Open Access
Journal of the Faculty of Medicine Baghdad
Print ISSN: 0041-9419, Online-ISSN: 2410-8057
DOI: https://doi.org/10.32007/jfacmedbaghdad.6642371
Research Article

# The Anti-Inflammatory Effect of *Chenopodium murale* in Comparison to *Salvia frigida* on Atopic Eczema

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*Received: April, 2024*
*Revised: Sept. 2024*
*Accepted: Oct. 2024*
*Published: Dec., 2024*

**Abstract:**

**Background:** Atopic dermatitis (AD) is a prevalent chronic inflammatory skin condition with a familial tendency. It affects approximately 10%-20% of children and 1%-3% of adults worldwide. *Chenopodium murale* is clinically proven for treating many medical conditions, such as AD, due to its easy application and efficacy. *Salvia* plant has an anti-inflammatory effect on AD cases treated with phenolic compounds.

**Objective:** To determine the anti-inflammatory effect of the phytosterol fraction of *Chenopodium murale* (CM) in comparison to *Salvia frigida* (SF).

Methods: This study was conducted from December 2020 to June 2021 in the Department of Pharmacology, College of Medicine, Al Nahrain University. Fifty mice were included in the study, subdivided equally into five subgroups [control, induction, Tacrolimus-1%, Phytosterol-3%, and Phenolic-5%]. Biological and histological parameters were measured, and their means were compared using the independent t-test, and the one-way ANOVA was used to estimate the mean of differences.

**Results:** The Tacrolimus-1% group showed a significant decrease in white blood cells, Ig-E, and inflammation means than other groups; a significant decrease in mean epidermal thickness than the Phytosterol-3% groups; and a significant decrease in IL-13 and erosion than the Phenolic-5% groups. The phytosterol-3% group showed a significant decrease in the mean parakeratosis, erosion, and observational severity (OS) score than other groups. The phenolic-5% group showed a significant decrease in the mean epidermal thickness than other groups and a significant decrease in OS score than the Tacrolimus-1% groups.

**Conclusion:** The topical applications of the phytosterol fraction of *Chenopodium murale* or the phenolic compound of *Salvia frigida* were effective and promising in treating atopic dermatitis. While the phenolic compound of *Salvia frigida* is effective, it is somewhat less than that of the phytosterol fraction of *Chenopodium murale*.

**Keywords:** Atopic dermatitis; *Chenopodium murale;* Phenolic compound; *Salvia frigida*; Tacrolimus

## Introduction

Atopic eczema dermatitis [AD] is a skin condition characterized by inflammation, itching, redness, drying, and scaling. Thirty percent of AD patients also have asthma. AD tends to be persistent with periods of relapse and remission. While some patients may improve during puberty, others may experience lifelong symptoms. Different microbial infection can occur as a result of AD. Restoring skin barriers by moistening is considered crucial in managing AD symptoms like itchiness and inflammatory response. (1-3)

A macrolide lactone, Tacrolimus, derived from fungi, is a widely utilized immune-suppressive medication. Its diminutive size grants it strong skin penetration capabilities. Despite the fact that it effectively treats severe AD and aids in controlling acute flare-ups and preventing new occurrences by its immune-regulating mechanism. However, it is associated with side effects such as skin burning and itchiness (4).

Natural plant extracts exhibit diverse pharmacological effects, including their ability to serve as antioxidants due to their redox property. This enables them to function like reducing agents, hydrogen donors, and quenchers of single oxygen. Phytosterol fraction (PF) shows promise as a nutritious factor in certain conditions like GIT disorders, harnessing both systemic metabolic and local anti-inflammatory effects. Previous studies have demonstrated the utility of plants across various ailments, including anthelmintic, gastric upset, anti-spasmodic, and excessive sweating, while providing relief from conditions such as dysmenorrhea, asthma, colds and migraines (5-6). Chenopodium murale (CM) exhibits similar pharmacological properties to PF; such as anti-

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oxidant, anti-bacterial, anti-inflammatory, alongside efficacy in treating skin diseases (6-10).

Salvia-frigida (SF) stands out as one of the extensively utilized medicinal plants in Turkey (11). Past research concentrated on analyzing acetone extract of SF's aerial parts, resulted in the discovery and characterization of two oleanane-type triterpenoids and two cycloartane-type triterpenoids, in addition to substances like α_amyrin and β_sitosterol (12-14). Antioxidant properties attributed to Phenolic Compounds (PC) of SF and flavonoids are believed to contribute to the upregulation or protection of the antioxidant defense system (15, 16).

The study aimed to assessment of *Chenopodium murale* anti-inflammatory effectiveness in comparison to that of *Salvia frigida* in treating atopic dermatitis**.**

**Subject, Materials and Methods:**

This study was randomized clinical trial, carried out on mice, for the period from January - July 2021 in the Department of Pharmacology, College of Medicine, Al-Nahrain University. Ethical and scientific procedures for the animal experiment protocols were rigorously reviewed and approved by the University Review Council (No. 857 on 28/9/2020).

