## Efficacy of Topical Flaxseed Oil on Hand Eczema: a **Randomized, Triple-Blind Clinical Trial**

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#### Article Info

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ABSTRACT

frequency of up to 10% and a lifetime prevalence of nearly 15% in the general population, typically involves inflammation of the dermis and Received: 2024/10/06; epidermis layers .The aim of this study was to investigate and emphasize Accepted: 2024/12/31; Published Online: 31 Dec 2024; the anti-inflammatory properties of flaxseed oil as well as its historical use in traditional medicine, which could help support its potential effectiveness in treating hand eczema and improving the quality of life of patients. Materials & Methods: The research conducted was a triple-blind, randomized controlled trial involving 68 patients diagnosed with mild to moderate eczema. The participants were assigned to receive either 1 gram of topical flaxseed oil applied twice daily or a control cream, Eucerin, over a period of four weeks. The effectiveness of the treatment was evaluated by measuring the severity of eczema and the quality of life of the patients before and after the intervention. This assessment was carried out using the Hand Eczema Harshness Index (HECSI) and the Dermatology Life Quality Index (DLQI). Results: Based on the gas chromatography (GC) analysis, the flaxseed oil contained 1.9 grams of linoleic acid per 100 grams of oil. There was no **Corresponding Information:** substantial variance in the baseline demographic and clinical characteristics Fatemeh Aliasl, of the two study groups. HECSI and DLQI(14.71 ± 1.89) scores Persian Medicine,Qom significantly improved in the flaxseed oil group compared to the control of Medical group (p=0.001). This effect was particularly pronounced among patients Sciences, Qom, Iran E-Mail: faliasl@muq.ac.ir with mild and moderate eczema (p<0.001). Conclusion: Flaxseed oil can improve eczema indications and quality of life in contact dermatitis patients. However, further research with a larger sample size and comparison to topical steroids is recommended.

Keywords: Flaxseed oil, Dermatitis, Herbal medicine, Persian medicine

Background & Objective: Hand contact dermatitis, with a one-year

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## Introduction

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Hand contact dermatitis, with a one-year frequency of up to 10% and a lifetime prevalence of nearly 15% in the general population, typically involves inflammation of the dermis and epidermis layers (1, 2). It presents symptoms such as redness, edema, scaling, crusts, papules, and vesicles (blisters) (3). In most cases, hand contact dermatitis develops due to two main factors, including increased skin sensitivity to various environmental allergens as well as activation of inflammatory and autoimmune pathways (4). The main pathophysiological mechanisms of these disorders include disruption of skin barrier function and hydration, impairment of the keratinized layer, and destruction of the dermis plus subcutaneous fat due to immune response activation (5, 6). The occurrence of such disorders can lead to the appearance of erythema (redness), edema (swelling), and severe dryness of the skin, along with oozing and hypopigmentation (7). Extensive research suggests a link between inflammatory skin diseases, particularly various types of dermatitis, and the emergence of these manifestations. The underlying cause is often an intensification of inflammatory and autoimmune responses, especially in individuals with sensitive skin and mucous membranes (8).

Consequently, pharmaceutical and beauty companies are increasingly focusing on developing safe and nonchemical treatments to alleviate symptoms of skin conditions such as dermatitis (9). Their primary focus is on herbal compounds and therapeutic extracts with the potential to improve skin structure. As Dini & Laneri (2021) point out, "green cosmetics" are not only used as eco-friendly beauty products to reduce pollution but are also gaining popularity for their use of natural vegetable oils that protect the skin and prevent itchy skin allergies such as eczema (10).

