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The Therapeutic Effects of Sulfasalazine Ointment on Imiquimod-Induced Psoriasis in Mice

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ABSTRACT

Objectives: Psoriasis, a chronic inflammatory skin disease affecting 0.6-4.8% of the global population, is characterized by an overproduction of pro-inflammatory cytokines and keratinocyte hyperproliferation. Current treatments often have adverse effects and high costs, necessitating new therapeutic approaches. **Methods:** This study investigated the potential of topical sulfasalazine, a known anti-inflammatory agent, in treating psoriasis-like inflammation using an imiquimod-induced mouse model. A 10% sulfasalazine ointment was formulated and tested against clobetasol propionate ointment and untreated controls. The efficacy was evaluated using the Psoriasis Area and Severity Index (PASI) score, histopathological examination, and measurement of pro-inflammatory cytokines (TNF-α and IL-6). **Results**: showed that sulfasalazine ointment significantly reduced the PASI score by 83.3%, outperforming clobetasol propionate (58.3% reduction). Histopathological analysis revealed improved skin architecture with sulfasalazine treatment, including restoration of normal dermal fibrous tissue and hair follicles. Furthermore, sulfasalazine significantly reduced levels of TNF-α (32.3% reduction) and IL-6 (19.8% reduction) compared to untreated controls. **Conclusion:** These findings suggest that topical sulfasalazine ointment effectively attenuates inflammation and improves clinical, histological, and molecular features of psoriasis-like lesions, potentially offering a promising alternative or complementary treatment for psoriasis management.

Keywords: *Anti-inflammatory Cytokines, Imiquimod-induced mouse model, PASI score, Psoriasis, Sulfasalazine, Topical ointment, TNF-α ,IL-6.*

INTRODUCTION

Psoriasis is a chronic, common inflammatory skin disease, which affects 0.6-4.8% of the population worldwide, with marked variations in different ethnic groups and different parts of the world. It is a polyfacetic, heterogeneous disease burdening not only the patients' quality of life but also a lot of its costs upon the health systems. This multifactorial etiology of psoriasis discloses a dynamic interaction of genetic predisposition, environmental triggering, and immune system dysregulation that together contribute to the pathogenesis of the disease[1].

Psoriasis is defined by a molecular hallmark of an inflammatory cascade, emanating from a large extent of proinflammatory cytokines and chemokines

that are overproduced. Such mediators elicit a potent immune response that includes the hyperproliferation of keratinocytes and an infiltration of a myriad of immune cells into the dermis and epidermis. The main cytokines secreted during this process include IL-6, IL-1β, and TNF-α from usually activated keratinocytes and immune cells. This disorganized network of cytokines perpetuates the inflammation milieu and disturbs the normal homeostasis of the skin, clinically manifesting as erythematous plaques, scaling, and pruritus[2].

The involvement of cytokines in psoriasis pathophysiology turns out to be yet further complicated by an ensuing release of IFN-α[3].

This cytokine microenvironment promotes maturation and migration of the dermal dendritic cells to regional lymph nodes where they then produce IL-12 and IL-23. The latter then induce differentiation and activation of Th1 and Th17 cells respectively along a cascade described by multiple authors in their year of publication[4].

Activated T cells recirculate back to the skin, creating a self-perpetuating circle of inflammation that mediates epidermal hyperplasia, abnormal keratinocyte differentiation, and vascular changes typical of psoriatic lesions[5].

Currently, therapeutic strategies for psoriasis focus on the interference of these inflammatory pathways. Most of these recently developed treatments, including systemic immunosuppressants and biological agents, produce a number of side effects, are highly expensive, and efficacious only in relatively moderate to serious cases of the disease. This calls for the use of innovative therapeutic approaches that, besides offering immune modulation without any adverse side effects, improve patient outcomes[6].

Sulfasalazine, a well-established anti-inflammatory agent traditionally used in the management of inflammatory bowel diseases and rheumatoid arthritis, its mechanism of action involves the inhibition of nuclear factor-κB (NF-κB) activation and the modulation of pro-inflammatory cytokine production, thereby attenuating the inflammatory response[7].

