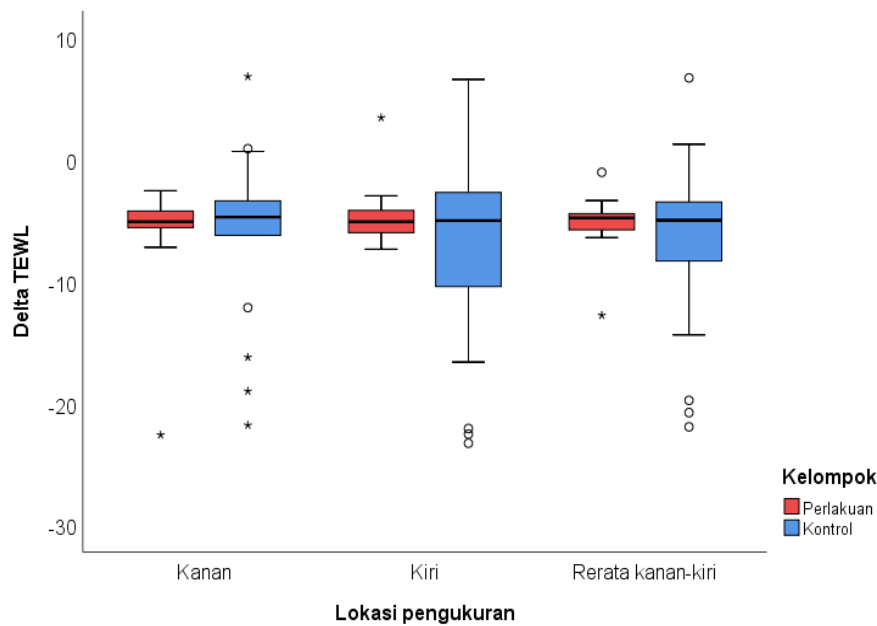


Figure 2. Box-plot graph of right, left TEWL delta values, as well as the average of right and left TEWL values.

Figure 2 shows that the median TEWL delta values for the right side, left side and the mean TEWL values for the right and left sides in the two study groups are approximately the same. The statistical test results also showed that the two groups did not show a significant difference in TEWL delta values ($p=0.7$ for the right side, $p=0.4$ for the left side and $p=0.9$ for the average of the right and left sides).

pH Value Before and After Using Fruit Extract Moisturizer Pomegranate and Petrolatum

The pH values before and after topical administration of 0.1% pomegranate extract and topical 100% petrolatum are shown in table 10.

Table 4. pH values before and after topical administration of 0.1% pomegranate extract and 100% petrolatum.

pH value	Group		p
	Pomegranate extract 0.1% (n=17)	Petrolatum 100% (n=17)	
Right side			
Baseline	5.7±0.72; 5,6 (4.8-6.8)	5.3±0.70; 4.9 (4.4-6.4)	0.07¥
4th week	5.7±0.71; 5.7 (4.7-6.8)	5.4±0.47; 5.3 (4.3-6.1)	0.4\$
p&	<0.001	0.5	

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Delta pH right	-0.5±0.07; -0.5 (-0.7--0.4)	0.1±0.65; 0.1 (-1.3-0.9)	<0.001¥
Left side			
Baseline	5.7±0.71; 5.7 (4.7-6.8)	5.4±0.47; 5.3 (4.3-6.1)	0.9\$
4th week	5.2±0.70; 5.1 (4.2-6.4)	5.4±0.35; 5.4 (4.5-6.0)	0.6\$
p&	<0.001	0.9	
Left pH delta	-0.5±0.15; -0.5 (-0.8--0.2)	0.0±0.57; 0.0 (-1.5-0.9)	0.003\$
Average pH value§			
Baseline	5.7±0.71; 5,6 (4.8-6.8)	5.3±0.57; 5.1 (4.4-6.2)	0.09\$
4th week	5.2±0.71; 5.2 (4.2-6.3)	5.4±0.31; 5.4 (4.7-5.8)	0.5\$
p&	<0.001	0.6	
Delta pH	-0.5±0.10; -0.5 (-0.6--0.4)	0.0±0.59; 0.1 (-1.4-0.9)	<0.001¥

