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Ameliorating effects of topical lornoxicam on acne-like lesions induced by Cutibacterium acnes and testosterone in mice: a randomized controlled animal study

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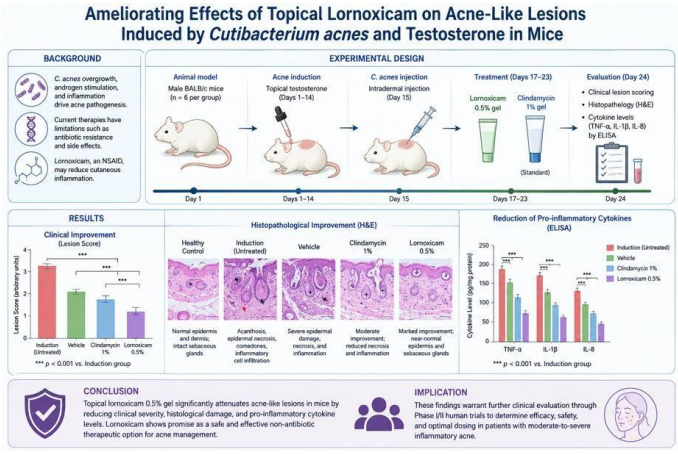
Abstract

Introduction: Alternative therapeutic approaches are required for acne vulgaris, as current treatments, such as antibiotics, are less effective due to antimicrobial resistance and side effects. **Objective:** It was to evaluate the efficacy of lornoxicam gel as a non-antibiotic treatment, an acne mouse model was established using *C. acnes* and testosterone. **Methods:** Thirty untreated male albino BALB/c mice weighing 25-35 grams and aged 6-8 weeks were randomly divided into five groups (n = 6 per group). After a one-week acclimatization period, acne induction was initiated by applying the testosterone solution topically once daily for 14 days. On day 15, C. acnes was injected intradermally into the dorsal skin, while topical testosterone application continued to the end of the experiment. On day 17, Lornoxicam gel (0.5%) was applied once daily for one week. Clindamycin gel was applied to the standard group. H&E staining was used to evaluate histopathological changes, and ELISA was used to measure the levels of inflammatory mediators (TNF-α, IL-1β, and IL-8) in skin homogenates. **Results:** Lornoxicam treatment significantly reduced clinical lesion scores, histological damage, and pro-inflammatory cytokine levels compared with the untreated induction group ($p<0.001$). **Conclusion:** Topical lornoxicam markedly improves acne-like lesions, indicating new therapeutic possibilities for acne management. Further testing is required to determine its clinical significance, including Phase I/II human clinical trials to assess efficacy, safety, and appropriate dose regimens in various patient populations with moderate-to-severe inflammatory acne.

Keywords: Lornoxicam. *Cutibacterium acnes. Acne vulgaris.* Cytokines. TNF-alpha.

Graphical Abstract



Source: Own authorship.

Introduction

Acne vulgaris is the most common chronic inflammatory dermatosis; approximately 85% of adolescents and young adults aged 12–25 years are affected, with a global prevalence estimated at ~9.4% [1]. Clinically, it is a heterogeneous disorder characterized by comedones, papules, pustules, nodules, and cysts, mainly involving the face, neck,

chest, and back [2]. The significance of acne lesions is no longer just cutaneous, as it clearly confers a considerable psychological morbidity with associations to low self-esteem, anxiety, depression, and social withdrawal, underscoring its importance as a major public health concern [3]. *Acne vulgaris* is a heterogeneous disease with several interlinked mechanisms, including androgen-mediated sebaceous hyperactivity, follicular hyperkeratinization, dysbiosis of the cutaneous microbiota (especially Cutibacterium acnes), and activation of the innate immune inflammatory pathway [4].

A significant component of the skin microbiome, *C. acnes* is a Gram-positive, anaerobic, lipophilic bacterium that contributes to cutaneous homeostasis under physiological circumstance, C. acnes transforms into an opportunistic pathogen in pilosebaceous units in acne-prone skin [5]. Bacterial lipases, which hydrolyze sebum triglycerides into free fatty acids and glycerol, contribute to this transformation by obstructing follicles and amplifying inflammation [6]. Tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-8 (IL-8) are among the pro-inflammatory cytokines that are produced when C. acnes activates Toll-like receptor 2 (TLR-2) on keratinocytes and sebocytes [7]. Acne pathophysiology is driven by androgens, particularly testosterone and its powerful 5α-reduced metabolite, dihydrotestosterone (DHT), which promote lipid synthesis and sebaceous gland growth [8].