One of these valuable and practical compounds for skin health and reducing inflammatory factors is unsaturated fatty acids, particularly omega-3 fatty acids (3, 11). Linoleic acid, particularly found in oilseeds such as flax seeds, is recognized for its potential benefits in treating skin disorders, including skin sensitivity and various forms of dermatitis. According to Marques et al. (2023), flaxseed is rich in bioactive compounds, notably  $\alpha$ -linolenic acid (approximately 60%) and lignans, which offer several beneficial properties, including anti-edema, antioxidant, and analgesic effects. These characteristics make flaxseed a valuable option for the topical treatment of skin conditions such as eczema. Furthermore, the mucilage present in flaxseed helps soothe the skin and forms a protective barrier which aids in preserving and enhancing moisture levels. (12). In an alternative study, Salhi et al. (2019) reported that flaxseed oil is a medicinal plant traditionally used by healers to reduce or heal skin burns and inflammation. This study identified flaxseed as the primary occurrence as a traditional treatment for skin burns in Morocco, and its use has expanded to treat other skin disorders over time (13). Several studies have shown evidence of flaxseed extract's effectiveness in improving skin inflammation, especially dermatitis, though further research is needed (14). The current study aims to compare the efficacy of flaxseed oil with Eucerin in improving the symptoms of contact dermatitis. By conducting this comparative analysis, we hope to provide empirical evidence that supports the use of flaxseed oil as a viable alternative or complementary treatment for contact dermatitis. This study not only seeks to validate the traditional uses of flaxseed oil but also aims to contribute to the growing body of literature advocating for natural treatments in dermatological care.

Furthermore, our research will address the need for more comprehensive studies on the mechanisms by which flaxseed oil exerts its anti-inflammatory and skin-soothing effects, thereby enhancing our understanding of its role in managing contact dermatitis

## **Materials and Methods**

This randomized, triple-blind clinical trial was carried out on patients with varying levels (mild to moderate) of contact dermatitis affecting the upper extremities, who were referred to the medical centers of Tehran University of Medical Sciences (TUMS) in 2022. These patients received definitive diagnoses from an experienced dermatologist based on Rajka criteria and physical examination. The trial employed a triple-blind design, where neither the participants, nor healthcare providers administering treatment, nor the researchers analyzing data were aware of group assignments (intervention or control). Identicallooking packaging for both treatments, combined with a concealed allocation method (e.g., sealed envelopes), accomplished this blinding strategy. Data analysts received coded data without identifiers linking participants to their assigned treatment group.

The study sought patients who demonstrated a willingness to cooperate in several ways. This included eliminating or reducing environmental irritants from their lives, applying the study medication regularly, and attending follow-up visits at scheduled times after signing the informed consent form. In this study, adherence to treatment was monitored through several methods. Participants were required to attend followup visits at scheduled times, during which healthcare providers assessed their compliance with the study medication. Additionally, participants were encouraged to maintain a diary to record their medication usage and any environmental irritants they encountered. This self-reporting, combined with regular check-ins, allowed us to gauge adherence levels effectively. Additionally, all participants needed a confirmed diagnosis of hand contact dermatitis, be between 5 and 70 years old, and not to be taking any anti-allergic or anti-itch medications. However, certain conditions excluded potential participants from the study. These included a history of neurological or mental illness, known specific skin sensitivities, current use of systemic anti-allergic, anti-itch, or immunosuppressive medications, use of topical medicines within two weeks before the study's start, obsessive handwashing habits, or the use of systemic immunosuppressant drugs within one month before the study began.

Our study used Cochran's formula to estimate the initial sample size, assuming equal proportions (p = q = 0.5) in both groups, a significance level of 0.05, and a critical Z score of 1.96. This formula yielded a target of 80 participants. However, due to exclusions during screening, the final sample size achieved was 68. These contributors were then dispersed at random into two groups of 34 each (control and intervention).

This study was approved by the Research Council of Qom University of Medical Sciences and proceeded in agreement with the ethical principles outlined in the Declaration of Helsinki. All study units were informed about the study's objectives and its significance. Potential participants were provided with a detailed clarification of the research and their right to choose participation. Additionally, they were assured of complete confidentiality regarding their information. Upon request, participants could receive a copy of the study results. The authors confirm that all study protocols adhered to the ethical standards set forth by the ethics committee of Qom University of Medical Sciences and Health Services (Ethics Code: IR.MUQ.REC.1401.023).