§Right-left side average

¥Mann_Whitney test

\$Unpaired t-test

&Baseline vs week 4; Wilcoxon test

After 4 weeks, the average pH value in the pomegranate extract group showed a significant decrease, from 5.7 ± 0.71 to 5.2 ± 0.71 (decrease of -0.5 ± 0.10 , $p < 0.001$), while the petrolatum group actually experienced an increase in pH from 5.3 ± 0.57 to 5.4 ± 0.31 (an increase of 0.0 ± 0.59), although this change was not statistically significant ($p = 0.6$). There was no significant difference between the average initial and final pH values of the two groups ($p=0.09$ and $p=0.5$), although the petrolatum group showed a lower pH at the start of the study, while the pomegranate extract group showed a lower pH. lower after 4 weeks. The decrease in pH in the pomegranate extract group was significantly greater than the petrolatum group ($p<0.001$). The graph of changes in pH values in the volar part of the right and left arms shows a decreasing trend in the pomegranate extract group, while the petrolatum group shows more varied results. The box-plot graph also shows that the median delta pH value and average TEWL on both sides of the arm in the pomegranate extract group were lower than those in the petrolatum group, with significant differences ($p<0.001$ for the right side, $p=0.003$ for the left side, and $p<0.001$ for the average of the right and left sides).

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Discussion

Patients with a history of atopic dermatitis (AD) often experience damage to the skin barrier which is characterized by increased transepidermal water loss (TEWL) and skin pH. This increase correlates with the severity of the disease, so TEWL and pH examinations can be used to evaluate post-therapy skin conditions. This study assessed the effect of topical administration of 0.1% pomegranate extract for 4 weeks on TEWL and skin pH in 34 subjects with AD, who were randomly divided into two groups: one group received pomegranate extract and the other received topical petrolatum. The two groups have a similar age and gender distribution and characteristics that are not significantly different, so the comparison data is considered valid. The majority of subjects showered twice a day and used antiseptic soap which can damage the skin barrier, while most did not use warm water for bathing. The method of drying the skin by wiping also has the potential to affect the skin barrier. Complaints of dry skin are the most common, associated with deficiencies of natural moisturizing factors and mutations in the filaggrin gene, which exacerbate damage to the skin barrier. Most patients had used moisturizers previously, but there was no significant difference in their use between the therapy and control groups. The use of moisturizers is recommended as initial and maintenance therapy to improve the condition of the skin barrier and prevent recurrence. All patients in this study had received previous therapy, either topical or a combination of topical and oral, with topical therapy generally used for mild to moderate AD, and combination therapy only for more severe cases or those that showed no improvement from long-term topical therapy (Silverberg, 2019).

Effect of Topical 0.1% Pomegranate Extract on TEWL

In this study, the group of patients who used topical petrolatum showed a significantly lower mean total TEWL value than the pomegranate extract group after 4 weeks of use ($p < 0.05$). Although topical 0.1% pomegranate extract also showed a significant reduction in TEWL with a mean reduction of -5.2 ± 2.31 g/m²/hour ($p < 0.001$), topical administration of petrolatum resulted in a slightly greater reduction in TEWL, namely -7.0 ± 7.95 g/m²/hour ($p < 0.05$), although the difference in total TEWL reduction between the two groups was not significant ($p > 0.05$). This shows that topical 0.1% pomegranate extract has comparable effectiveness to petrolatum in reducing TEWL and improving the skin barrier in sufferers of atopic dermatitis (AD). In addition, the pathogenesis of AD involves dysbiosis of the skin microbiome, Th2 and Th1 immune reactions, as well as inflammatory conditions triggered by pro-inflammatory cytokines and reactive oxygen species (ROS) such as superoxide and hydrogen peroxide. Increased ROS can increase oxidative stress, modulate pro-inflammatory signaling pathways, and exacerbate damage to the extracellular lipid matrix at the skin barrier. Pomegranate

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extract, which has antioxidant and anti-inflammatory effects, can help improve the condition of the skin barrier by increasing the skin's water content, improving the skin microbiome, and reducing TEWL. Polyphenol compounds in pomegranate extract are known to have a strong antioxidant effect by donating hydrogen atoms to free radicals, as well as inhibiting lipid peroxidation and cyclooxygenase-2 expression. Previous research shows that pomegranate extract can reduce TEWL and improve skin condition in animal models and cell cultures. Although research on topical pomegranate extract for AD is still limited, existing results support its use as a therapeutic alternative with promising effectiveness (Cervi et al., 2021).

