Original Article

Potential Therapeutic Role of Aescin in a Model of Psoriasis in Male Rats

Rafal Wadhah Taher, Ghaith Ali Jasim[1], Basma Talib Al-Sudani[2]

Department of Pharmacology and Toxicology, College of Pharmacy, Mustansiriyah University, [1]Department of Pharmacology and Toxicology, College of Pharmacy, Al-Bayan University, [2]Department of Pharmacology and Toxicology, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq

Abstract

Background: Psoriasis is a complex chronic inflammatory skin condition that is influenced by both genetic and environmental factors. Aescin is a natural mixture from *Aesculus hippocastanum* seeds. It exhibits powerful anti-inflammatory, anti-edematous, anti-oxidant, and vasoprotective properties. **Objective:** The purpose of this study is to examine the potential effects of aescin on psoriasis inflicted on male rats. **Materials and Methods:** Thirty-six apparently healthy male rats were divided into six groups, each group were given different treatment for psoriasis. The duration of study was 24 days (10 days induction period + 14 days of treatment). **Results:** Enzyme-linked immunosorbant assay results showed that the difference among groups was significant ($P < 0.05$) according to *post hoc* test (multiple comparison). Interleukin-1 beta (IL-1β) mean values were lowest in the combination group. Nuclear factor kappa-B (NF-κB) mean values show the lowest reduction in group VI. Malondialdehyde (MDA) values were decreased by the use of all types of treatments in compared with the induction group. The mean values of superoxide dismutase (SOD) were higher in groups III, IV, V, and VI in compared with the induction group. The lowest values of caspase 3 were seen with the use of oral aescin. **Conclusion:** Aescin, either alone or in combination with clobetasol, was found to decrease IL-1β and NF-κB levels. The highest anti-inflammatory effect was observed with the combination of aescin and clobetasol. Aescin were found to increase SOD and decrease MDA levels.

Keywords: Aescin, caspase 3, enzyme-linked immunosorbent assay, interleukin-1 beta, imiquimod, malondialdehyde, nuclear factor kappa-B, psoriasis, rat model, superoxide dismutase

Introduction

Psoriasis is a chronic, multisystem inflammatory condition that mostly affects the skin and joints.[1] Psoriasis has a significant emotional and psychosocial impact on patients that extends beyond the physical aspects of the disease, impacting social functioning and interpersonal interactions.[2] Epidermal hyperplasia, dilated blood vessels, and a leucocyte infiltration are the main characteristic of psoriasis.[3] Psoriasis may be triggered by infection, cold weather, injury to the skin, smoking, and heavy alcohol consumption.[4] Many inflammatory biomarkers increase in psoriasis, including interleukin-1 beta (IL-1β), tumor necrosis factor alpha (TNF-α), interferon alpha, interferon gamma, nuclear factor kappa-B (NF-κB), C-reactive protein, and others.[5,6] Oxidative stress biomarkers also affected by psoriasis,[7] including superoxide dismutase (SOD; a crucial anti-oxidant defense mechanism in the body against oxidative stress) and malondialdehyde (MDA; one of the end products of the cells peroxidation of polyunsaturated fatty acids).[8] Common pathophysiological mechanisms of psoriasis include the resistance of keratinocytes to apoptosis.[9] In this study, psoriasis was induced using imiquimod,[10] a non-nucleoside heterocyclic amine that binds to Toll-like receptors 7 and 8 and acts by enhancing both the

Access this article online

Quick Response Code:

Website: https://journals.lww.com/mjby

DOI: 10.4103/MJBL.MJBL_1559_23

Address for correspondence: Mrs. Rafal Wadhah Taher, Department of Pharmacology and Toxicology, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq.
E-mail: rafelwadah769@yahoo.com,
orcid = http://orcid.org/0000-0001-5153-4094

Submission: 13-Oct-2023 **Accepted:** 05-Dec-2023 **Published:** 30-Apr-2026

How to cite this article: Taher RW, Jasim GA, Al-Sudani BT. Potential therapeutic role of aescin in a model of psoriasis in male rats. Med J Babylon 2026;23:641-7.