Seborrhea and follicular occlusion are believed to be stimulated by androgen receptor activation in sebocytes, which also creates a lipid-rich milieu that promotes C. acnes growth and inflammation [9]. Therefore, androgenic stimulation is a major endocrinological cause of acne, particularly in hyperandrogenic diseases and throughout puberty [10]. Retinoids, anti-inflammatory medications, and antibiotic therapies are among current therapeutic approaches with drawbacks, including antibiotic resistance in 40–60% of cases and retinoid-induced irritation that are requires careful monitoring [11].

Such challenges mandate novel, safe alternatives capable of controlling inflammation. Lornoxicam is an oxicam-class nonsteroidal anti-inflammatory drug (NSAID) that reduces prostaglandin-mediated inflammation by potent inhibition of cyclooxygenase-1 and cyclooxygenase-2 (COX-1/COX-2) enzymes [12]. Beyond its well-established systemic anti-inflammatory and analgesic effects, lornoxicam may represent a promising new therapeutic approach for *Acne vulgaris* by modulating local inflammatory pathways. In a murine model of *Acne vulgaris* caused by *Cutibacterium acnes* and testosterone, this study examined the potential of topical lornoxicam 0.5% as a novel therapeutic and anti-inflammatory agent.

Materials and Methods

This research is a randomized, prospective, controlled animal study approved by the Institutional Review Board (IRB) of the College of Medicine at Al-Nahrain University. The ethical code for this study is as follows (IRB/111, No.: 20250924) dated 2 February 2026.

Chemicals and Reagents

Lornoxicam pure powder (purity 99.035%, Lot No. C15115777) and testosterone propionate (purity 99.537%, CAS No. 57-85-2) were acquired from Shanghai Macklin Biochemical Technology Co., Ltd. (Shanghai, China); clindamycin hydrochloride gel 1% was sourced from Medpharma (UAE); all other chemicals and solvents utilized for gel formulation and solution were of analytical grade.

Bacterial Strain and Cultivation Conditions

The reference strain of Cutibacterium acnes (previously Propionibacterium acnes; ATCC 6919) was acquired from Hangzhou Hyper Chemicals Limited in Hangzhou, China. The strain was cultivated anaerobically at 37 °C for 48 hours in Brain Heart Infusion (BHI) broth utilizing a GasPak anaerobic apparatus. After incubation, bacterial cells in the logarithmic growth phase were collected, and the inoculum concentration was calibrated to a turbidity of 0.5 McFarland's standard (1×10^8 CFU/mL) [13].

Animals

A total of 30 untreated male albino BALB/c mice, weighing 25-35 g and aged 6-8 weeks, were randomly assigned to five groups (n = 6 per group) and housed in experimental cages with wood-chip bedding, which was changed biweekly. They were granted complimentary access to sustenance and hydration. The animal housing facility of the College of Medicine, Al-Nahrain University, is provided with a 12-hour light-dark cycle, adequate ventilation, a relative humidity of 50–60%, and a temperature of 23±2 °C. Prior to the initiation of the trial, mice were allotted one week to acclimatize to their new surroundings. All procedures adhered to the ARRIVE standards 2.0.

Experimental Design

Group I (healthy control, induced but untreated), Group II (acne model, induction without intervention), Group III (vehicle control, gel base only), Group IV (standard treatment, topical clindamycin), and Group V (lornoxicam gel 0.5%).