**Experimental Animal and Study Design:** The study involved 50 apparently-healthy adult male Albino-mice weighing 25 to 30 grams. The mice acclimatized for seven days with well-ventilation and isolation in 24 Celsius. They were housed at the College of Veterinary, with a 12-hour light cycle. The study's practical component took place at the College of Veterinary Medicine, University of Baghdad, Iraq. Out of the 50 mice, 10 were apparently-healthy (Control Group), while 40 mice were induced with 1 – Chloro - 2, 4 - dinitrobenzene [DNCB][15] to develop AD. The induced mice were divided into four groups: Not treated (Induction group); managed by Tacrolimus ointment 0.1% (Tacrolimus-1% group), managed by 5% topically applied SF cream (Phenolic-5% group), managed by 3% topically applied CM cream (Phytosterol-3% group) (17). Topical treatments were administered once per day for three weeks. (18-20)

**Inductions:**

**Mice Models of DNCB; AD-Induction:** Atopic dermatitis was induced in mice by shaving hair from the dorsal skin, followed by the topical application of 150 µL of 1% Dinitrochlorobenzene (DNCB) in a 3:1 (v/v) acetone/olive oil solution. After four days, 0.2% DNCB dissolved in an acetone/olive oil mixture (3:1 vol/vol) was applied three times a week for three weeks. Once skin sensitization was visually confirmed, the mice were managed by the test sample (21). Figure 1 for details.

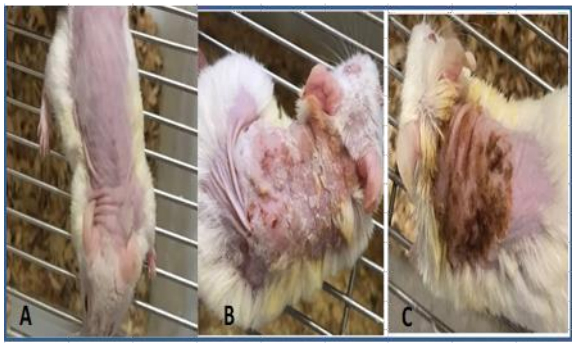


**Figure 1: Skin condition: Healthy [A] and Lesions after induction [B and C]**

**Plant material:** Identifying and authentication of the CM and SF plants was done by a specialist professor. Herbs were extracted and verified at the Pharmacognosy department and Medicinal Plants in the College of Pharmacy/ Al-Mustansiriyah University. The plant leaves were processed thorough washing, shade drying, and grinding into coarse powder using a mechanical grinder.

**Extractions and fractionations of PF from *CM*:** The shade-dried leaves, totaling 250 grams, were subjected to extraction with a 90% ethanol solution (600 milliliters) using a reflux apparatus until complete exhaustion and evaporation, yielding a crude fraction. The crude extracts were then acidified with 5% hydrochloric acid to reach a pH of 2, followed by partitioning with an equal volume of ethyl acetate to obtain 2 layers (aqueous and ethyl acetate). The ethyl acetate layer was collected, evaporated, and subsequently basified with 300 milliliters of NaOH-5%. The mixture was then separated with chloroform to produce two layers: A methanol-80% layer and a petroleum ether layer. The chloroform layer was further treated with petroleum ether to extract the phytosterol in the petroleum ether fraction. This fraction was then transferred to a Petri dish coated with tinfoil and stored at freezer temperature (-8 $c^{o}$). (18) High-performance liquid chromatography was conducted to examine the PF of CM, revealing significant presence of Beta-sitosterol as a primary component.

**Preparations of** PF-**3% cream:** Extraction of 3-grams from the PF of CM were weighed and dissolved with alcohol-3 milliliters. The mixture was shaken for 4 minutes until complete dissolution, resulting in a clear solution. One-hundred grams was subsequently weighted and adjusted with Aquasoft cream further shaking was done for five-minutes using a spatula (19).

***Salvia frigida* Extraction:** A total of 150 grams of shade dried and crushed leaves underwent defatting through soaking in hexane for 24-hours, followed by drying at 25$^{o}$c. Then, further extraction with Soxhlet apparatus with powder-packed into thimbles and 1.75 liters of 85% aqueous methanol was extracted as solvents after 24 hours. Then, the extracted material was filtered and evaporated through reduced pressure, yielding 12 grams of dry extract. Of the residue, 4 grams

were suspended in 100 ml of wate,, adding approximately four milliliters NaOH-5% to obtain basic-solution with a pH of 10. The mixture was then aliquoted with ethyl acetate (19). Finally, collection, evaporation, and dryness of the aqueous layer were done, representing the phenol-rich fraction was stored for further use.

**Preparations of PC-5% Cream:** Extraction of five grams PC from SF were weighed and dissolved with alcohol-3 milliliters. The solution was shaken for 4 minutes until complete dissolution and clarity were achieved. Subsequently, the weight was adjusted with Aquasoft cream and further shaking was done for five-minutes using a spatula (22).

**Phytochemical tests:** Two chemical tests [(I) Liebermann-Burchard test and (II) H2SO4 test)] were conducted on ethanol extraction through standard procedure to assess PF of CM (18).

**Topical Treatment Application, parameter, and animals sacrificing**: Topical administrations of Tacrolimus-0.1% ointment (20), Phenolic-5% cream (22), and Phytosterol-3% cream (18) was done to the AD areas of animals for 21 days, once/day (9-am), commencing from 5$^{th}$ day of induced AD. The comparison parameters included white blood cells, eosinophil%, s. Ig-E levels, IL-4 and IL-13 concentrations, and histopathological examination of AD skin lesions. These results were then compared with those of the control groups, and an observational severity score was determined.

**Sample Collection and Histopathological Analysis**
After 21 days of treatment, the mice were anesthetized using ether, and blood samples were collected in EDTA tubes for CBC and serum Ig-E analysis. Subsequently, the mice were euthanized using cervical dislocations, and the affected skin area of AD was removed for histological examination and homogenized skin preparation. Dorsal skin samples were fixed in 10% formaldehyde, paraffin-embedded, and cut into 6 µm sections. These sections were stained with hematoxylin and eosin (H & E) for histological evaluation of the inflammatory degree and AD-associated changes (23). Histopathological analysis was performed on skin for all groups in the 21$^{st}$ day of therapy. The sections were evaluated and scored by a pathologist using a semi-quantitative scoring system, assessing parameters such as epidermal thickness, erosions, inflammations, and oedema (0-3 scores, with 0 indicating no abnormalities, 1 indicating mild abnormalities, 2 indicating mild to moderate abnormalities, and 3 indicating moderate abnormalities) (21). These evaluations were performed in the department of histopathology/Ibn Sina Medical and Pharmaceutical Sciences University.