innate and adaptive immune systems.[11] This study aims to examine the potential effects of aescin on psoriasis inflicted on male rats. Aescin is a mixture of triterpene saponins.[12] The active component of the mixture, beta aescin, is the chemical form present in the majority of commercially marketed pharmaceuticals.[13] Aescin has been the focus of numerous studies due to its diverse range of pharmacological activities.[14] Due to its strong anti-inflammatory, venotonic, and anti-odematous actions, it is used to treat arthritis, chronic venous insufficiency, edema, hemorrhoids, varicose veins, hematoma, and venous congestion.[15] Its venotonic impact has been demonstrated to be mediated by its ion channel sensitizing activity in the vessel wall, particularly to calcium, which causes a rise in contractility.[16] Additionally, it has been suggested that it increases prostaglandin F2 release, which inhibits the vasodilator effects of histamine and serotonin.[17]

Materials and Methods

Chemicals

Aescin powder was purchased from Arkure Health Care, India. The powder with Carbopol 940, triehanolamine, and propylene glycol was used to prepare aescin gel at the Department of Pharmaceutical Chemistry, College of Pharmacy, Mustansiriyah University.[18] Carbopol 940 was purchased from ASESCHEM, India. Triethanolamine was purchased from Charco, India. Propylene glycol was purchased from Brouwland, Belgium. Imiquimod cream was purchased from MEDA, Sweden. Clobetasol ointment was purchased from GSK, United Kingdom. IL-1β, NF-κB, MDA, SOD, and caspase 3 enzyme-linked immunosorbent assay (ELISA) kits were purchased from MyBioSource, United States.

Methods

The National Center for Drug Control and Research/ Ministry of Health provided 36 male albino rats. They were 12–16 weeks old and weighed between 150 and 200 g. These rats were kept in cages that were properly ventilated and kept at a temperature of 25°C ± 5°C throughout the cycles of natural light and darkness. They also had free access to food and water. The rats were left to acclimatize for 3 days before the beginning of the study. The rats were divided into six groups, with each group containing six rats. Group I served as a control group and received vaseline only. In group II, psoriasis was induced with 120 mg of 5% W/W imiquimod cream for 10 days. Group III received 120 mg of 5% W/W imiquimod cream for 10 days to induce psoriasis then was treated with 0.04 g/kg aescin gel for 14 days. Group IV received 120 mg of 5% W/W imiquimod cream for 10 days then was treated with 0.42 mg/g clobetasol ointment for 14 days. Group V received 120 mg of 5% W/W imiquimod cream for 10 days then was treated with combination of 0.04 g/kg topical aescin and 0.42 mg/g topical clobetasol for 14 days (which were given separately). Group VI received 120 mg of 5% W/W imiquimod cream for 10 days then was treated with 10 mg/kg of oral aescin for 14 days. In all groups, imiqumod and all other treatments were