Induction of Acne-Like Lesions

Hair Removal and Skin Maintenance

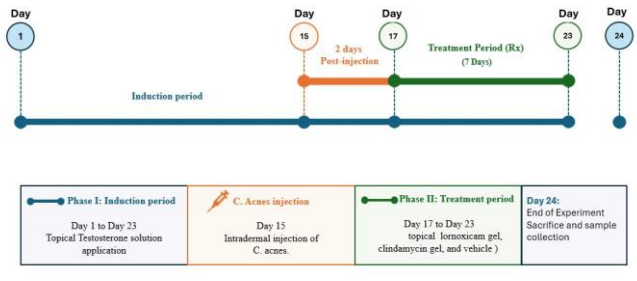
Dorsal hair was first removed with an electric clipper, and then a depilatory cream was applied to the dorsal hair **[14]**. During the investigation, shaving was only performed twice since testosterone therapy massively suppressed any future hair growth. This finding is in agreement with published reports that testosterone retards the hair follicle cycle and prolongs the anagen phase in mice **[15]**. The less frequent shavings also decreased skin irritation and prevented perplexing inflammatory reactions.

Testosterone Preparation and Application

Testosterone propionate was dissolved in a mixture of ethanol and olive oil. The final solution, 2% (w/v), was applied topically once daily for 23 consecutive days to the shaved dorsal skin to increase the sebaceous gland activity and prepare the skin for bacterial inoculation **[16]**. *Cutibacterium acnes* inoculation Day 15: Intradermal injection of *C. acnes* suspension (1×10^8 CFU/mL, 50 µL) into the dorsal skin using a meso needle (31-gauge; 4 mm).

Drug Treatment

Lornoxicam gel (0.5% w/w) was prepared using Carbopol 940 as the gelling agent. In the presence of a magnetic stirrer, Carbopol 940 (1% w/w) was gradually added to distilled water, which was then hydrated overnight at room temperature. For a co-solvent and penetration booster, propylene glycol at 20% w/w was also added. Lornoxicam and methylparaben (0.2% w/w) were then added to the hydrated Carbopol dispersion gradually under constant stirring after dissolution in propylene glycol. The pH of the formulation was adjusted to 5.5–6.0 with triethanolamine, yielding a clear, uniform-composition gel as the final product. The weight was calibrated using distilled water, and the jelly was stored in amber vials at 4 °C for later use **[17]**. The selected dorsal region was treated topically once daily for 7 days after acne induction, as shown in Figure 1. Figure 1. Experimental timeline for acne-like lesion induction and treatment. Source: Own



Source: Own authorship.

Clinical Evaluation

Clinical severity was evaluated using a modified Draize-based semi-qualitative rating system. On a scale of 0 to 4, an impartial, double-blind observer assessed erythema, edema, and the formation of papules/plaques as shown in Table 1. The sum of the scores for each criterion was used to calculate the overall clinical score (maximum score = 12).

Table 1. A semi-quantitative scoring system was developed based on the Draize method for the evaluation of acne-like lesions **[18]**.

score	Erythema	Edema	Lesion formation
0	No redness	No edema	No visible lesions
1	Slight redness	Very Slight edema	Minimal lesions
2	Well-defined redness	Slight edema	Mild lesions
3	Moderate to severe redness	Moderate edema	Moderate lesions
4	Severe redness	Severe edema	Sever lesions

Source: Own authorship.

Sample collection

A ketamine-xylazine mixture comprising a 10% ketamine solution (100 mg/mL; Atlas) and a 2% xylazine solution (20 mg/mL; Interchemie, Holland) was injected intraperitoneally to induce anesthesia. The dosages were 10 mg/kg of xylazine and 100 mg/kg of ketamine. Each animal's body weight was used to calculate the required volume. Euthanasia was carried out by cervical dislocation after adequate anesthetic depth was confirmed. A disposable, sterile punch biopsy tool was used to obtain 4-mm skin biopsies from the dorsal surface. For histopathological analysis, tissue samples were quickly preserved in 10% neutral-buffered formalin. For biochemical studies, samples were placed in sterile cryotubes, frozen for 24 hours at -80°C, and then processed.