**Preparations of Skin-Tissue Homogenates (STH):** The 2$^{nd}$ part of the mice skin underwent a washing process using normal saline, with chilled phosphate buffered saline (1X PBS) being used. After weighing, homogenization; for every 100-grams of tissue with one-milliliters of 1X PBS was done using a tissue homogenizer (24). The homogenate was stored overnight at 20°C, and two freeze-thaw cycles were performed to break the cell membrane. After centrifugation, the supernatant was collected and preserved at -20°C to examine the level of IL-4 and IL-13.

**Serum Ig-E, IL-4, and IL-13 Assays:** Serum Ig-E, IL-4, and IL-13 levels were assessed using an ELISA Kit from CUSABIO/China Kit (23).

**Assessing the Observational Severity Score (OS score):** On day 21 of treatment, the severity of atopic dermatitis on the dorsal area was evaluated for each group. Erythema, dryness, erosion, and edema were scored as 0 (none), 1 (mild), 2 (moderate), and 3 (severe). The clinical skin score was defined as the sum of individual scores, ranging from 0-12 (25).

**Statistical Analysis:**
The data was entered into Microsoft excel 365 and loaded into the Statistical Package for Social Sciences (SPSS) version 26. Parametric data are presented as mean ± standard deviation. Categorical data are presented as numbers and percentages. The Independent t-test and one-way ANOVA test were used to measure the differences between groups parametric variables. A P value of $<0.05$ was considered statistically significant.

**Results:**
All biomarkers and histological parameters showed significantly higher levels in the induction-group than that of the control, $P<0.05$, Figure 2.

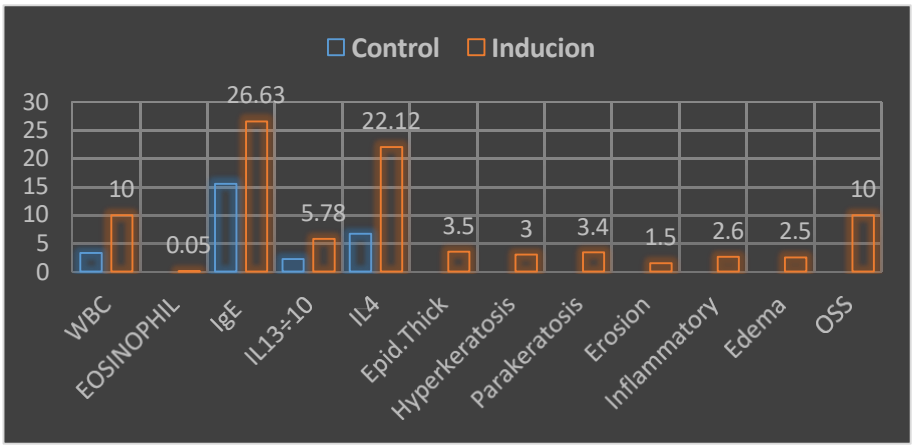


**Figure 2: Biological and histological comparisons between control and induction groups**

Biological comparisons between all studied groups showed significant decreases in the level of (WBC, Eosinophil, Ig-E, IL-13, and IL4) among Tacrolimus-1%, Phytosterol-3%, and Phenolic-5% groups compared to the induction group (P<0.001). Tacrolimus-1% group showed a significantly lower mean WBC count and Ig-E than other groups (<0.05) and a significantly lower mean IL-13 than Phenolic-5% groups (P<0.05). No significant differences were observed in biological parameters between Phytosterol-3% and Phenolic-5% groups (P>0.05), table 1.

**Table 1: Biological comparisons between all study groups**

| Variables | | Induction | Tacrolimus-1% | Phytosterol-3% | Phenolic-5% |
|---|---|---|---|---|---|
| WBC [x103 /µl] | Mean±SD | 10.0±2.10 | 6.0± 2.02 | 7.1± 2.01 | 7.6± 3.03 |
| | P-*a* | | < 0.001 | < 0.001 | <0.001 |
| | P-*b* | | | 0.04 | 0.04 |
| | P-c | | | | 0.56 |
| Eosinophil [x103 /µl] | Mean±SD | 0.05±0.02 | 0.02± 2.02 | 0.03±0.09 | 0.03± 0.03 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | 0.11 | 0.12 |
| | P-c | | | | 0.34 |
| Ig-E [ng/ml] | Mean±SD | 26.6±5.15 | 16.0±6.08 | 17.5±6.61 | 20.4±5.92 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | 0.9 | 0.045 |
| | P-c | | | | 0.91 |
| IL-13 [pg/ml] | Mean±SD | 57.8±10.52 | 31.8±21.29 | 31.6±12.31 | 37.2±18.00 |
| | P-*a* | | < 0.001 | < 0.001 | <0.001 |
| | P-*b* | | | 0.06 | 0.031 |
| | P-c | | | | 0.42 |
| IL4 [pg/ml] | Mean±SD | 22.1±6.21 | 9.1±4.03 | 9.7±2.88 | 11.6±2.23 |
| | P-*a* | | < 0.001 | < 0.001 | <0.001 |
| | P-*b* | | | .49 | .07 |
| | P-c | | | | .57 |

***a= Comparisons among Induction and others; b= Comparisons among tacrolimus-1% and Phytosterol-3%; Phenolic-5%; c= Comparisons among Phytosterol-3% and Phenolic-5%***