Furthermore, the study was registered with the Iranian Registry of Clinical Trials (IRCT registration number: IRCT20200229046641N1, registration date is 2022-06-01)

#### **Flaxseed Oil Preparation and Analysis**

#### - Flaxseed oil preparation

Flaxseed oil, sourced from brown seeds, was purchased from Niri Organic Company (Tehran, Iran). This oil was then used to prepare a 30% flaxseed oil cream in the Faculty of Pharmacy at the University of Tehran. To ensure an identical appearance to the Eucerin cream, the flaxseed oil cream was formulated to match the color and overall look. Following cream preparation, the active ingredient, linoleic acid, was quantified at Mehr Laboratory, a collaborating laboratory of the Food and Drug Deputy of the Ministry of Health.

#### **Determining Linoleic acid Content in Flaxseed oil**

Gas chromatography (GC) was employed to separate and quantify the linoleic acid content in flaxseed oil. The experiment utilized a 1000GC device from Dany Company, Italy. Following a standard protocol (15), linoleic acid in the oil was methylated. This involved mixing 0.1 g of flaxseed oil with 3 ml of n-heptane and 0.05 ml of 2 N methanolic potassium hydroxide solution. The combination was mixed and shaken for 20 minutes using a mixer. Once glycerol was settled, the supernatant containing the methyl esters dissolved in n-heptane was injected into the GC device. The linoleic acid content was recognized by comparing the retention time and peak of the sample with a synthetic linoleic acid standard.

#### **Study interventions**

Figure 1 illustrates the study design. Patients visiting the Skin and Stem Cell Research Center (SSRC) within the research timeframe were screened by specialists using the Hanifin and Rajka criteria (as a gold standard) for atopic dermatitis diagnosis. Those who met the inclusion criteria were then randomly assigned to either the control or experimental group. After providing a detailed explanation of the study's objectives, the written informed agreement was obtained from all contributors (or their parents for minors). Demographic information (age, sex, medical history) was collected using a checklist. Baseline assessments were conducted to evaluate eczema severity using the Hand Eczema Severity Index (HECSI) and the Dermatology Life Quality Index (DLQI). The ICC (Internal Correlation Coefficient) for the total HECSI score showed good reliability (0.79 at the first assessment, 0.84 at the second valuation), and interobserver agreement was excellent (ICC = 0.90) (16).

The DLQI is a recognized instrument for evaluating how skin conditions affecting patients' quality of life, whose validity and reliability have been confirmed in Iranian patients with vitiligo and psoriasis. (**3**, **17**). The HECSI questionnaire is a scoring system designed explicitly for hand eczema. It evaluates symptoms such as erythema, vesicles, papules, scaling, and edema in various hand regions (fingertips, back, palm, wrist). The total score varies withi 0-360, with 0 demonstrating no eczema and 360 indicating the most extreme type. In this research, participants with a score of 0-11 were in the mild group, 12-27 were in the moderate group and above, and 28 were in the severe group.

The DLQI questionnaire, with ten questions, explores the impact of skin problems on patients' daily activities, social interactions, work, and overall wellbeing. Scores vary from 0 (no impact) to 30 (highest impact), with more outstanding scores indicating a poorer quality of life. These scores are further categorized into five levels, including no impact (0 to 1), low impact (between 2 and 5), medium impact (between 6 and 10), high impact (between 11 and 20), and very high impact (between 21 and 30). Both questionnaires have been translated into Farsi and validated for content plus formal validity (17, 18). Validation by experts yielded a Content Validity Index (CVI) of 0.69 for the HECSI and 0.93 for the DLQI, indicating good tool quality. These high scores indicate that these tools are excellent and reliable (3).