Preparation of tissue homogenate

Samples of frozen skin tissue were thawed, carefully weighed, and put into homogenization tubes with one milliliter of ice-cold homogenization buffer. To prevent enzymatic protein degradation, the buffer consisted of phosphate-buffered saline (PBS) supplemented with 1% Triton X-100 and a protease inhibitor cocktail (cOmpleteTM, Mini, EDTA-free, Roche, Germany). A bead mill homogenizer (Precellys® 24, Bertin Technologies, France) with 2.8 mm ceramic beads was used to mechanically rupture tissue. To avoid heat denaturation, the samples are homogenized at 6,000 rpm for three cycles and 20 seconds each, with ice between cycles. After that, the crude homogenates were centrifuged in a chilled

centrifuge at 12,000 × g for 10 minutes at 4 °C. The translucent supernatant was swiftly used for subsequent ELISA experiments after being meticulously collected and aliquoted **[19]**.

Histopathological Examination

Skin samples from the induction sites were collected and preserved in 10% neutral buffered formalin for 24 hours. The specimens underwent conventional paraffin embedding, and 5-µm-thick sections were cut and stained with hematoxylin and eosin (H&E) for light-microscopy analysis. Two blinded pathologists evaluated histology, focusing on alterations in the epidermis, inflammation, depletion of pilosebaceous structures, vascular congestion, edema, and A semi-quantitative grading system, spanning from 0 to 3, was employed as shown in Table 2 **[20,21]**.

Table 2. A semi-quantitative scoring system.

score	Congestion	Severity leukocyte infiltration	Gland change	Acanthosis
0	No congestion	No leukocyte infiltration	No gland change	Normal epidermal thickness (no acanthosis)
1	Mild congestion	Few leukocyte infiltrations	Few white and blackhead comedones	Mild epidermal hyperplasia
2	Moderate congestion	Moderate leukocyte infiltration	Moderate white and blackhead comedones	Moderate epidermal hyperplasia
3	Severe congestion	Plenty of leukocyte infiltration	plenty white and blackhead comedones	Severe epidermal hyperplasia with marked thickening of the epidermis

Source: Own authorship.

Analysis of Cytokines

The concentrations of IL-1β (ELK Biotechnology, USA) (ELK1271MS), IL-8 (ANTIBODIES ONLINE, USA) (ABIN6968034), and TNF-α (ELK Biotechnology, USA) (ELK1387) in the homogenate were quantified utilizing enzyme-linked immunosorbent assay (ELISA) kits in accordance with the manufacturers' protocols.

Statistical analysis

Cytokine values are presented as mean ± standard deviation (SD). In instances where the assumption of homogeneity of variances was violated, statistical significance was assessed utilizing Welch's one-way analysis of variance (ANOVA) and Dunnett's T3 post hoc test for multiple comparisons. Visual and histological scores (nonparametric data) were reported as median and interquartile range (IQR); group differences were assessed using the Kruskal-Wallis test, followed by Dunn's multiple comparisons post hoc test. All statistical analyses were conducted utilizing GraphPad Prism version 11.0.0 (84). Statistical significance was established at a p-value < 0.05.

Results

Visual Evaluation of Cutaneous Lesions

The intensity of acneiform skin lesions was evaluated with the modified Draize score, with a maximum attainable score of 12. Control group scores had a median of 0.0 and an IQR of 0.0. The median scores for the induction and vehicle groups were 9 (IQR 10–8) and 8 (IQR 9–7), respectively. Compared with the induction and vehicle groups, the median score in the lornoxicam 0.5% gel group was 1 (IQR = 2–1; $p < 0.05$), as illustrated in Table 3. This statistical improvement and lesion clearance were visually confirmed by macroscopic evaluation, as illustrated in Figure 2.

Table 3. Median (IQR) Draize scores for each experimental group.

Groups	Modified Draize score Median (IQR)
Healthy control	0.0(0.0) ****
induction	9 (10-8)
vehicle	8 (9-7) ns
standard	1 (2-1) *
Lornoxicam 0.5%	1 (2-1) *
Healthy control	0.0(0.0) ****

Source: Own authorship.

All comparisons were conducted with the model (induction) group. *, **, ***, and **** denote significant differences at $p < 0.05$, $P < 0.01$, $p < 0.001$, and $p < 0.0001$, respectively. ns: not statistically significant; IQR = Interquartile Range; IQR (Q3-Q1); Q3 (75th percentile); Q1 (25th percentile).