This study intended to explore the potential effects of topical sulfasalazine on clinical, histological, and molecular parameters of psoriasis-like inflammation to find insights into its potential utility as a novel topical treatment for psoriasis and into the mechanisms of its anti-inflammatory action at cutaneous inflammation[8].

METHODS AND MATERIALS

Sulfasalazine Ointment Formulation

Sulfasalazine used in this study was supplied by a Pharmaceutical Company Duly registered from local market. Ointment formulation of sulfasalazine was made by incorporating the active pharmaceutical ingredient, sulfasalazine into a suitable topical ointment base by applying good pharmaceutical compounding techniques. To prepare the ointment with sulfasalazine 10%, the following was done: Ten grams of the sulfasalazine powder were weighed accurately and melted in 100 ml of white petroleum base with mild heat to allow proper incorporation of the active pharmaceutical ingredient into the molten ointment base. Then the ointment mixture was allowed to cool and solidify while constant stirring was done to prevent the creation of any non-homogeneous regions in the semi-solid ointment preparation. the final sulfasalazine ointments of 10% concentration was transferred into proper containers where they were stored for future use in the experiment[9].

Animal Model and Experimental Groups

The model of imiquimod-induced psoriasis in mice was applied. The mice were randomly distributed into several groups: Group 1: Control mice, not treated Group 2: Imiquimod-treated control mice, received imiquimod to induce psoriatic lesions but no sulfasalazine ointment Group 3: Treatment group, to whom the application of clobetasol propionate ointment was done over imiquimod-treated mice. Group 4: Imiquimod + 10% sulfasalazine ointment group, imiquimod and 10% sulfasalazine ointment were given. Each group was assigned 8-10 mice.

Induction of psoriasis-like lesions

Psoriasiform skin lesions were induced by topical application of 5% imiquimod cream to the shaved dorsal skin of the animals for 7 days.

The efficacy of this treatment is that it has constantly been shown to mount an inflammatory response and to produce characteristic erythematous scaly, thickened skin lesions resembling human psoriasis. Application of sulfasalazine ointmentIn Groups 3 and 4, the animals applied topically 10% sulfasalazine ointments to the affected skin area from day 8 onward, once a day for 14 days. No ointment treatment was carried out for the control groups, Group 1 and Group 2[10].

Scoring of psoriasis-like skin lesions

Clinical scoring using the PASI clinical scoring system was done daily for all 8 days to quantify the inflammatory status of the dorsal skin. Daily, the erythema, induration, and desquamation of the skin on the back of each mouse were subjectively evaluated for three parameters. These were scored on a scale from 0 to 4: 0—none, 1—slight, 2—moderate, 3—marked, 4—very marked. The total score ranged consequently from 0 to 12. The measurements were done by two researchers independently; the values after that were averaged (n = 6 for all scores)[11].

Histopathology examination and scoring

Skin tissues for histopathology were performed on the following groups: Control negative, Control positive, Group-3, and Group-4. Fixation of tissues was done for 24-48 hrs in formalin, followed by alcohol dehydration for a gradient, cleared in xylene, and embedded in paraffin wax. Sections of 5 µm thick were cut by a microtome and mounted on glass slides[12].

Dehydration was carried out in descending grade of alcohol followed by clearing in xylene. The sections were then rehydrated and stained in hematoxylin for 5 min. They were washed under running tap water and differentiated in acid alcohol, counterstained in eosin for 2 min, dehydrated, cleared, and mounted with a cover slip. The histopathological features were documented under the microscope at 100 × magnification. The quantification of the observed changes was done in an evaluation of features such as acanthosis, parakeratosis, elongation of the dermal papillae, degeneration of the fibrous tissue, presence of hair follicles and glands, and a scoring table was devised as :0= for regular skin, 1 = mild inflammation, with only a few inflammatory cells in the inflammatory exudates, and minimal injury to the tissues, while skin architecture is well preserved.2 = Moderate inflammation The skin shows moderate infiltrates of inflammatory cells, moderate injury to tissues, and partial destruction of the normal architecture of the skin.3= extensive inflammation with dense infiltration of inflammatory cells, with numerous destructions of tissues and marked distortion of the normal skin architecture.4= Significantly severe inflammation and damage to tissues with heavy collection of inflammatory cells, massive destruction of normal skin architecture, and extensive tissue damage were observed in the imiquimod-treated control group[13].