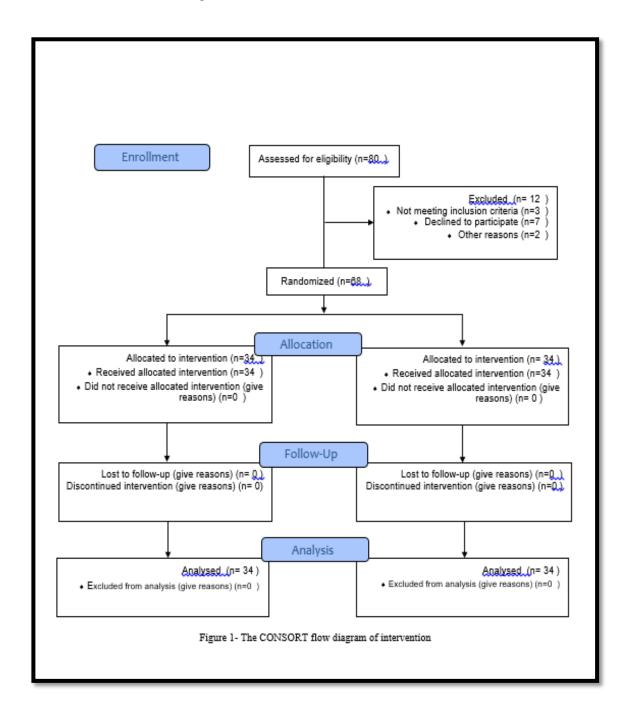
Flaxseed oil and Eucerin were packaged in identical tubes to maintain anonymity. A person uninvolved in the study assigned a code to the tubes, ensuring patients, researchers, and pharmacists remained blind to the contents throughout the trial.

Patients were then randomly designated to groups A and B using a coin toss. Both groups received flaxseed oil or Eucerin cream (prepared in the laboratory of Tehran's Faculty of Pharmacy), which was applied topically to the affected area twice daily for four weeks. The dosage was approximately 1 gram, equivalent to a knuckle-sized flaxseed oil. A Finger Tip Unit (FTU) was a reference to estimate the ointment use. Baseline assessments using the HECSI and DLQI questionnaires were conducted at the beginning of the study and repeated at the four-week follow-up visit.

#### Statistical analysis

Data analysis was conducted using SPSS software version 21. Descriptive statistics were employed, with means and standard deviations (mean  $\pm$  SD) reported for quantitative variables as well as pre-test and posttest scores. A mean level of 0.05 was accepted for all statistical tests. For evaluations of qualitative variables,

the chi-square test was employed, and p-values below 0.05 were considered statistically significantfrequencies and percentages for qualitative variables. Independent samples t-tests were used to compare quantitative means between unrelated groups, while paired t-tests were utilized to compare.





### Results

#### Content of Linoleic acid present in flaxseed oil

Based on the gas chromatography (GC) analysis, the flaxseed oil contained 1.9 grams of linoleic acid per 100 grams.

#### Demographic and disease-related characteristics

This study included 68 patients separated into two groups: an intervention group treated with flaxseed oil and a control group treated with Eucerin only. Table 1 indicates that the two study groups (intervention and control) exhibited comparable baseline characteristics. This includes gender, age, mean time of eczema appearance, and medical history (asthma, rhinitis, hypertension, diabetes mellitus, hyperlipidemia, thyroid disorders, and fatty liver disease). No statistically significant differences were observed between the groups regarding demographics or medical histor. (P > 0.05).

#### Eczema severity

As reported in Table 2, results show no significant differences in baseline eczema severity scores among the treatment and control groups ( $35.65 \pm 10.17$  vs.  $33.53 \pm 9.52$ , P = 0.719). However, after the intervention, the treatment group displayed a significant improvement in eczema severity about the control group ( $14.41 \pm 7.06$  vs.  $25.26 \pm 8.71$ , P =

0.001). Furthermore, the improvement in eczema severity was particularly significant for patients with mild eczema (P=0.0015) compared to the control group (P>0.99). Patients with moderate eczema in the treatment group also showed a significant decline in scores (P=0.019). These findings suggest that the flaxseed oil intervention is more effective than Eucerin in improving eczema severity, especially for mild and moderate cases. It also improved the quality of life of patients. These findings demonstrate that flaxseed oil is significantly more effective than Eucerin in reducing eczema severity post-treatment.

#### **Dermatology Life Quality Index**

As outlined in Table 2, the average severity score on quality of life, measured by DLQI scores, before the intervention was  $(25.12 \pm 4.21)$  and  $(25.88 \pm 3.80)$  in the treatment and control groups, respectively, with no critical variance found between the two groups (P = 0.435). However, after the intervention, the average scores reached  $(14.71 \pm 1.89)$  and  $(20.18 \pm 5.16)$ , respectively. These findings indicate that the positive effect on the quality of life of participants in the flaxseed oil group was greater than that in the control group (P = 0.009). This indicates a substantial improvement in the quality of life for participants using flaxseed oil compared to those using Eucerin."