Histological comparisons between all study groups showed a significantly lower levels of (Epidermal thickness, hyperkeratosis, parakeratosis, erosion, inflammatory cells, extracellular edema, and OSS) among Tacrolimus-1%, Phytosterol-3%, and Phenolic-5% groups from that of the induction group (P<0.001). The tacrolimus-1% group; showed a significantly lower mean inflammatory cells than other groups (P<0.05), a significantly lower mean epidermal thickness than Phytosterol-3% group (P<0.05), and a significantly lower mean erosion than Phenolic-5% group (P<0.05). The phytosterol-3% group showed a significantly lower parakeratosis, erosion and OS score than other groups (P<0.05). The phenolic-5% group showed a significantly lower mean epidermal thickness than the other groups (P<0.05), and a significantly lower OS score than Tacrolimus-1% groups (P<0.05), Table 2. Figure 3 (a, b and c) shows some of the above histological changes.

**Table 2: Histological c ɔmparisons betv een all study groups**

| Variables | | Induction | Tacrolimus-1% | Phytosterol-3% | Phenolic-5% |
|---|---|---|---|---|---|
| Epidermal Thickness | Mean±SD | 3.5±0.52 | 1.2±1.22 | 2.2±0.78 | 1.0±0.66 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | 0.025 | 0.04 |
| | P-c | | | | 0.002 |
| Hyperkeratosis | Mean±SD | 3.0±0.81 | 1.6±0.51 | 1.6±0.51 | 1.6±0.51 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | 0.99 | 0.99 |
| | P-c | | | | 1 |
| Parakeratosis | Mean±SD | 3.4±0.69 | 1.2±0.78 | 1.0±0.003 | 1.2±0.78 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | <0.001 | 0.9 |
| | P-c | | | | 0.43 |
| Erosion | Mean±SD | 1.5±0.52 | 0.2±0.42 | 0.2±0.35 | 0.4±0.51 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | 0.17 | .045 |
| | P-c | | | | .035 |
| Inflammatory Cells | Mean±SD | 2.6±0.51 | 1.7±0.42 | 1.8±0.42 | 1.8±0.78 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | .046 | .81 |
| | P-c | | | | 1 |
| Extracellular Edema | Mean±SD | 2.5±0.52 | 1.2±0.51 | 1.2±0.42 | 1.1±0.56 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | 0.45 | 0.46 |
| | P-c | | | | 0.66 |
| OSS* | Mean±SD | 10.0±.81 | 4.5±1.08 | 3.5±0.97 | 3.7±1.33 |
| | P-*a* | | < 0.001 | < 0.001 | < 0.001 |
| | P-*b* | | | 0.028 | .03 |
| | P-c | | | | .7 |

***a= Comparisons among Induction and others; b= Comparisons among tacrolimus-1% and Phytosterol-3% and Phenolic-5%; c= Comparisons among Phytosterol-3% and Phenolic-5%; *OSS= observation-severity-score.***

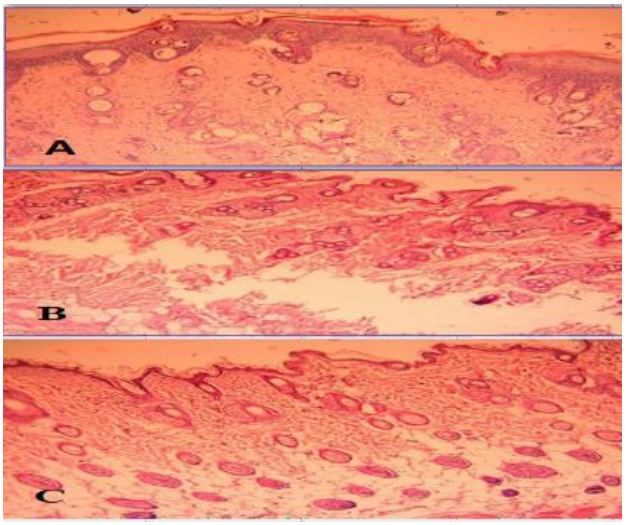


**Figure 3: Histological changes [10x] among a. Induction group; b. Phytosterol-3% group; and c. Phenolic-5% group. H and E -stain**

**Discussion:**

Atopic dermatitis (AD) is detrimentally impacting the quality of life and daily activities, with a comparable or even more severe impact than other chronic skin and systemic diseases (26).

In the current study, the comparison between the selected parameters in the untreated group with induced atopic dermatitis (AD) showed noticeable signs of inflammation and a significant increase in thickness, as well as elevated OS scores. This aligns with a previous study reporting a substantial increase in various WBC components in untreated AD-induced groups (27). Eosinophil counts were found to be significantly elevated in AD induced non-treated group in agreement with another study which showed increased eosinophil in patients having eczema with persistent lesions (28). In addition, a significant increase in skin tissue IL-13 and IL-4, and serum Ig-E were observed in the AD non-treated group, in congruency with other studies (29, 30). Another difference was found in OS score in the AD induced non-treated group, in agreement with a study reporting significantly more severe symptoms and high OS score, Gil, et al (31).

Upon the application of the topical 3% cream of phytosterol fraction of CM, a significant decrease in signs of inflammation, histopathological changes, and OS score were evident in comparison to the induction group, which may be explained by the β Sitosterol anti-atopic effects of CM. The anti-inflammatory action of β Sitosterol has been linked to the regulation of mediators of inflammation, demonstrating the therapeutic potential in inflammatory skin conditions like AD. Animal studies also support this, indicating that β Sitosterol decreases the release of inflammatory cytokines and oedema, He *et al.* (32)

Several studies supported our findings that the extracts of the Chenopodium murale significantly suppressed the test fungal growth (33) and exhibited mild to moderate inhibitory activities against different bacteria (34).