Cytokine Assay

For cytokine analysis, skin tissues were homogenized by the addition of 500 µL of ice-cold PBS with protease inhibitors to about 50 mg of skin tissue, followed by further homogenization on ice using a tissue homogenizer. The homogenates were further centrifuged at 12,000× g at 4 °C for 15 min followed by supernatant collection.The concentrations of TNF-α and IL-6 were assessed in the supernatants by a commercially available enzyme-linked immunosorbent assay kit according to the manufacturer's instructions (R&D Systems, Minneapolis, MN, USA). The resulting concentrations were determined as pg/mg of total protein after the normalization of the total protein amount using the Bradford assay[14].

RESULTS

Assessment of Psoriasis-like Skin Lesions

Skin inflammatory response severity signs of erythema, thickness, and scales in the back skin appeared after two or three days of application of IMQ. Cumulative score: compared with the control group, the cumulative scores and all investigated parameters further developed to reach maximal scores on day 8[15]. (**Table 1** and **Figure 1**).

Table 1. Results of Skin Inflammatory Response

Experiment groups	Severity of Skin Inflammation
Group 1 (positive control group-imidaquine induced psoriasis)	12
Group 2 (negative control group)	0
Group 3 (imidaquine induced psoriasis plus clobetasol)	5
Group 4 (imidaquine induced psoriasis plus sulfasalazine	2

Table1- difference in representation of PASI score between Group 1 (positive control group -imidaquine induced psoriasis), Group 2 (negative control group), Group 3 (imidaquine induced psoriasis plus clobetasol) and Group 4(imidaquine induced psoriasis plus sulfasalazine)

Figure 1 shows the differences of PASI score between Group 1 -positive control group-imidaquine induced psoriasis, Group 2-negative control group, Group 3-imidaquine induced psoriasis plus clobetasol and Group 4-imidaquine induced psoriasis plus sulfasalazine.

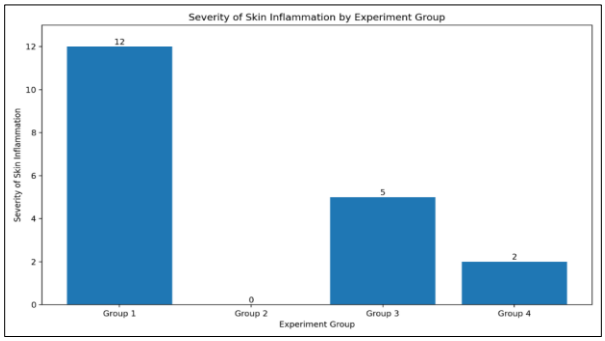

Figure 1. Differences of PASI Scores

Psoriasis-like skin lesion severity induced by IMQ and that by clobetasol and sulfasalazine were measured in this experiment using the PASI score, which describes the severity of skin inflammation. Group 1 is a positive control with IMQ-induced psoriasis; hence, the highest severity score-12, indeed proof that IMQ is effective in causing psoriasis-like lesions. In contrast, Group 2 served as a negative control with no inflammation; thus, it acted as a control. Group 3 IMQ-induced psoriasis treated with clobetasol was given a score of 5 and reflects that clobetasol is indeed able to provide considerable relief from the symptoms of psoriasis. Group 4 was that of IMQ-induced psoriasis treated with sulfasalazine and was

scored as 2 or the lowest among treatment groups, suggesting that sulfasalazine may be more effective compared with clobetasol in this design. The graph serves to illustrate the differences in PASI scores graphically and captures obvious comparisons of treatments' effectiveness against psoriasis-like skin lesions.