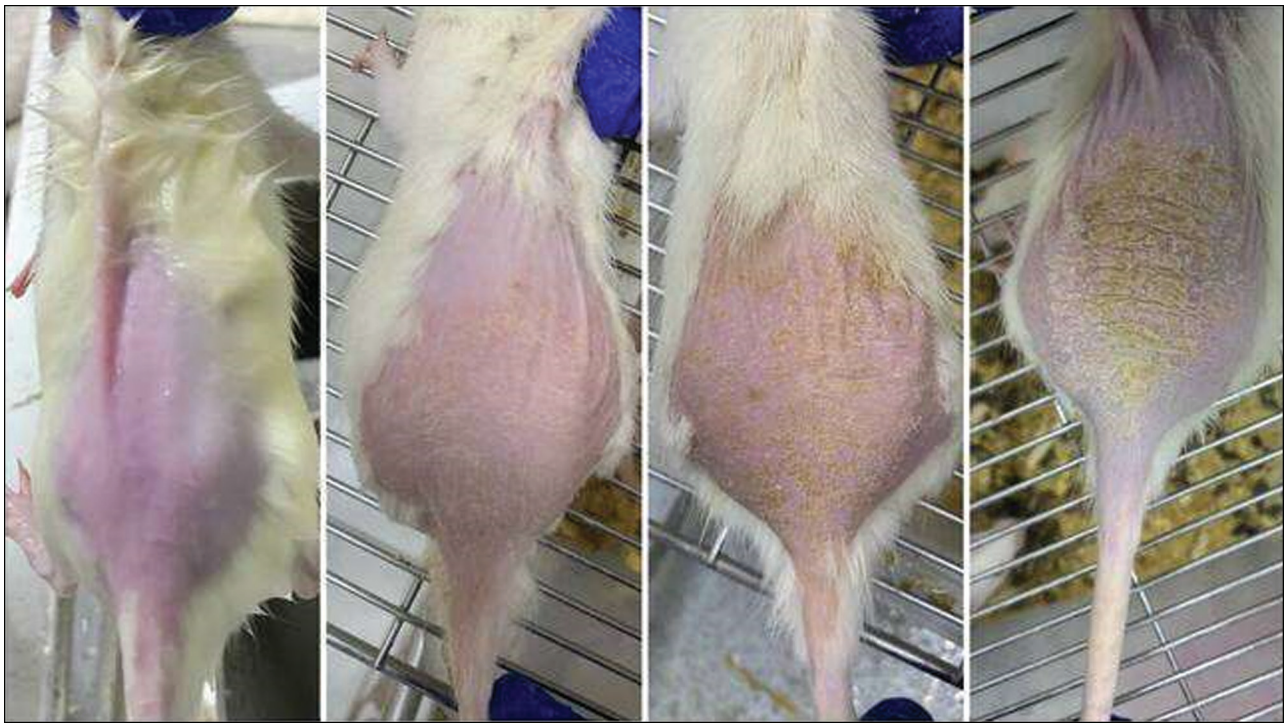

Figure 1: Development of psoriasis after the application of imiquimod during the induction period

applied once daily. At the end of the study, the rats were injected with xylazine and ketamine and were sacrificed. About 1 cm^2 of the skin from the dorsal back was taken [Figures 1 and 2].

Enzyme-linked immunosorbent assay

The effects of aescin on IL-1β, NF-κB, MDA, SOD, and caspase 3 were assessed using rat-specific ELISA kits (IL-1β, NF-κB, MDA, SOD, and caspase 3), respectively, according to MyBioSource manufacturer's guidelines. The procedure began by adding 100 µL of each standard and sample into the appropriate wells. The plate was then covered and left to sit at room temperature for 90 min. The solution was removed, the cover was removed, and the plate was washed twice with a washing buffer solution before being blotted with paper towels. The plate was then incubated at 37°C for 60 min with 100 µL of a detection antibody solution that had been Bioten-labeled. The wells were washed twice with buffer washing solution and then blotted with paper towels. After that, each well received 100 µL of the streptavidin-horse reddish peroxide solution, and the plate was incubated at 37°C for 45 min. The plate was then thoroughly cleaned twice. The plate was then given a second round of washing, the washing buffer was discarded, and the plate was dried with paper towels. The plate was then incubated at 37°C for 30 min in the dark with 100 µL of tetramethylbenzidine substrate solution added to each well. The color then quickly became yellow after the addition of 100 mL of stop solution. Within 30 min of administering the stop solution, the optic density absorbance was measured at 450 nm with a microplate reader.

Statistical analysis

Data were subjected to Shapiro–Wilk test to identify their normality. One way analysis of variance (ANOVA) and least significant difference *post hoc* test were used to assess the significant differences among means.

Ethical approval

This study was approved by the animal ethical committee at Mustansiriyah University, College of Pharmacy (File no.: 13) on December 1, 2022).

Results

Since the study included six groups of rats ANOVA test should be used but since ANOVA is a general test and do not identify which group differ from the other we adopted *post hoc* test (lsg-multiple comparison) to assess the results whether its significant or not. The results showed that means with different letters are significant $P < 0.05$ according to *post hoc* test as shown in Figures 3–7.

Regarding IL-1β, results revealed that the difference among groups was significant. The induction group showed the highest mean of IL-1β (2013.85 pg/mL), while the lower mean values were observed in group I (749 pg/mL), group III (897.48 pg/mL), group IV (721.05 pg/mL), and group VI (715.92 pg/mL). The lowest value was detected in the combination group (697.24 pg/mL) as shown in Figure 3.

Figure 4 shows that the results among rat groups were significant, with the highest mean of NF-κB observed in the induction group (6.36 ng/mL) and the lowest in group VI (oral aescin group) (1.79 ng/mL).