The results of the current study are in agreement with those of TrivellatoGrassi et al on the anti-inflammatory and anti-nociceptive effects of Chenopodium, identifying the mechanism of action as the inhibition of mediators and enzymes involved in the inflammatory and pain processes. (17) This confirms the validity of the common use of this plant for treating inflammation and pain and helping wound healing processes.

Han et al found that β-sitosterol reduced AD clinical symptoms such as dryness, eczematous, erythema and serum histamine and Ig-E levels in induced AD in mice. Additionally, β-sitosterol inhibited the IL-6 expression in AD like skin lesions, significantly reduced the levels of inflammation-related mRNA and protein in the AD skin lesions, significantly reduced the levels of histamine, Ig-E, and IL-4, and reduced the activation of mast cell when used in the treatment of AD skin lesions (20), which supports the current results.

In the current study, the application of the topical 3 phenolic compounds resulted in a significant decrease in the signs of inflammation, histopathological changes, and OS score in comparison to the induction group, supporting the role of the phenolic compounds of SF. Studies on Salvia plants, specifically those treated with phenolic compounds showed the anti-inflammatory effects in AD-treated groups, and highlighted the diverse properties of Salvia plants, including anti-inflammatory, anti-cancer, anti-cholinesterase, anti-microbial, anti-malarial, and antioxidant effects (35-41).

In the present study a significant decrease was found in the WBC count and IL-4 between 5% phenolic compound treatment group and AD induced non-treated group after three weeks of treatment, in consistence with Paulin et al study who found that salvia plant has anti-inflammatory effects (42). Paulin et al and Raal et al reported that Salvia species have also been used for a long time in folk medicine against fever, rheumatism, perspiration, sexual debility, chronic bronchitis, mental and neurological conditions. Essential oil of salvia and their preparations are externally used for inflammations and infections of the mucous membranes of throat and mouth (43, 44).

Histo-pathologically, a highly significant reduction in epidermal thickness, hyperkeratosis, parakeratosis, erosion, inflammatory cells, extracellular edema, and OS score was found after phenolic compound treatment. Many studies confirm these results, highlighting the properties of Salvia plant and its effects on AD and other skin lesions (45, 46). Dai et al reported that Phenolic compounds, especially flavonoids, have a great antioxidant effect that has been shown to be more effective than vitamins C and E and carotenoids (47). Upon comparing the effects of the phenolic compound of Salvia frigida and the phytosterol fraction of *Chenopodium murale*, it is noted that the phenolic compound reduces epidermal thickness significantly after three weeks of treatment. In contrast, the phytosterol fraction-treated group displays a more significant decrease in IL-13, parakeratosis, and OS score. The Tacrolimus-1% group exhibits a highly significant decrease in WBCs and inflammation but a comparable reduction of erosion to the phytosterol fraction-treated group.

The topical applications of various treatments in AD in the current study successfully mitigated responses of inflammation. This suppression led to a decrease in blood concentrations of histamine due to the reduction of IL-13 and the inactivation of mast cells, similar to the results reported (48).

**Limitations of the Study:**

This study did not include clinical data from human participants. Although animal models offer valuable insights into human diseases, they may not fully capture the complexity of atopic dermatitis as it occurs in humans. While the findings in the mouse model are encouraging, further research is required to evaluate the safety and effectiveness of *Chenopodium murale* and *Salvia frigida* on Atopic Eczema in human subjects.

**Conclusions:**

The topical applications of phytosterol fraction of *Chenopodium murale* or phenolic compound of *Salvia frigida* was effective and promising in treating atopic dermatitis. While the phenolic compound of *Salvia frigida* is effective, it is somewhat less than that of the phytosterol fraction of *Chenopodium murale*.

**Authors' declaration:**

The manuscript is an original work, not previously published or sent to other journals. We hereby confirm that all the figures and tables in the manuscript are ours. The project was approved by the local ethical and scientific care procedures for the animal by Al Nahrain University Review Council; code no. = 857 on 28/9/2020.

**Conflicts of Interest:** None

**Funding:** None

**Authors' contributions:**

Study conception & design: (Zahraa Y. Hassan). Literature search: (Zahraa Y. Hassan). Data acquisition: (Tuka Y. Hassan). Data analysis & interpretation: (Tuka Y. Hassan). Manuscript preparation: (Ahmed Al-Kinany). Manuscript editing & review: (Ahmed Al-Kinany)

***References:***

*1. Ahn K, Kim BE, Kim J, Leung DY. Recent advances in atopic dermatitis. Current Opinion in Immunology, 2020;66:14-21. https://doi.org/10.1016/j.coi.2020.02.007.*

2. *Kim J, Kim BE, Leung DY. Pathophysiology of atopic dermatitis: Clinical implications. Allergy Asthma Proc. 2019;40(2):84-92.* https://doi.org/10.2500/aap.2019.40.4202

3. *Tanei R. Atopic Dermatitis in Older Adults: A Review of Treatment Options. Drugs Aging 2020:37(3):149-160.* https://doi.org/10.1007/s40266-020-00750-5

4. *Mohamed AA, El Borolossy R, Salah EM, Hussein MS, Muharram NM, Elsalawy N, et al. A comparative randomized clinical trial evaluating the efficacy and safety of tacrolimus versus hydrocortisone as a topical treatment of atopic dermatitis in children. Front. Pharmacol. 2023; 14:1202325.* https://doi.org/10.3389/fphar.2023.1202325