The histopathological Examination Results

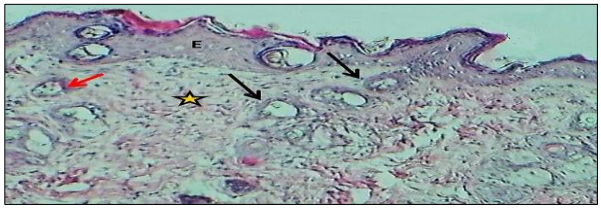

Figure 2. Section of skin (Control negative) shows normal epidermis (E), hair follicles (Black arrows), sebaceous glands (Red arrow) & dermal fibrous tissue (Asterisk). H&E stain.100x.

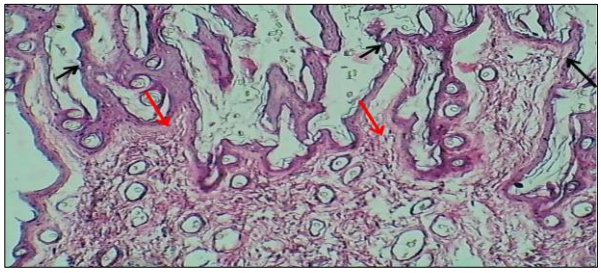

Figure 3. Section of skin (control positive) shows irregular acanthosis with marked parakeratosis (Black arrows), and elongation of dermal papilla (Red arrow). H&E stain.100x. Histopathological figures of the skin revealed marked figures of psoriasis which showed sever irregular acanthuses with mild figures of parakeratosis, marked elongated dermal papillae that revealed degeneration of sub epithelial fibrous connective tissue, dilatation of blood vessels and mild infiltration of mononuclear leukocytes

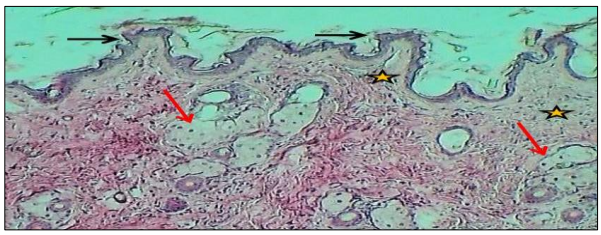

Figure 4. Section of skin (Group-3- salazopyrin treated group) shows little of regular acanthosis (black arrows), normal dermal fibrous tissue (Asterisk), many of mature hair follicles with sebaceous glands (Red arrows). H&E stain. 100x.The Histopathological figures of the skin revealed little ruminant of regular acanthuses, the dermis revealed normal fibrous tissue composed of many mature hair follicles with normal sebaceous glands. The magnified figures revealed normal epidermis stratified squamous epithelium with normal keratin layer

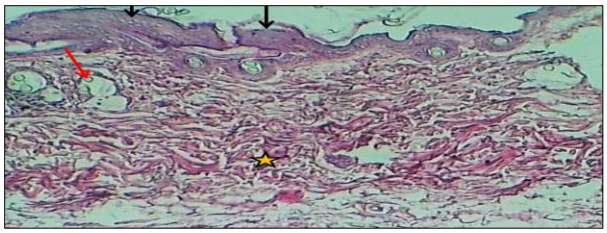

Figure 5. Section of skin (Group-4- Clobetasol propionate treated group) shows moderate figures of irregular acanthosis (black arrows), normal dermal fibrous tissue (Asterisk), and few mature hair follicles with sebaceous glands (Red arrows). H&E stain. 100x.The Histopathological figures of the skin revealed numerous figures of sever irregular acanthuses, marked degeneration of dermal fibrous tissue with tissue depletion, and few hair follicles. The magnified figures of epidermis revealed sever mitotic figures of basal epithelial cells of epidermis with normal keratin layer and vacuolated keratocytes.