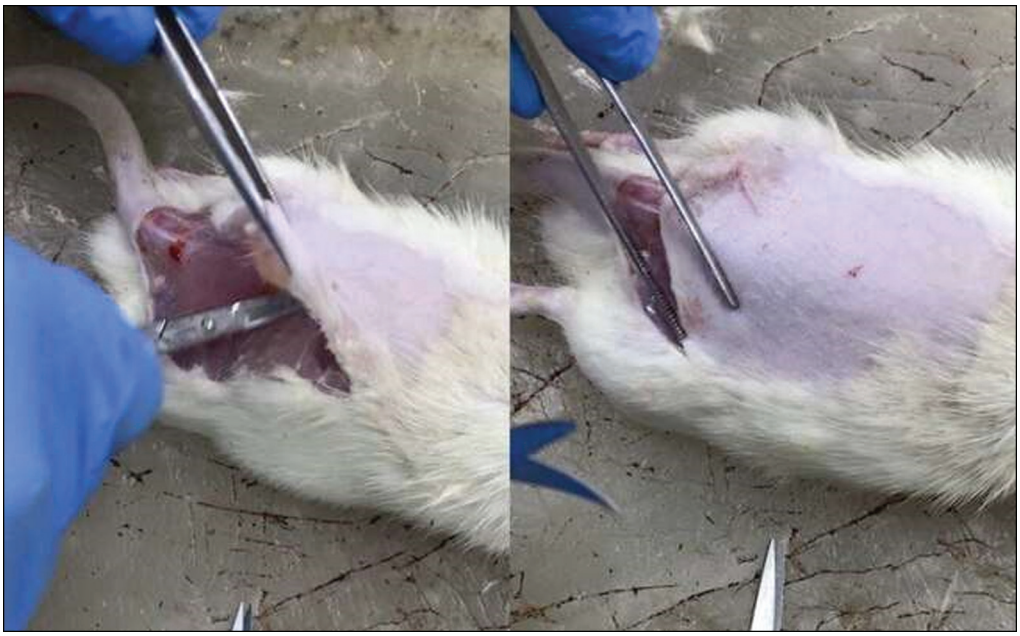

Figure 2: The removal of the dorsal back skin of the rats

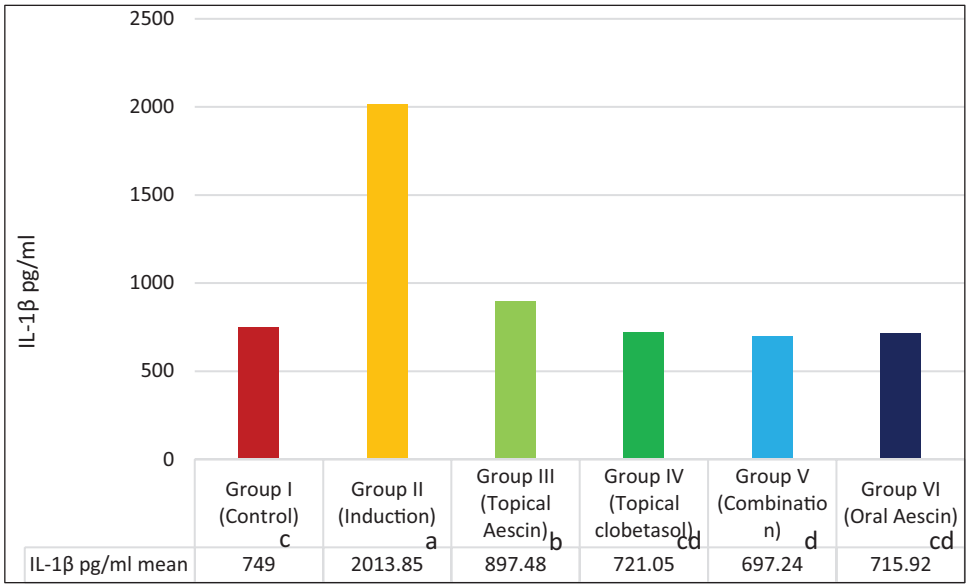

Figure 3: Bar chart of interleukin-1β mean values among different rat groups. Means with different letters are significantly different ($P < 0.05$)