#### Table 1.The demographic and disease-related characteristics of the participants

Characteristics		<b>Eucerin group</b> (Control group) (n=34) N%	<b>Flaxseed oil group</b> (Intervention group) (n=34) N%	Chi-square test	
Gender	Male	15 (44.1%)	14 (41.2%)		
Gender	Female	19 (55.9%)	20 (58.8%)	P value=0.806	
			Flaxseed oil group		
		Eucerin group	(Intervention group)		
Character	ristics	(Control group)		P value	
		Mean±SD	Mean±SD		
Age (years)		26.47±9.15	26.88±9.25	0.854	
Mean time of appearing eczema (month)		15.00±3.45	14.18±3.57	0.337	
History of	asthma	8.8	5.9	0.642	

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History of rhinitis	8.8		11.8		0.690	
History of hypertension	5.9		14.7		0.197	
History of diabetes mellitus	5.9		2.9		0.999	
History of hyperlipidemia	8.8		5.9		0.642	
History of thyroid disorders	2.9		5.9		0.999	
History of fatty liver disease	0.0		8.8		0.239	
*: Significant deference (Chi-square test). SD: standard deviation						

#### Table 2. The severity of eczema in the two groups using independent sample t-test

Characteristics		Eucerin group (Control group)		Flaxseed oil group (Intervention group)		p Value
		Mean±SD	95% confidence intervals	Mean±SD	95% confidence intervals	
	Before	33.53±9.52	±4.21	35.65±10.1 7	±4.50	0.7 9
Eczema severity	After	25.26±8.71	±3.85	14.41±7.06	±3.12	0.00 1*
	Before	10.35±0.35	±0.15	10.51±1.13	±0.50	>0.9 9
Mild	After	10.12±1.43	±0.63	8.4±0.97	±0.43	0.01 5*
Moderate	Before	25.11±1.04	±0.46	26.21±0.95	±0.42	0.07 1
	After	24.7±1.17	±0.51	14.19±2.23	±0.98	0.01 9
Quality of life	Before	25.88±3.80	±1.68	25.12±4.21	±1.86	0.43 5
	After	20.18±5.16	±2.28	14.71±1.89	±0.83	0.00 9*

#### Discussion

This research assessed the efficacy of flax oil in improving the severity of hand contact dermatitis and its impact on a patient's quality of life. Flaxseed oil is rich in alpha-linolenic acid (ALA), an omega-3 fatty acid, and linoleic acid, an omega-6 fatty acid. Both of these fatty acids play crucial roles in maintaining skin barrier function and overall dermatological health. Our findings revealed that flaxseed oil was more

efficacious than Eucerin (control group) in mitigating eczema harshness. Notably, the improvement in patients with mild eczema treated with flaxseed oil was significantly greater compared to the control group (p=0.0015, control group P>0.99). Additionally, patients with moderate eczema in the treatment group showed a substantial decline in severity compared to the control group (p=0.019). These results suggest that flax oil may benefit mild and moderate eczema. However, due to the limited sample size, more extensive studies are needed to confirm these findings and establish definitive causal relationships. The relatively small sample size and lack of long-term follow-up are other limitations of this study, which may affect the generalizability of the results.

Flaxseed oil, compared to Eucerin, not only significantly reduced eczema severity but also led to a significant development in patients' quality of life (p = 0.009), lowering the disease's impact on their daily lives. Skin disorders, including skin hydration, transepidermal water loss (TEWL), and surface condition, can be improved by dietary fatty acids (FAs), incredibly polyunsaturated FAs (PUFAs). Given the positive effects of unsaturated fatty acids, particularly linoleic acid, on the skin, flaxseed oil, rich in these FAs, deserves greater attention. Plants containing primary unsaturated fatty acids (UFAs), such as the three C18 types oleic (18:1), linoleic (18:2), and  $\alpha$ -linolenic acid, are evidently of great importance (19).