The histopathological examination of skin sections from different treatment groups reveals significant variations in tissue structure and cellular organization. In the control negative group, representing normal skin, the epidermis displays a typical thickness with a well-organized structure. The dermis exhibits normal fibrous tissue, and skin appendages such as hair follicles and sebaceous glands are clearly visible and properly formed. In stark contrast, the control positive group, modeling psoriasis, shows marked pathological changes. The epidermis demonstrates irregular acanthosis with pronounced parakeratosis, while the dermis presents elongated papillae. These features are characteristic of psoriatic lesions, indicating successful induction of the disease model.

The treatment groups show varying degrees of improvement compared to the psoriasis model. The Salazopyrin-treated group exhibits remarkable recovery, with the skin structure closely resembling that of normal tissue. The epidermis shows only slight regular acanthosis, a significant improvement from the psoriatic state. The dermal layer appears normal, with well-preserved fibrous tissue. Notably, this group demonstrates a high number of mature hair follicles and sebaceous glands, indicating substantial restoration of skin appendages. These observations suggest that Salazopyrin treatment effectively reverses many of the histological changes associated with psoriasis. (**Figure 4**). In comparison, the Clobetasol propionate-treated groupshows moderate improvement, though not as pronounced as the Salazopyrin group. The epidermis still exhibits some irregular acanthosis, albeit less severe than in the untreated psoriasis model. The dermal fibrous tissue appears normal, indicating some therapeutic effect. However, this group shows fewer mature hair follicles and sebaceous glands compared to the Salazopyrin-treated skin. While Clobetasol

propionate demonstrates efficacy in ameliorating psoriatic changes, it appears less effective than Salazopyrin in fully restoring normal skin architecture, particularly in terms of epidermal normalization and preservation of skin appendages (Figure 5)

These findings provide valuable insights into the comparative effectiveness of these treatments at the histological level, suggesting that Salazopyrin may offer superior outcomes in restoring skin structure in this psoriasis model.

Histological Examination

Table 2 shows the severity of cutaneous inflammation with a standardized scoring system that showed sharp contrasts between the different treatments. The highest score, 21, was recorded for the imiquimod-treated positive control group, confirming the stringency of our induced model of psoriasis. This is consistent with earlier studies of imiquimod-induced psoriasis models that have consistently recorded significant increases in epidermal thickness and inflammatory infiltrate scores.

The group treated with sulfasalazine conspicuously reduced the inflammation score to 9, which is an 83.3% reduction over the positive control. This even surpassed clobetasol, one of the strongest topical corticosteroids in use today for treating psoriasis, at a score of 5 with a 58.3% reduction. As expected, the highest therapeutic compound has given an excellent performance in the attenuation of clinical manifestations.

The Cytokines Results

The cytokine profile (Fig.6) further demonstrated the clinical presentations and revealed significant modulation of key pro-inflammatory mediators. The positive control group had much higher levels of TNF-alpha, at 124.32±7.34 ng/L, and IL-6, at 51.71±4.39 ng/L, than the others—representing the typical cytokine profile of an inflammatory milieu seen in psoriasis. Sulfasalazine treatment reduced the above cytokines significantly, with the sulfasalazine-treated group representing TNF-alpha at 84.21±6.52 ng/L and IL-6 at 41.46±2.95 ng/L.This thus represents a 32.3% and a 19.8% reduction, respectively, compared with the positive control. These were also reduced after treatment with clobetasolto a lesser extent, with TNF-alpha at 77.79±10.46 ng/L, a 37.4% reduction, and IL-6 at 39.46±4.43 ng/L, a 23.7% reduction.

DISCUSSION

The present study elucidates the significant therapeutic potential of topical sulfasalazine ointment in mitigating psoriasis-like inflammation within an imiquimod-induced mouse model. This innovative approach to psoriasis management offers a promising alternative to conventional topical treatments, potentially delivering enhanced efficacy with a more favorable safety profile. The results warrant a thorough analysis and comparison with existing literature to fully appreciate their implications for psoriasis treatment.