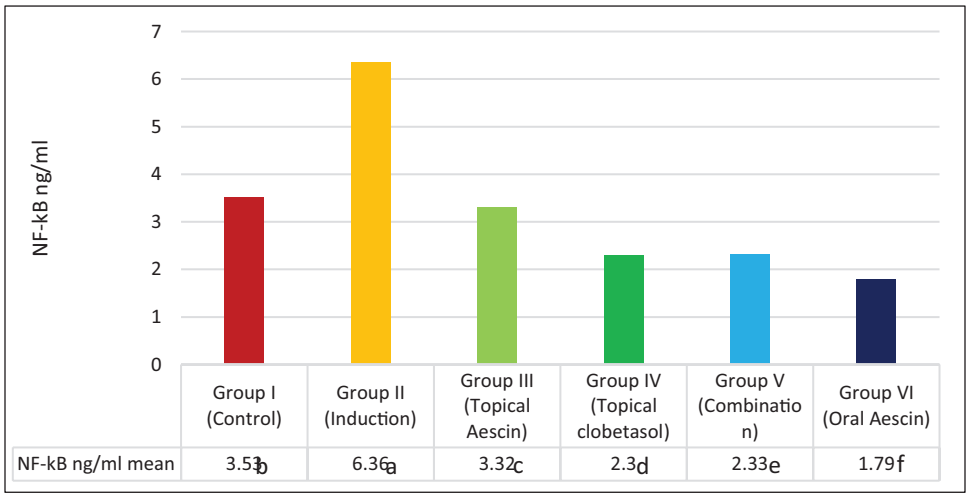

Figure 4: Bar chart of nuclear factor kappa-B mean values among different rat groups. Means with different letters are significantly different ($P < 0.05$)

Figure 5 shows that the results among rat groups were significant, and the means of MDA in groups I, II, III, V, and VI were 4.81, 3.61, 2.99, 2.57, and 3.22 nmol/mL, respectively, with the lowest mean value in group IV (topical clobetasol group) (1.49 nmol/mL).

Figure 6 shows that the results among rat groups were significant, and SOD mean values were 69.09, 111.56, 127.58, 153.47, and 135.02 U/mL for groups I, II, III, IV, and VI, respectively, with the highest mean value (160.38 U/mL) in group V (the combination group).

Figure 7 shows that the results among rat groups were significant, and caspase 3 mean values were 33.53, 26.60, 26.09, 32.28, and 21.54 pmol/L for groups I, II, III, IV, and V, respectively, with the lowest mean value (16.00 pmol/L) in group VI.

Discussion

Psoriasis is a common chronic inflammatory disease, characterized by red, scaly plaques that can affect any part of the skin.[19] It is primarily an immune-mediated illness with hereditary and environmental roots where activation of keratinocytes and immune cells results in the hyper proliferation.[20,21] Regarding IL-1β, the highest reduction was noticed in group V with the use of a combination of topical aescin and clobetasol. Aescin alone was also able to decrease IL-1β significantly in compared with the induction group. NF-κB level was reduced by the use of topical aescin, topical clobetasol, and the combination of topical aescin and clobetasol with the highest reduction noticed in the oral aescin group. These results came in agreement with previous studies that investigated the anti-inflammatory activity of aescin,

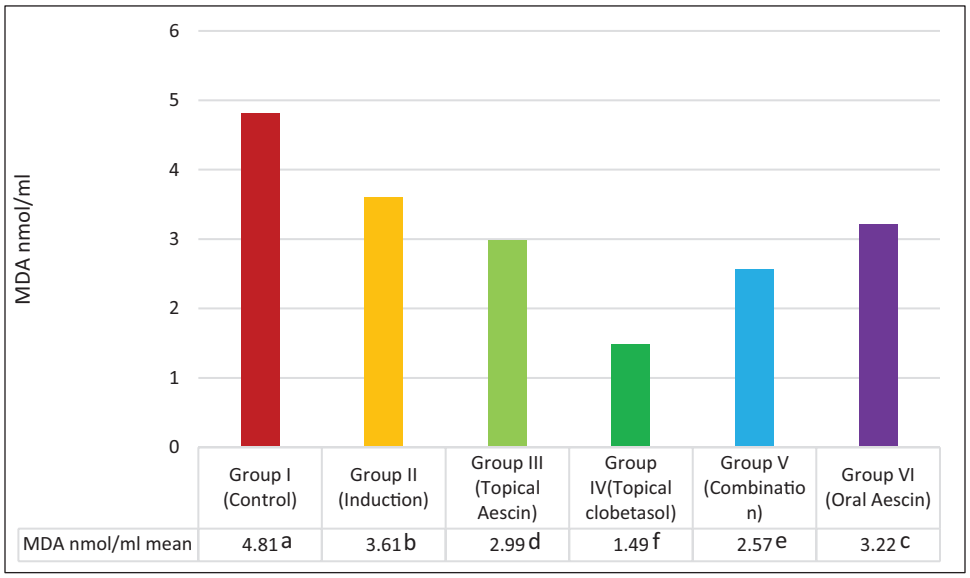

Figure 5: Bar chart of malondialdehyde mean values among different rat groups. Means with different letters are significantly different ($P < 0.05$)