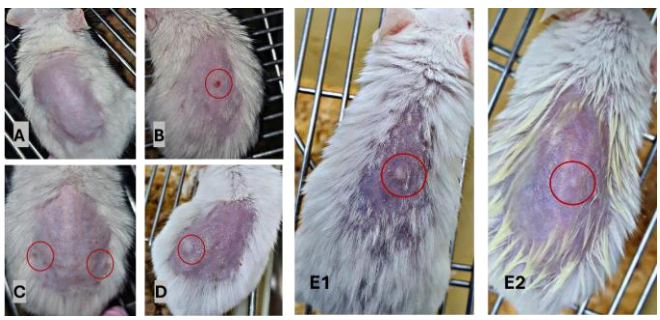


Figure 2. Macroscopic pictures of the dorsal skin of mice from several experimental groups: (A) Control, (B) Induction, (C) Standard, (D) Vehicle. Pictures were captured on day 24 (end of experiment). (E1) before application of 0.5% lornoxicam, (E2) after application of 0.5% lornoxicam. Source: Own authorship.

Histopathological Findings

The histological evaluation of skin specimens verifies the disease development indicators during the procurement period and the subsequent therapeutic efficacy of Lornoxicam as shown in Table 4.

Table 4. Semi-quantitative scoring system

Groups	Congestion Median (IQR)	Leukocyte Median (IQR)	Gland change median (IQR)	Acanthosis Median (IQR)
Healthy control	0 (0-0) ***	0 (0-0) **	0 (0-0) **	0 (0-0) **
Model (induction)	3 (3-2)	3 (3-2)	2 (3-2)	3 (3-2)
vehicle	2 (3-2) ns	2 (3-2) ns	3 (3-2) ns	2 (3-2) ns
standard	0 (1-0) ns	0 (0-0) **	1 (1-0) ns	1 (1-0) ns
Lornoxicam 0.5%	0 (0-0) **	0 (0-0)**	0 (0-0) **	0 (0-0) **

All comparisons were conducted with the model (induction) group. *, **, ***, and **** denote significant differences at $P < 0.05$, $P < 0.01$, $P < 0.001$, and $P < 0.0001$, respectively. ns: not statistically significant; IQR = Interquartile Range; IQR (Q3 - Q1); Q3 (75th percentile); Q1 (25th percentile). Source: Own authorship.

A-The Healthy Control group (Figure 3 A1, A2): exhibited normal epidermal lining cells (red arrow), normal dermal fibrous tissue (asterisk), and normal sebaceous glands (black arrow).

B-The induction group (Figure 3 B1, B2): exhibited significant histological changes indicative of severe acneiform lesions. Acanthosis is marked by significant thickening of the stratum spinosum, accompanied by superficial epidermal necrosis and the formation of depression scars (red arrow). The superficial dermis exhibited necrosis accompanied by leukocyte infiltration and bacterial colonies (asterisk). Numerous sebaceous glands had comedones (w) packed with sebum and germs, occluded by the epidermis. The deep dermis exhibited dermatitis characterized by congestion, edema, and leukocyte infiltration (black arrow).

C-Vehicle group (Figure 3 C1, C2): Histopathological examination of the skin revealed a substantial crust on the superficial epidermis, necrosis inside the dermis, accompanied by leukocyte infiltration, vascular congestion, and perifollicular involvement (shown by black arrows).

D-Standard group (Figure 3 D1, D2): Histopathological images of the skin revealed normal epidermal lining cells (red arrow), a limited number of non-inflamed whiteheads and black comedones (w), minor follicular changes with sebaceous gland atrophy (black arrows), and normal fibrous tissue in the dermis (asterisk). Another image revealed typical epidermal lining cells exhibiting follicular atrophy; the dermis displayed normal sebaceous glands with discharges of those chemicals, alongside those present in the papillary dermis, in fibrous tissue D , and in dilated ductal areas**.**

E-Lornoxicam 0.5% (Figure 3 E1, E2): All histopathological images of the skin exhibited normal keratinocytes,the epithelial cells of the epidermis, located within the fibrous dermal tissue (asterisk), while sebaceous glands (S) and hair follicles (black arrow) began to revert from their dilated state to their anatomical lobular structure.