5. *Ahmed AA, Abu-Raghif AR. Effect of Topical Phytosterol Fraction of Chenopodium murale on Induced Hypertrophic Scar in Rabbits. Journal of Global Pharma Technology, 2020;12(02):115-124.* https://www.jgpt.co.in/index.php/jgpt/article/view/3231/2567

6. *Abd Elkarim AS, Ahmed AH, Taie HAA, Elgamal AM, Abu-elghait M, Shabana S. Synadenium grantii hook f.: HPLC/QTOF-MS/MS tentative identification of the phytoconstituents, antioxidant, antimicrobial and antibiofilm evaluation of the aerial parts. Rasayan. J. Chem. 2021;14:811–828.* https://doi.org/10.31788/RJC.2021.1426165

7. *Hassan ZY, Hassan TY, Abu Raghif AR. Evaluation the Effect of Phytosterol Fraction of Chenopodium murale in Comparison with Tacrolimus on Mice Induced Atopic Dermatitis. Iraqi J Pharm Sci, Vol.32(1) 2023.* https://doi.org/10.31351/vol32iss1pp84-91

8. *Batcha O, Gnatoulma K, Gérard T, Laura L, Efui G, Manuel R, et al. Anti-inflammatory, antibacterial and antioxidant activities of Chenopodium ambrosioides L. (Chenopodiaceae) extracts 2021;162: 16764 - 16794.* https://doi.org/10.35759/JABs.162.7

9. *El-Newary SA, Abd Elkarim AS, Abdelwahed NAM, Omer EA, Elgamal AM, ELsayed WM. Chenopodium murale Juice Shows Anti-Fungal Efficacy in Experimental Oral Candidiasis in Immunosuppressed Rats in Relation to Its Chemical Profile. Molecules. 2023 May 24;28(11):4304.* https://doi.org/10.3390/molecules28114304

10. *Ahmed Z, Uddin Z, Shah S, Zahoor M, Alotaibi A, Shoaib M, et al. Antioxidant, antidiabetic, and anticholinesterase potential of Chenopodium murale L. extracts using in vitro and in vivo approaches. Open Chemistry. 2022;20(1): 1171-1186.* https://doi.org/10.1515/chem-2022-0232

11. *Akgül H, Korkmaz N, Dayangaç A, Sevindik M. Antioxidant Potential of Endemic Salvia absconditiflora. Turkish Journal of Agriculture - Food Science and Technology, 2020;8(10): 2222-2224.* https://doi.org/10.24925/turjaf.v8i10.2222-2224.3697

12. *Asgarpanah J. A review on the essential oil chemical profile of Salvia genus from Iran. Nat. Volatiles and Essent. Oils, 2021; 8(3): 1-28* https://doi.org/10.37929/nveo.852794

13. *Esmaeili G, Fatemi H, Baghani avval M, Azizi M, Arouiee H, Vaezi J, et al. Diversity of Chemical Composition and Morphological Traits of Eight Iranian Wild Salvia Species during the First Step of Domestication. Agronomy. 2022; 12(10):2455.* https://doi.org/10.3390/agronomy12102455

14. *Sunar S, Korkmaz M, Sığmaz B, Ağar G. Determination of the Genetic Relationships Among Salvia Species by RAPD and ISSR Analyses. Turk J Pharm Sci. 2020;17(5):480-485.* https://doi.org/10.4274/tjps.galenos.2018.24572

15. *Al-Hussaini A, Al-Mousawi AH, Al-Musawi AHE. The ecology and geographical distribution for the species of the genus Salvia L. of labiatae in Iraq. Baghdad Sci. J., 2013; 10 (4), 1082-1087.* https://doi.org/10.21123/bsj.2013.10.4.1082-1087

16. *Hassan ZY, Hassan TY, Abu Raghif AR. Evaluation the Effectiveness of Phenolic Compound of Salvia frigida on Induced Atopic Dermatitis in Experimental Mice. Iraqi J Pharm Sci, Vol.31(1) 2022.* https://doi.org/10.31351/vol31iss1pp154-166

17. *TrivellatoGrassi L, Malheiros A, Meyre-Silva C, Buss Z, Monguilhott ED, Fröde TS, et al. From popular use to pharmacological validation: A study of the anti-inflammatory, anti-nociceptive and healing effects of Chenopodium ambrosioides extract, Journal of Ethnopharmacology 2013;145(1):127-138.* https://doi.org/10.1016/j.jep.2012.10.040

18. *Harborne, J.B. Textbook of Phytochemical Methods. A Guide to Modern Techniques of Plant Analysis. 5th Edition, Chapman and Hall Ltd, London, 1998;21-72.* https://link.springer.com/book/10.1007/978-94-009-5570-7

19. *Mohammed NJ, Wisam A. Ameen W A. The effect of topical finasteride in treatment of idiopathic hirsutism. AJBM 2015; 3(9):552 – 566.* https://doi.org/10.18081/2333-5106/015-09/552-566

20. *Han JS, Won KH, Chang SE, Kim JE. Tacrolimus 0.1% ointment in the treatment of allergic contact dermatitis: a new approach. Int J Dermatol, 2014;53: e470-e471.* https://doi.org/10.1111/ijd.12641

21. *Kim H, Kim JR, Kang H, Choi J, Yang H, Lee P, et al. 7,8,49-Trihydroxyisoflavone Attenuates DNCB-Induced Atopic Dermatitis-Like Symptoms in NC/Nga Mice. PLoS ONE 2014;9(8):e104938.* https://doi.org/10.1371/journal.pone.0104938

22. *Tungmunnithum D, Thongboonyou A, Pholboon A, Yangsabai A. Flavonoids and other Phenolic Compounds from Medicinal Plants for Pharmaceutical and Medical Aspects: An Overview. Medicines. 2018; 5(3):93.* https://doi.org/10.3390/medicines5030093