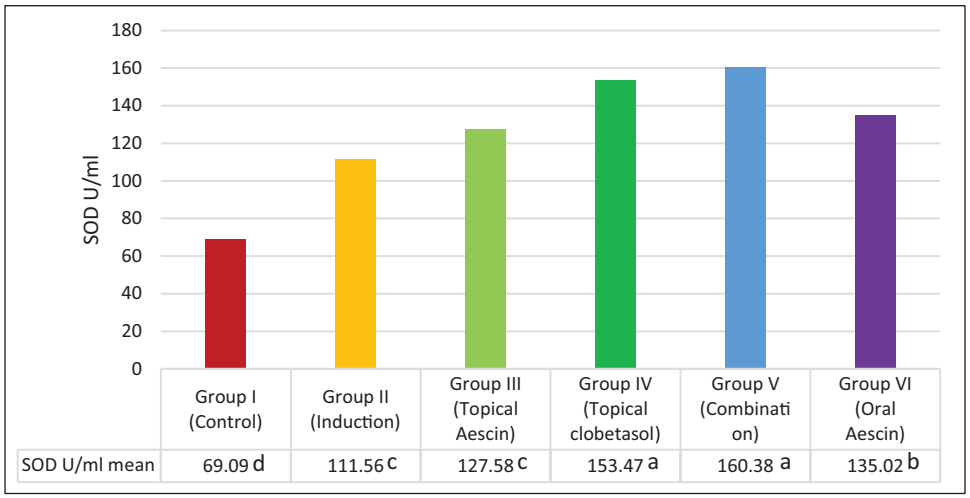

Figure 6: Bar chart of superoxide dismutase mean values among different rat groups. Means with different letters are significantly different ($P < 0.05$)

and concluded that the anti-inflammatory effect of aescin is through the inhibition of the TNF-/NF-B, TNF-/JNK, and IL-22/STAT3 signaling pathways, as well as the reduction of neutrophil, CD4+ T cell, and monocyte infiltration.[22,23] MDA level was decreased with the use of topical aescin, topical clobetasol, the combination of topical aescin and clobetasol, and oral aescin, while SOD level was significantly increased by the use of aescin both topically and orally with the greatest increase was noticed in the combination group. These results came in agreement with previous studies that highlighted the anti-oxidant activity of aescin, including scavenging of free radicals ($OH^{\bullet}$, $O_2^{\bullet -}$), transition metal ion chelation, inhibition of lipid peroxidation, lowering the effects of oxidative stress induced by lipopolysaccharide, decreasing myeloperoxidase, increasing activity of SOD and glutathione peroxidase, decreasing MDA, and decreasing nitric oxide release.[24,25] The development of numerous skin conditions is significantly influenced by dysfunctional apoptosis. Psoriasis characterized by decreased keratinocyte apoptosis.[26,27] The present study showed that aescin reduced the level of caspase 3 which came in agreement with some previous studies that showed that aescin has the potential to significantly reduce the activation of caspase 3 and the release of cytochrome c while raising the expression of Bcl-2.[28,29] However, other previous studies have shown an increase in the activation of caspase 3 with aescin.[30,31] The variation in the outcomes may be due to the various aescin doses that had been utilized in each study and the various conditions that aescin had been administered for. Corticosteroids such as clobetasol are known to decrease inflammatory biomarkers, making them valuable in the treatment of various inflammatory diseases.[32]