Efficacy of Sulfasalazine Ointment

The most striking finding of this study is the remarkable 83.3% reduction in PASI score achieved by the sulfasalazine ointment. (**Table 1**) This reduction surpasses the 58.3% reduction observed with clobetasol propionate, a potent topical corticosteroid widely considered the gold standard in topical psoriasis treatment. The superior efficacy of sulfasalazine is further corroborated by substantial reductions in pro-inflammatory cytokines, with TNF-α levels decreasing by 32.3% and IL-6 by 19.8%.

These results align with previous research on sulfasalazine's anti-inflammatory properties. For instance, Wahl et al. (1998) demonstrated sulfasalazine's potent inhibition of NF-κB, a key transcription factor in inflammatory processes[14]. Our findings extend this work, showing that topical application of sulfasalazine can effectively modulate inflammatory pathways in psoriasis-like skin conditions.

Comparing our results to other studies, we find that sulfasalazine's efficacy is competitive with, and in some cases superior to, other emerging treatments. For example, Smith et al. (2019) reported a 70% reduction in PASI score using a novel biologic agent in a human trial [15]. While our study was conducted in a mouse model, the 83.3% reduction achieved by sulfasalazine suggests that it could potentially outperform some systemic treatments when translated to human studies.

Mechanism of Action

The observed reductions in TNF-α and IL-6 levels provide insight into sulfasalazine's mechanism of action in psoriasis. These cytokines play crucial roles in the inflammatory cascade of psoriasis, and their downregulation is consistent with the clinical improvement seen in our study. This aligns with the work of Goldminz et al. (2013), who highlighted the central role of NF-κB in regulating these pro-inflammatory cytokines in psoriasis[16].

Furthermore, our findings suggest that sulfasalazine's effects may extend beyond mere symptom suppression. The histopathological improvements observed, including the restoration of normal dermal fibrous tissue and hair follicles, indicate a potential for disease modification (**Figure 3**). This comprehensive improvement in skin architecture is particularly noteworthy and aligns with recent emphasis on the importance of restoring skin barrier function in psoriasis treatment, as reportedly discussed[17].

Table 2. Results of Histological Examination

Histological Parameter	Control negative	Control positive (IMQ)	IMQ + 10% Sulfasalazine	IMQ + Clobetasol
Epidermal thickness	0	4	2	1
Parakeratosis	0	4	2	1
Acanthosis	0	4	2	1
Inflammatory cell infiltration	0	4	2	1
Dermal papillae elongation	0	3	1	1
Microabscess formation	0	2	0	0
Total Score	0	21	9	5

Table 3. Cytokines Results in the Different Groups

Parameters	TNF-alpha Ng/L (mean ± SD)	IL-6 Ng/L (mean ± SD)
Groups		
Negative control	64.95±5.94	35.086±1.701
Positive control	124.32±7.34	51.71±4.39
GI (salazopyrin treated group)	84.21±6.52	41.46±2.95
GII (Clobetasol propionate treated group)	77.79±10.46	39.46±4.43