*23. Ghasemzadeh A, Ghasemzadeh N. Flavonoids and phenolic acids: role and biochemical activity in plants and human. J. Med. Plants Res., 2011; 5 (31P): 6697-6703. https://doi.org/10.5897/JMPR11.1404*

*24. Roberts MD, Young KC, Fox CD, Vann CG, Roberson PA, Osburn SC, et al. An optimized procedure for isolation of rodent and human skeletal muscle sarcoplasmic and myofibrillar proteins. J Biol Methods. 2020; 7(1): e127. https://doi.org/10.14440/jbm.2020.307*

*25. Drislane C, Irvine AD. The role of filaggrin in atopic dermatitis and allergic disease. Ann Allergy Asthma Immunol. 2020 Jan;124(1):36-43. https://doi.org/10.1016/j.anai.2019.10.008.*

*26. Birdi G, Cooke R, Knibb RC. Impact of atopic dermatitis on quality of life in adults: a systematic review and meta-analysis. Int J Dermatol. 2020;59(4):e75-e91. https://doi.org/10.1111/ijd.14763*

*27. Liu Y, Zienkiewicz J, Qiao H, Gibson-Corley KN, Boyd KL, Veach RA, et al. Genomic control of inflammation in experimental atopic dermatitis. Sci Rep 2022;12,18891. https://doi.org/10.1038/s41598-022-23042-x.*

*28. Celakovská J, Bukac J, Ettler K, Vaneckova J, Krcmova I, Ettlerova K, et al. Evaluation of Peripheral Blood Eosinophilia in Adolescent and Adult Patients Suffering from Atopic Dermatitis and the Relation to the Occurrence of Allergy to Aeroallergens. Indian J Dermatol. 2019; 64(1):34-40. https://doi.org/10.4103/ijd.IJD_509_17.*

*29. Simon D, Von Gunten S, Borelli S, Braathen LR, Simon HU. The interleukin-13 production by peripheral blood T cells from atopic dermatitis patients does not require CD2 costimulation. Int Arch Allergy Immunol. 2003; 132(2):148-55. https://doi.org/10.1159/000073716*

*30. Ju Ho P, Jun Sung J, Ki Cheon K, Jin Tae H. Anti-inflammatory effect of Centella asiatica phytosome in a mouse model of phthalic anhydride-induced atopic dermatitis. Phytomedicine. 2018; 43:110-119. https://doi.org/10.1016/j.phymed.2018.04.013.*

*31. Gil TY, Kang YM, Eom YJ, Hong CH, An HJ. Anti-Atopic Dermatitis Effect of Seaweed Fulvescens Extract via Inhibiting the STAT1 Pathway. Mediators Inflamm. 2019; 20193760934. https://doi.org/10.1155/2019/3760934.*

*32. He D, Wang S, Fang G, Zhu Q, Wu J, Jianling Li, et al. LXRs/ABCA1 activation contribute to the anti-inflammatory role of phytosterols on LPS-induced acute lung injury. Journal of Functional Foods. 2022; 89:104966. https://doi.org/10.1016/j.jff.2022.104966*

*33. Cardona ID, Cho SH, Leung DY. Role of bacterial superantigens in atopic dermatitis: implications for future therapeutic strategies. Am J Clin Dermatol. 2006;7(5):273-9. https://doi.org/10.2165/00128071-200607050-00001*

*34. Flohr C, Pascoe D, Williams HC. Atopic dermatitis and the 'hygiene hypothesis': too clean to be true? Br J Dermatol. 2005;152(2):202-16. https://doi.prg/10.1111/j.1365-2133.2004.06436.x.*

*35. Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ. Fitzpatrick's Dermatology in General Medicine. 7th Edition. Vol. 1, United States: The McGraw-Hill Companies. 2008. https://doi.org/10.1111/j.1524-4725.2008.34211.x*

*36. Awad AB, Chinnam M, Fink CS, Bradford PG. beta-Sitosterol activates Fas signaling in human breast cancer cells. Phytomedicine. 2007 Nov;14(11):747-54. https://doi.org/10.1016/j.phymed.2007.01.003*

*37. Askari SF, Avan R, Tayarani-Najaran Z, Sahebkar A, Eghbali S. Iranian Salvia species: A phytochemical and pharmacological update. Phytochemistry. 2021 Mar;183:112619. **doi**: 10.1016/j.phytochem.2020.112619.*

*38. Gad HA, Mamadalieva RZ, Khalil N, Zengin G, Najar B, Khojimatov OK, et al. GC-MS Chemical Profiling, Biological Investigation of Three Salvia Species Growing in Uzbekistan. Molecules. 2022; 27(17):5365. https://doi.org/10.3390/molecules27175365*

*39. Al-Dabbagh MA, Shihab SA, Kadhim EJ. Effects Of Phenolic Compounds Extracted from Salvia frigida On Induced Hyperuricemia In Mice. Asian J Pharm Clin Res, 2019;12(4):211-217. http://dx.doi.org/10.22159/ajpcr.2019.v12i4.32096*

*40. Alwan NK, Shakir SA, Waheeb HH. Epidemiology of Skin Diseases among Displaced People in Diyala Province. JFacMedBagdad. 2018; 60(1):52-6. https://doi.org/10.32007/jfacmedbagdad.60145*

*41. Mustafa Thamer S, Q. Yahya M. The Effect of Lenalidomide Ointment on TNF-α Tissue Levels in Mice with Imiquimod-Induced Psoriasis. JFacMedBagdad. 2023;64(4):252-60. https://doi.org/10.32007/jfacmedbagdad.6441959*