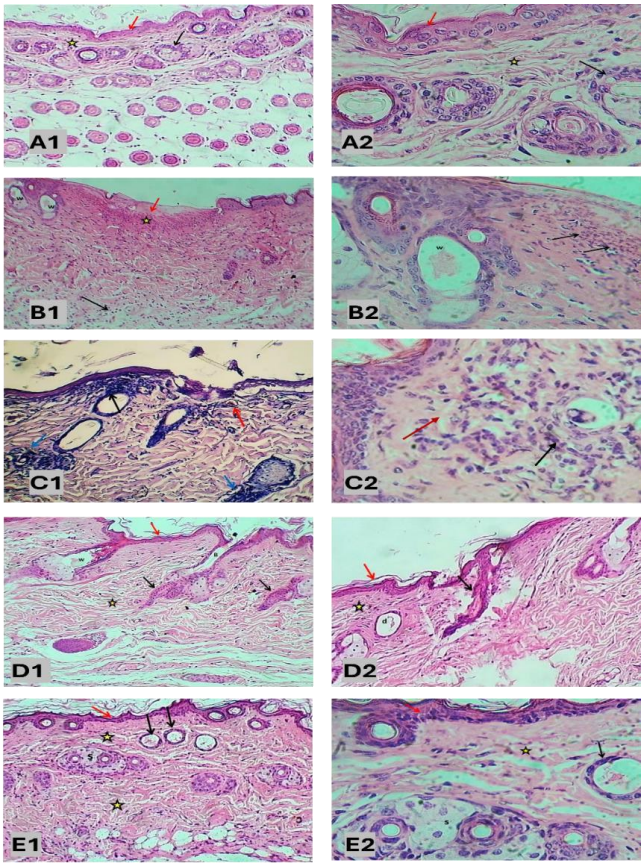


Figure 3. Histopathological pictures of the dermis (Hematoxylin and Eosin stain). Panels A1, B1, C1, D1, and E1 are presented at 100x magnification, whilst panels A2, B2, C2, D2, and E2 are magnified at 400x. The experimental groups are categorized as follows: control (A1, A2), induction (B1, B2), vehicle (C1, C2), standard (D1, D2), and lornoxicam 0.5 (E1, E2). Source: Own authorship.

Markers

Levels of the pro-inflammatory cytokines IL-1β, IL-8, and TNF-α were quantified in all experimental groups, as shown in Table 5. Compared with the healthy control group, the induction group exhibited markedly elevated levels of IL-1β, IL-8, and TNF-α ($p< 0.0001$), thereby confirming the successful establishment of the inflammatory model. A significant reduction in IL-1, IL-8, and TNF-alpha was observed in

the standard medication group compared with the induction group ($p < 0.001$), with values approaching normal levels. The cytokine levels in the vehicle-treated group were comparable to those in the induction group and hence did not exhibit a significant drop. The lornoxicam 0.5% group showed a significant reduction in cytokine levels ($p < 0.0001$), demonstrating efficacy comparable to that of the standard drug group.

Table 5. Comparison of inflammatory cytokine levels between experimental groups.

Groups	TNF-α (pg/ml) Mean ± SD	IL-1β (pg/ml) Mean ± SD	IL-8 (pg/ml) Mean ± SD
Healthy control	117.48±36.70 ****	139.36±34.37 ****	241.34±47.33 ****
Model (induction)	748.43±91.85	956.79±18.76	821.93±93.23
vehicle	599.06±27.19 ns	738.46±104.71 *	715.31±118.28 ns
standard	177.36±35.51 ***	165.97 ± 23.5 ****	253.88±51.36 ****
Lornoxicam 0.5%	154.86±22.06 ****	153.75±6.58 ****	235.10±19.78 ***

Note: All comparisons were conducted with the model (induction) group. *, **, ***, and **** denote significant differences at $P < 0.05$, $P < 0.01$, $P < 0.001$, and $P < 0.0001$, respectively. ns: not statistically significant. TNF-α: tumor necrosis factor-alpha; IL-1β: interleukin-1 beta; Interleukin-1 beta; IL-8: interleukin-8. Source: Own authorship.