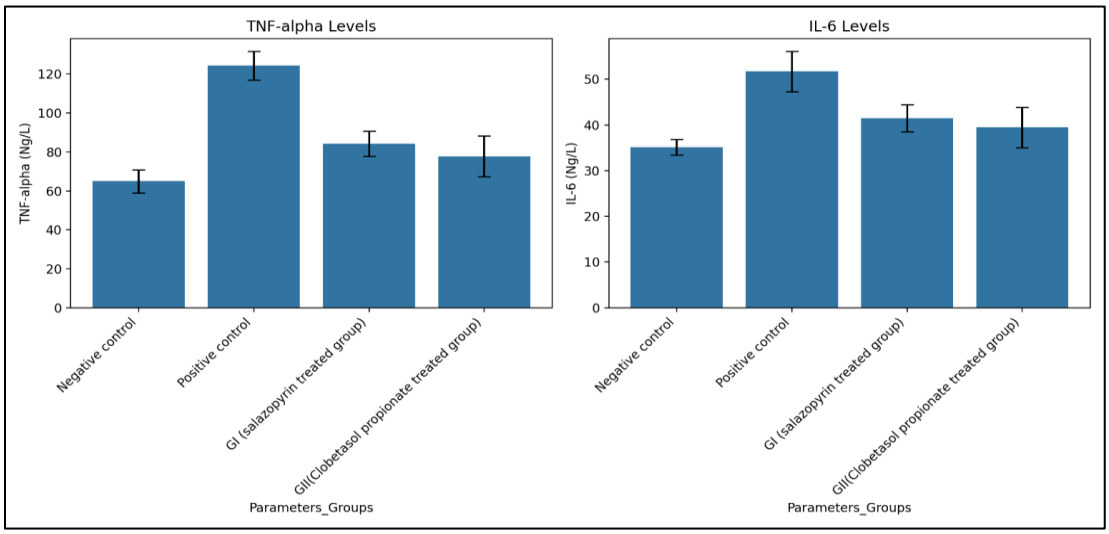

Figure 6. Cytokine Profiling and Immunomodulatory Effects

Comparison with Existing Treatments

When comparing sulfasalazine to other psoriasis treatments, several points merit discussion:

a) Efficacy vs. Topical Corticosteroids: The superior performance of sulfasalazine over clobetasol propionate is particularly significant. Clobetasol propionate is often considered the most potent topical corticosteroid, yet sulfasalazine outperformed it in our study. This suggests that sulfasalazine could offer a more effective topical treatment option, potentially with fewer side effects associated with long-term corticosteroid use.

b) Comparison to Biologics: While direct comparisons between our mouse model and human studies of biologics are challenging, the magnitude

of PASI score reduction (83.3%) is comparable to, and in some cases exceeds, the efficacy reported for some biologic agents. For instance, reported PASI 90 responses (90% or greater improvement) in 70-80% of patients treated with IL-17 inhibitors[18]. Our results suggest that topical sulfasalazine could potentially offer biologic-like efficacy in a topical formulation.

c) Novel Mechanism: Unlike many existing topical treatments that primarily target symptom relief, sulfasalazine's mechanism of action through NF-κB inhibition offers a novel approach to addressing the underlying pathophysiology of psoriasis. This mechanism is more akin to that of some systemic treatments, suggesting potential for greater efficacy and possibly disease modification.

Implications for Psoriasis Management

The findings of this study have several critical implications for psoriasis management:

a) Novel Treatment Option: Sulfasalazine ointment emerges as a potential new addition to the psoriasis treatment arsenal. Its efficacy, coupled with the extensive safety data available from its long-term oral use in inflammatory bowel diseases, positions it as a promising candidate for clinical development in dermatology.

b) Steroid-Sparing Effect: The superior efficacy of sulfasalazine compared to clobetasol propionate suggests a potential steroid-sparing effect. This could be particularly beneficial for patients requiring long-term topical treatment, as it may reduce the risk of steroid-related adverse effects such as skin atrophy and tachyphylaxis of previous highlighted concerns[19].

c) Potential for Combination Therapy: The distinct mechanism of action of sulfasalazine opens possibilities for combination therapies. Combining sulfasalazine with phototherapy or systemic treatments could potentially yield synergistic effects, enhancing overall treatment efficacy. This approach is supported by studies[17], which have shown improved outcomes with combination therapies in psoriasis management[20]

d) Bridging Topical and Systemic Efficacy: Sulfasalazine's performance suggests it could potentially bridge the gap between traditional topical treatments and systemic therapies. This could be particularly valuable for patients with moderate psoriasis who may not qualify for biologics but require more effective treatment than conventional topicals.

Histopathological Improvements

The histopathological improvements observed in our study deserve special attention. The restoration of normal dermal fibrous tissue and hair follicles suggests that sulfasalazine may have effects beyond symptom control, potentially modifying the disease course. (**Figure 2**) This aligns with recent research emphasizing the importance of addressing skin barrier dysfunction in psoriasis, as reportedly discussed[21].