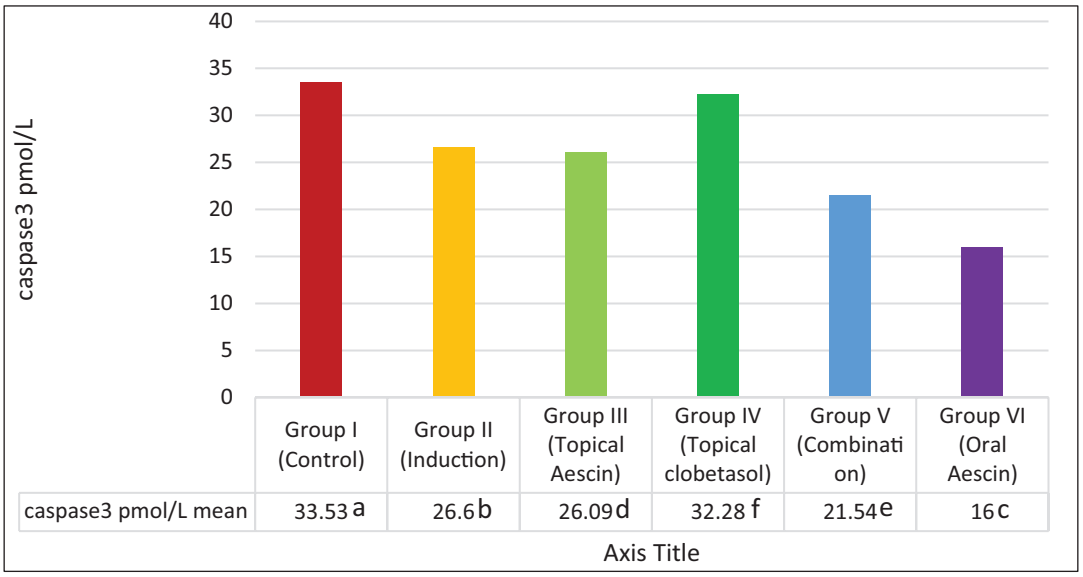

Figure 7: Bar chart of caspase 3 mean values among different rat groups. Means with different letters are significantly different ($P < 0.05$)

Conclusion

Aescin effectiveness in relieving the signs of psoriasis was demonstrated through its anti-inflammatory, venotonic, and anti-oxidant capabilities, which were demonstrated by decreasing IL-1β, NF-κB, and MDA levels while increasing SOD levels. The study found that topical aescin applied directly to the site of a psoriasis lesion, has a greater positive effect in compared with oral aescin which was administered systemically. The study also demonstrated the advantages of combining aescin and clobetasol for treating psoriasis.

Acknowledgments

The authors sincerely thank Mustansiriyah University (www.uomustansiriyah.equ.iq), Baghdad, Iraq, for their support with this work.

Financial support and sponsorship

Nil.

Conflicts of interest

No conflicts of interest to declare.

References

1. Al-Saba AH, Shemran KA, Al-Hattab MK. Study of serum Chitinase-3-like-1 protein (CHI3L1) and C-reactive protein (CRP) in patients suffering from chronic plaque psoriasis. Med J Babylon 2022;19:729-35.
2. Agarwal K, Das A, Das S, De A. Impact of psoriasis on quality of life. Indian J Dermatol 2022;67:387-91.
3. Rendon A, Schäkel K. Psoriasis pathogenesis and treatment. Int J Mol Sci 2019;20:1475.
4. Green A, Shaddick G, Charlton R, Snowball J, Nightingale A, Smith C, *et al*. Modifiable risk factors and the development of psoriatic arthritis in people with psoriasis. Br J Dermatol 2020;182:714-20.
5. Blagov A, Sukhorukov V, Guo S, Zhang D, Eremin I, Orekhov A. The role of oxidative stress in the induction and development of psoriasis. Front Biosci (Landmark Ed) 2023;28:118.
6. Ramessur R, Corbett M, Marshall D, Acencio ML, Barbosa IA, Dand N, *et al*. Biomarkers of disease progression in people with psoriasis: A scoping review. Br J Dermatol 2022;187:481-93.
7. Dobrică EC, Cozma MA, Găman MA, Voiculescu VM, Găman AM. The involvement of oxidative stress in psoriasis: A systematic review. Antioxidants (Basel) 2022;11:282.
8. Yadav MR. Characterization and Comparison of oxidative and inflammatory biomarkers in psoriatic arthritis patients.
9. Chimenti MS, Sunzini F, Fiorucci L, Botti E, Fonti GL, Conigliaro P, *et al*. Potential role of cytochrome c and tryptase in psoriasis and psoriatic arthritis pathogenesis: Focus on resistance to apoptosis and oxidative stress. Front Immunol 2018;9:2363.
10. Jabeen M, Boisgard AS, Danoy A, El Kholti N, Salvi JP, Boulieu R, *et al*. Advanced characterization of imiquimod-induced psoriasis-like mouse model. Pharmaceutics 2020;12:789.
11. Parmar KM, Jagtap CS, Katare NT, Dhobi M, Prasad SK. Development of a psoriatic-like skin inflammation rat model using imiquimod as an inducing agent. Indian J Pharmacol 2021;53:125-31.
12. Geisler R, Prévost S, Dattani R, Hellweg T. Effect of cholesterol and ibuprofen on DMPC-β-Aescin bicelles: A temperature-dependent wide-angle x-ray scattering study. Crystals. 2020;10:401.
13. Khushnuma R, Dakshina G, Anubhav D, Yatendra S. A review on β-ESCIN. Indian J Med Res Pharmac. Sci. 2021;8:10-6.
14. Gözcü S. *Aesculus hippocastanum* L. In: Novel Drug Targets with Traditional Herbal Medicines. Cham: Springer; 2022. p. 23-36.
15. Gallelli L. Escin: A review of its anti-edematous, anti-inflammatory, and venotonic properties. Drug Des Devel Ther 2019;13:3425-37.
16. Moleiro HL, Martin Romero MT, Herraez D, Santiago JA, Caselli N, Dargel C, *et al*. Dual mechanical impact of β-escin on model lipid membranes. bioRxiv 2023;2023:06.
17. Yang Y, Wang L, Yuan M, Yu Q, Fu F. Anti-inflammatory and gastroprotective effects of escin. Nat Prod Commun 2020;15:1934578X2098211.
18. Sailaja AK, Supraja R. An overall review on topical preparation-gel. Innovat Int J Med Pharmac Sci 2016;1:17-22.
19. Camela E, Potestio L, Fabbrocini G, Ruggiero A, Megna M. New frontiers in personalized medicine in psoriasis. Expert Opin Biol Ther 2022;22:1431-3.
20. de Alcantara CC, Reiche EM, Simão AN. Cytokines in psoriasis. Adv Clin Chem 2021;100:171-204.