Discussion

Managing inflammatory acne with conventional topical therapies often encounters limitations, including localized irritation, antibiotic resistance, and safety concerns associated with retinoids [22]. As a result, there is an increasing interest in non-antibiotic and non-retinoid strategies, including repurposed anti-inflammatory agents such as H1 antihistamines (e.g., Meclozine) [23]. Meclozine predominantly targets histamine-mediated pathways, whereas lornoxicam may provide a more comprehensive, multi-targeted anti-inflammatory profile. To evaluate its therapeutic efficacy, we employed a murine model induced by testosterone propionate and C. acnes. Here, Testosterone propionate serves to drive sebaceous gland hyperplasia and sebocyte differentiation, generating a hyperseborrheic lipid-rich microenvironment optimal for C. acnes colonization [24]. An intradermal inoculation with C. acnes subsequently elicits a local acute inflammatory response due to the secretion of lipases that hydrolyze triglycerides in sebum into free fatty acids, which contribute to irritation and inflammation. These are detected by keratinocytes, macrophages, monocytes, and sebocytes via pattern-recognition receptors (TLR2; TLR4). Initiating intracellular cascades via the NF-κB and MAPK pathways leads to increased transcription of several inflammatory cytokines, including TNF-α, IL-1β, and IL-8 [25,26]. This cascade closely mimics the inflammatory processes in human acne lesions.

In the current study, topical 0.5% lornoxicam gel significantly improved the appearance of acne-like lesions, as evidenced by a significant reduction in modified Draize scores compared to the untreated induction group. Conversely, the vehicle group demonstrated a median change of no effect, indicating that the observed clinical benefit was attributable to the active drug and not its gel base. The testosterone propionate/Cutibacterium acnes-induced murine model efficiently gave rise to the inflammatory skin lesions observed clinically, such as erythema and irritation in line with features of acne vulgaris [27]. The clinical improvement observed after topical administration of lornoxicam may be due to its potent anti-inflammatory properties through inhibition of cyclooxygenase-mediated prostaglandin production and the regulation of inflammatory mediators [28]. These findings support earlier research demonstrating the anti-inflammatory benefits of several NSAIDs in dermatological inflammatory models [29].

The histological and molecular studies in this work provide significant support for the visual evaluation. Our results show a specific correlation between the observed histological improvements and a reduction in key pro-inflammatory cytokines, suggesting that lornoxicam acts through multiple anti-inflammatory mechanisms.

A- Dermal Congestion and TNF-α Modulation

Congestion in the induction group substantiated by the heightened level of TNF-α. TNF-α induces vasodilation and increases vascular permeability by upregulating adhesion molecules and releasing vasoactive mediators (e.g., prostaglandins, nitric oxide). lead to the accumulation of plasma leakage and tissue swelling, which appear as congestion [30]. In contrast, topical lornoxicam significantly reduced cutaneous congestion compared with healthy controls. Simultaneously, we observed a dramatic reduction in TNF-α levels after lornoxicam administration, comparable to that of the standard drug treatment group. Lornoxicam, which is working as a COX inhibitor, consecutively inhibits prostaglandin synthesis and thus reduces vasodilation induced by prostaglandins. In addition, its ability to modulate inflammatory mediators such as TNF-α likely helps restore vascular homeostasis and minimize hyperemia and edema, as previously shown for NSAIDs in dermal inflammation models [31,32].

B- Leukocyte Infiltration and IL-8 Suppression

IL-8 is a dominant cytokine in the development of neutrophil migration to inflamed tissues in acne [33]. Our molecular analysis confirmed markedly increased IL-8 levels compared with healthy controls, as shown in Table 5. Through the release of reactive oxygen species and proteolytic enzymes, inflammatory cell accumulation contributes to tissue damage, thus maintaining a perpetuating environment rich in inflammation [34]. 0.5% lornoxicam gel treatment significantly reduced leukocyte infiltration, potentially linked to suppression of IL-8 to nearnormal levels. Thus, the data provide strong evidence that the anti-inflammatory action of lornoxicam depends on blockade of IL-8-mediated chemotactic activity and on a decrease in upstream inflammatory signaling pathways that regulate leukocyte recruitment and skin migration. Previous studies have highlighted the importance of IL-8 in acne pathogenesis and the potential of targeting it as a treatment strategy through inhibition of its synthesis [35].