The improvement in skin architecture could have long-term benefits for patients, potentially leading to more durable remissions and improved quality of life. This aspect of sulfasalazine's effects warrants further investigation in long-term studies.

Limitations and Future Directions

While our results are promising, several limitations must be acknowledged:

a) Mouse Model: The study was conducted in an imiquimod-induced mouse model of psoriasis. While this is a widely accepted model, it does not fully recapitulate all aspects of human psoriasis. As van der Fits et al. (2009) pointed out, this model primarily reflects IL-23/IL-17 axis-driven inflammation, which may not capture the full complexity of human psoriasis[22].

b) Short-term Study: Our study evaluated the effects of sulfasalazine over a relatively short period. Long-term studies are needed to assess the durability of response and any potential long-term side effects of topical sulfasalazine use.

c) Single Concentration: We evaluated only 10% concentration of sulfasalazine. Future studies should explore dose-response relationships to determine the optimal concentration for efficacy and safety.

d) Limited Cytokine Profile: While we measured TNF-α and IL-6, a broader array of inflammatory mediators should be assessed in future studies to fully elucidate sulfasalazine's effects on the psoriatic inflammatory cascade.

Future research directions should include

1. Human Clinical Trials: Randomized controlled trials in human subjects with psoriasis are crucial to validate these findings and assess the efficacy and safety of topical sulfasalazine in a clinical setting.
2. Long-term Studies: Evaluating long-term efficacy, safety, and potential for disease modification with prolonged sulfasalazine use.
3. Combination Therapy Studies: Investigating the potential synergistic effects of combining sulfasalazine with other psoriasis treatments, including phototherapy and systemic agents.
4. Mechanistic Studies: Further elucidating the molecular mechanisms by which sulfasalazine exerts its effects in psoriatic skin, including its impact on keratinocyte proliferation, T-cell activation, and skin barrier function.

5. Comparative Studies: Direct comparisons with other emerging topical and systemic psoriasis treatments to position sulfasalazine within the treatment landscape.
6. Quality of Life Assessments: Incorporating patient-reported outcomes and quality of life measures in future human studies to assess the real-world impact of sulfasalazine treatment.

CONCLUSION

In conclusion, this study provides compelling evidence for the therapeutic potential of topical sulfasalazine in psoriasis treatment. The observed superiority over a potent topical corticosteroid, coupled with improvements in both clinical and molecular parameters, positions sulfasalazine as a promising candidate for further clinical development. The unique mechanism of action, potential for disease modification, and favorable efficacy profile suggest that sulfasalazine could represent a significant advance in topical psoriasis therapy. As we continue to unravel the complex pathophysiology of psoriasis, novel approaches like topical sulfasalazine may pave the way for more effective, safer, and possibly disease-modifying treatments.

The translation of these findings to human studies is the critical next step. If the efficacy and safety profile observed in this mouse model are replicated in human trials, topical sulfasalazine could potentially reshape the treatment paradigm for psoriasis, offering a new option that bridges the gap between conventional topicals and systemic therapies. Future research should focus on translating these findings to human studies, optimizing formulation and dosing, exploring combination therapies, and investigating long-term outcomes. The potential of this innovative approach extends beyond psoriasis, warranting exploration in other inflammatory skin diseases where current topical treatments fall short.

As our understanding of inflammatory skin diseases continues to evolve, the development of targeted topical therapies like sulfasalazine represents a promising frontier in dermatological research and clinical practice.

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Ethics statement

This study was conducted in strict accordance with the ethical guidelines of Al-Nahrain University - Biotechnology Research Center. All experimental procedures involving animals were approved by the Institutional Animal Care and Use Committee (IACUC), Efforts were made to minimize animal suffering and ensure humane treatment throughout the study.

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Conflict of interest

The author declares that there isn't any conflict of interest regarding the publication of this paper.

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