21. Medovic MV, Jakovljevic VL, Zivkovic VI, Jeremic NS, Jeremic JN, Bolevich SB, *et al*. Psoriasis between autoimmunity and oxidative stress: Changes induced by different therapeutic approaches. Oxid Med Cell Longevity 2022;2022:2249834.
22. Park S, Park JM, Park M, Ko D, Kim S, Seo J, *et al*. β-Escin overcomes trastuzumab resistance in HER2-positive breast cancer by targeting cancer stem-like features. Cancer Cell Int 2022;22:289.
23. Elshal M, Hazem SH. Escin suppresses immune cell infiltration and selectively modulates Nrf2/HO-1, TNF-α/JNK, and IL-22/STAT3 signaling pathways in concanavalin A-induced autoimmune hepatitis in mice. Inflammopharmacology 2022;30:2317-29.
24. Suryavanshi SV, Kulkarni YA. Escin alleviates peripheral neuropathy in streptozotocin induced diabetes in rats. Life Sci 2020;254:117777.
25. Kaliyamoorthi K, Loordhurani A, Subashchandrabose O, Lakshmanan V, Ganapathi S, Sathiavakoo VA. Cardioprotective effect of aescin on antioxidant and lipid profile in isoproterenol-induced myocardial infarction in rats.
26. Xu R, Feng S, Ao Z, Chen Y, Su C, Feng X, *et al*. Long-acting β2 adrenergic receptor agonist ameliorates imiquimod-induced psoriasis-like skin lesion by regulating keratinocyte proliferation and apoptosis. Front Pharmacol 2022;13:865715.
27. Wroński A, Wójcik P. Impact of ROS-dependent lipid metabolism on psoriasis pathophysiology. Int J Mol Sci 2022;23:12137.
28. Ramadoss H, Kathiresan S, Kathiresan S. Anti-proliferative activity of aescin on human oral carcinoma (KB) cells and human laryngeal carcinoma (Hep-2) cells-via cell sensitivity assays. Ann Romanian Soc Cell Biol 2021:3559-73.
29. Zeng M, Zhang R, Yang Q, Guo L, Zhang X, Yu B, *et al*. Pharmacological therapy to cerebral ischemia-reperfusion injury: Focus on saponins. Biomed Pharmacother 2022;155:113696.
30. Li B, Wu GL, Dai W, Wang G, Su HY, Shen XP, *et al*. Aescin-induced reactive oxygen species play a pro-survival role in human cancer cells via ATM/AMPK/ULK1-mediated autophagy. Acta Pharmacol Sin 2018;39:1874-84.
31. Ming ZJ, Hu Y, Qiu YH, Cao L, Zhang XG. Synergistic effects of β-aescin and 5-fluorouracil in human hepatocellular carcinoma SMMC-7721 cells. Phytomedicine 2010;17:575-80.
32. Al-Mosawi RH, Alebadi NAM. Usage of corticosteroids as therapeutic agents in diseases. Med J Babylon 2023;20:447-50.