Studies show that linoleic acid is the most remarkable rich fatty acid in the skin layer. Its variations are crucial for the structure and function of the epidermal barrier (20). Flaxseed oil besides having a beneficial fatty acid composition rich in linoleic acid, also possesses mucilaginous properties. These properties give it water-holding capacity, allowing it to naturally moisturize and heal inflamed skin (19, 21, 22). The effects of plant extracts, particularly flaxseed oil, on reducing the severity of dermatitis have been investigated in other studies, yielding more or less similar results. A similar survey of Somjorn et al. (2021) studied the effectiveness of a combination of black currant seed oil, sunflower oil, and balloon vine compared to 5% urea cream on 38 patients with atopic dermatitis. Their findings indicated that the combination cream was more effective than 5% urea cream in improving atopic dermatitis and may be utilized for treating mild to moderate cases.

#### (23).

In another study, Ahmad Nasrollahi et al. (2018) evaluated the effectiveness of a linoleic acidcontaining product compared to urea-containing waterin-oil (w/o) emulsions in 20 patients with atopic dermatitis. After four weeks, their results revealed that linoleic acid significantly reduced local SCORAD, TEWL, erythema, and severity of atopic dermatitis compared to urea emulsions and improved barrier dysfunction (20).

In Yu et al.'s 2022 study (24), mice treated with flaxseed extract showed a significant increase in enterolactone, an intestinal bacterial metabolite, along with more remarkable improvement in skin dermatitis. This study identified secoisolariciresinol-diglycoside (SDG), a natural lignan in flaxseed extract, as the key contributor to the improvement. Feeding affected mice SDG extract was associated with diminished serum IgE levels and, consequently, reduced skin inflammation. Additionally, the extract consumption lowered the number and inflammatory response of TH2 lymphocytes.

In Yang et al.'s 2017 study (25), to explore the immunological and therapeutic effects of fermented flaxseed oil (FFSO) on eczema symptoms (redness, pruritus) induced by atopic dermatitis (AD) in NC/Nga mice, researchers measured Fc receptor expression and beta-hexosaminidase concentration. They concluded that FFSO could alleviate AD symptoms such as epithelial damage, redness, swelling, and pruritus. This was achieved by reducing the number of cells expressing NF- $\kappa$ B p65 and iNOS while significantly enhancing PKC expression.

Prior research and our current findings suggest that linoleic acid plays a significant role in improving atopic dermatitis. Flaxseed oil, derived from the flaxseed plant, is exceptionally rich in linoleic acid. This highlights the potential of flaxseed oil as a natural therapeutic option for managing atopic dermatitis. Further investigation into the efficacy and optimal dosage of flaxseed oil for treating atopic dermatitis is warranted.

## Conclusion

As a conclusion, the administration of flaxseed oil, as compared to routine treatment regimens for the treatment of contact dermatitis, would boost the effectiveness of the drug regimen by reducing the harshness of eczema and augmenting the quality of life of patients. Finally, it can be recommended that the study should be conducted with a larger sample size and compared in terms of efficacy with topical corticosteroids such as betamethasone.

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Not applicable.

## **Authors' Contribution**

S.D: Responsible for data curation, conceptualization, methodology, formal analysis, validation, and writing original draft. F.A: Involved in conceptualization, methodology, validation, supervision, project administration, original draft writing, and reviewing and editing. P.M, M.A, and S.F: Contributed to conceptualization, methodology, investigation, and writing the original draft.

## **Conflict of Interest**

The authors declare that they have no conflict of interest.

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# Ethics Approval and consent to participate

This study was approved by the Research Council of Qom University of Medical Sciences and led in agreement with the ethical principles outlined in the Declaration of Helsinki. The authors confirm that all study protocols adhered to the moral standards set forth by the ethics committee of Oom University of Medical Sciences and Health Services (Ethics Code: IR.MUQ.REC.1401.023). This study received approval from the Research Council of Qom University of Medical Sciences and was carried out in alignment with the ethical principles specified in the Declaration of Helsinki. The authors affirm that all study protocols complied with the ethical standards established by the ethics committee of Qom University of Medical Sciences and Health Services (Ethics Code: IR.MUQ.REC.1401.023).

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