Effects of Topical 0.1% Pomegranate Extract on Skin pH

Skin barrier function is influenced by complex interactions between stratum corneum pH, filagrin, pH-influenced lipid processing, serine proteases, and the condition of the skin microbiome, where skin pH plays a role in regulating the antimicrobial barrier, permeability, and skin barrier integrity. Changes in pH in the stratum corneum often indicate impaired epidermal barrier function, with the pH of healthy skin ranging between 4.0–6.0 and the ideal value around 4.5. In this study, the initial pH value in atopic dermatitis (AD) patients was within the normal range, namely an average of 5.7 ± 0.71 in the pomegranate extract group and 5.3 ± 0.57 in the petrolatum group, probably due to history previous use of a moisturizer that improves the initial skin condition. AD skin may show an increase in pH toward a more neutral state (>6.5) due to decreased filagrin expression and active lesions, which is associated with slower recovery and more severe skin barrier damage. Increased pH can exacerbate skin barrier damage and trigger desquamation through kallikrein protease activity. In this study, topical administration of 0.1% pomegranate extract for 4 weeks showed a significant decrease in pH with an average decrease of -0.5 ± 0.10 ($p < 0.001$), while the petrolatum group experienced an increase in pH although not significantly statistics ($p < 0.05$). A better reduction in pH in the pomegranate extract group probably occurred through improved skin barrier conditions and the balance of skin microbiota, where commensal bacteria such as *Staphylococcus epidermidis* and *Bacillus* spp. produces fatty acids that help maintain acidic skin pH and prevent the colonization of pathogenic bacteria.^{18,60}

Difference between Topical 0.1% Pomegranate Extract and Petrolatum

Petrolatum is the gold standard moisturizer for the initial therapy of atopic dermatitis (AD) due to its proven ability to reduce TEWL and repair the skin barrier effectively through its role as an occlusive agent, with a minimum concentration of 5% which can reduce TEWL by more than 98%. However, many patients avoid petrolatum because of its thick, oily consistency, which can stick to clothing and cause discomfort. In this study, AD sufferers showed significant discomfort with petrolatum compared with topical 0.1% pomegranate extract, which caused no complaints during 4 weeks of use. Although topical administration of 0.1% pomegranate extract and petrolatum

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showed similar effectiveness in reducing TEWL without significant differences, petrolatum showed statistically lower TEWL values at the end of week 4, possibly due to its greater occlusive effect. In contrast, topical 0.1% pomegranate extract was more effective in lowering skin pH than petrolatum, thanks to its additional antioxidant and anti-inflammatory effects as well as improving the skin microbiome. Topical 0.1% pomegranate extract is also more comfortable to use and does not cause side effects, so it can be an effective and safe alternative moisturizer to repair the skin barrier without discomfort, as well as increasing patient compliance in long-term use. The use of pomegranate extract in concentrations of 0.1% in skin care products is generally considered safe and effective, as proven by previous research and expert panel evaluations.

Research Shortcomings

This research was carried out by dividing research subjects into 2 groups, each of which was given different treatment, and does not provide two different types of therapy on the left and right arms of each patient. This may increase the risk of variability in the baseline characteristics of patients in the two study groups and influence the results obtained. In this study, there were no significant differences in mean initial TEWL or pH values between the two research groups, although the petrolatum group generally showed a lower mean initial TEWL value (21.2 ± 8.21 versus 22.6 ± 4.27 g/m²/hour; $p=0.5$) as well as a lower average initial pH value (5.3 ± 0.57 versus 5.7 ± 0.71 ; $p=0.09$) when compared to the pomegranate extract group.

CONCLUSION

The conclusion of this study shows that the TEWL value after topical administration of 0.1% pomegranate extract in patients with a history of atopic dermatitis (AD) is significantly lower than before treatment, likewise the TEWL value after topical administration of 100% petrolatum is also significantly lower. Although the TEWL value after administering 0.1% pomegranate extract was higher than after administering 100% petrolatum, the difference was not statistically significant. The skin pH value after topical administration of 0.1% pomegranate extract was significantly lower than before treatment, while the skin pH value after topical application of 100% petrolatum was higher than before treatment although the difference was not significant. Topical 0.1% pomegranate extract has been shown to be more effective in lowering skin pH compared to 100% petrolatum, but both have equivalent effectiveness in reducing TEWL. For future research, it is recommended that multicenter studies be conducted with a larger number of subjects to increase statistical power, as well as compare the effectiveness of two types of moisturizers by applying them to both arms of one subject for more representative results.

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