*42. Kamatou GP, van Zyl R, Van vuuren S, Viljoen A, Figueiredo A, Barroso J, et al. Chemical Composition, Leaf Trichome Types and Biological Activities of the Essential Oils of Four Related Salvia Species Indigenous to Southern Africa. Journal of Essential Oil Research. 2006;18. 72-79. https://doi.org/10.1080/10412905.2006.12067125.*

*43. Kamatou GP, Viljoen A, Steenkamp PA. (2010). Antioxidant, anti-inflammatory activities and HPLC analysis of South African Salvia species. Planta Medica. 2010;76. https://doi.org/10.1055/s-0030-1264458*

*44. Raal A, Orav A, Arak E. Composition of the essential oil of Salvia officinalis L. from various European countries. Natural product research. 2007;21(5):406-11. https://doi.org/10.1080/14786410500528478*

*45. Altun M, Ünal M, Kocagöz T, Gören AC. Essential Oil Compositions and Antimicrobial Activity of Salvia Species. Journal of essential oil-bearing plants, 2007;10 (3): 251 -258. https://doi.org/10.1080/0972060X.2007.10643550*

*46. Kürşat M, Erecevit P, Sarı A, Emre İ, Kırbağ S, Civelek Ş. The Antimicrobial Activities of Seed Fatty Acid Extracts from Some Salvia L. Species. Turkish Journal of Science and Technology, 2012;7(1):31-36. https://www.researchgate.net/publication/290606992*
*47. Dai J, Mumper RJ. Plant phenolics: extraction, analysis and their antioxidant and anticancer properties. Molecules. 2010;15(10):7313-52. https://doi.org/10.3390/molecules15107313*
*48. Oettgen HC. Fifty years later: Emerging functions of IgE antibodies in host defense, immune regulation, and allergic diseases. J Allergy Clin Immunol. 2016 Jun;137(6):1631-1645. https://doi.org/10.1016/j.jaci.2016.04.009*

***How to Cite this Article***
*Hassan ZY, Hassan TY, Kanany AY. The Anti-Inflammatory Effect of Chenopodium Murale in Comparison to Salvia Frigida on Atopic Eczema. J Fac Med Baghdad. 2024;66(4).*
*Available from:*
*https://iqjmc.uobaghdad.edu.iq/index.php/19JFacMedBaghdad36/article/view/2371*

# التأثير المضاد للإلتهاب لنبات العفينة بالمقارنة مع نبات القصعين برودي في علاج الأكزيما التأتبية لدى الفئران

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**الخلاصة**

**الخلفية:** إلتهاب الجلد التأتبي هو حالة جلدية مزمنة شائعة ذات طبيعة إلتهابية ولها ميل وراثي. يصيب حوالي 10%-20% من الأطفال و1%-3% من البالغين في جميع أنحاء العالم. لقد ثبت سريريا أن نبات العفينة فعال في علاج العديد من الحالات الطبية مثل التهاب الجلد التأتبي بسبب إمكانية تطبيقه وفعاليته. كما أن لنبات القصعين برودي تأثيرا مضادا للإلتهابات بين مجموعة مرضى إلتهاب الجلد التأتبي الذين عولجوا بمركبات الفينول.

**الهدف:** تحديد التأثير المضاد للإلتهابات لنبات العفينة بالمقارنة مع نبات القصعين برودي في علاج الأكزيما التأتبية لدى الفئران.

**المنهجية:** أجريت هذه الدراسة في الفترة من كانون الأول 2020 إلى حزيران 2021 في قسم الصيدلة-كلية الطب-جامعة النهرين. تم تضمين خمسين عينة من الفئران في الدراسة، وتم تقسيمهم إلى خمس مجموعات فرعية بالتساوي ]الضابطة، المحفزة بدون علاج، تاكروليموس-1%، فيتوستيرول-3%، وفينوليك-5%[. تم قياس المعايير البيولوجية والنسيجية باستخدام إختبار تي المستقل (أو تحليل التباين الأحادي ANOVA) لتقدير متوسط الفروقات.

**النتائج:** أظهرت مجموعة التاكروليموس-1% إنخفاضا ملحوظا في عدد خلايا الدم البيضاء والغلوبيولين المناعي-إي والخلايا الإلتهابية مقارنة بالمجموعات الأخرى، وإنخفاضا أكبر في متوسط سمك البشرة مقارنة بمجموعة فيتوستيرول-3%، وانخفاضا أكبر في الإنترلوكين-13 والتآكل مقارنة بمجموعة الفينول5 ٪. كما أظهرت مجموعة فيتوستيرول-3% إنخفاضا أكبر في متوسطات نظير التقرن والتآكل ودرجة شدة الملاحظة مقارنة بالمجموعات الأخرى. كما أظهرت مجموعة الفينول -5% إنخفاضا أكثر في متوسط سماكة البشرة مقارنة بالمجموعات الأخرى وإنخفاضا أكثر في درجة شدة الملاحظة من مجموعة التاكروليموس-1٪.

**الإستنتاج:** كانت التطبيقات الموضعية لجزيئات الفيتوستيرول من نبات العفينة أو مركبات الفينول من نبات القصعين برودي فعالة وواعدة في علاج إلتهاب الجلد التأتبي. في حين أن المركب الفينولي لنبات القصعين برودي فعال، إلا أن تأثيره أقل قليلا من تأثير جزيئات الفيتوستيرول من نبات العفينة.

**الكلمات المفتاحية:** جزيئات الفيتوستيرول، نبات العفينة، التهاب الجلد التأتبي، مركب الفينول، نبات القصعين برودي، تاكروليموس