C-Acanthosis and IL-1β Attenuation

Epidermal hyperplasia, defined as acanthosis, was observed in the induction group, indicating ongoing inflammatory activation within acneiform lesions. This epidermal hyperplasia is often driven by pro-inflammatory cytokines such as IL-1β, which promote keratinocyte proliferation and disrupt normal epidermal differentiation [36]. The data showed that IL-1β levels of the induction group were significantly higher than those of healthy controls, as shown in Table 5. Prolonged IL-1β signaling facilitates thickening of the stratum spinosum and follicular hyperkeratosis, which are features of acne pathogenesis [37]. Topical lornoxicam therapy led to a significant reduction of acanthosis and almost completely restored the normal epidermal architecture. This improvement is closely related to the marked reduction of IL-1β levels in the treated group. Although the present study has not directly assessed inflammatory activity, reduced IL-1β levels suggest reduced inflammasome-mediated inflammatory activity, since IL-1β maturation and release are tightly regulated by inflammasomes, particularly NLRP3 [38].

D- Sebaceous Gland Changes and Inflammatory Milieu

Changes in sebaceous glands observed in the induction group were primarily attributable to combined androgenetic stimulation and inflammatory stress induced by C. acnes, characterized by comedone development and architectural distortion. Simultaneously, inflammation due to C. acnes, mediated by cytokines such as TNF-α and IL-1β, disrupts the innate structure of glands and promotes perifollicular inflammation. Topical 0.5% lornoxicam gel remarkably restored sebaceous gland morphology and reduced inflammatory changes. This improvement is likely a consequence of thinning of the local pro-inflammatory microenvironment in the pilosebaceous unit. Despite persistent androgenic action, lornoxicam treatment reduced tissue inflammation and secretion of key pro-inflammatory mediators (TNF-α, IL-1β, and IL-8); therefore, it re-established sebaceous gland integrity and restored follicular structure.

Limitations

An animal model was used in this investigation, which might not adequately simulate the human character of acne vulgaris. The small sample sizes and the short treatment period may limit the generalizability and strength of these results. The chronic safety, potential for irritation, and pharmacokinetics of lornoxicam following topical administration were not investigated. Most of the available knowledge relied on clinical scoring, histology, morphometry, and cytokine measurements, but detailed mechanistic studies using techniques such as immunohistochemistry for MMP-9, COX-2, and NF-κB are lacking. Species differences in sebaceous gland biology and sebum composition (human skin contains higher proportions of wax esters and squalene than mouse skin) may further limit translational relevance. Thus, further studies are required to validate formulation design parameters, better elucidate the molecular signaling pathways, and evaluate clinical efficacy in human subjects.

Conclusion

In conclusion, these data suggest that topical lornoxicam can treat acne-like lesions by modulating several inflammatory pathways. The improved macroscopic severity of lesions, dermal congestion, leukocyte infiltration, acanthosis, and differences in sebaceous gland morphology represent a mechanistic basis for these findings, which correlate with the efficacy of lornoxicam in greatly reducing the pro-inflammatory cytokines TNF-α, IL-8, and IL-1β. Overall, Lornoxicam has a profound impact on inflammation and is an emerging treatment for inflammatory acne, affecting both clinical parameters and molecular pathology.

CRediT

Author contributions: Conceptualization; Data

Curation; Formal Analysis: Jasim, and Gatea; Investigation: Methodology: Project Administration: Supervision: Hassan, and Gatea and Tahir; Writing-Original Draft, Writing -Review & Editing: Jasim

Acknowledgment

Not applicable.

Ethical Approval

This research is a randomized, prospective, controlled animal study approved by the Institutional Review Board (IRB) of the College of Medicine at Al-Nahrain University. The ethical code for this study is as follows (IRB/111, No.: 20250924) dated 2 February 2026.

Informed Consent

Not applicable.

Funding

Not applicable.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request, and all data is stored following privacy and ethical guidelines.

Conflict of Interest

The authors declare no competing interests.

Similarity Check

It was applied by Ithenticate[@].

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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