

Effect of Topical Benzoyl Peroxide on Skin Barrier Integrity Assessed by Transepidermal Water Loss in an Experimental Model

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ABSTRACT

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Benzoyl peroxide is a topical agent widely used in the treatment of acne vulgaris; however, its use is associated with cutaneous adverse effects related to impairment of epidermal barrier function. The aim of the present study was to evaluate the effect of topical benzoyl peroxide on skin barrier integrity by measuring transepidermal water loss (TEWL) in an experimental model. An experimental, controlled, and prospective study was conducted comparing a group treated with 5% topical benzoyl peroxide and a control group without active treatment. Transepidermal water loss was measured under controlled environmental conditions before the intervention, during the treatment period, and at the end of the study. The results showed a progressive and statistically significant increase in TEWL in the treated group compared with the control group, demonstrating a time-dependent effect. In addition, the treated group more frequently presented clinical signs of skin irritation, including erythema, dryness, and desquamation, which correlated with increased TEWL. In conclusion, topical application of benzoyl peroxide is associated with a significant impairment of skin barrier function, highlighting the importance of considering therapeutic strategies aimed at preserving epidermal integrity during its clinical use.

KEYWORDS: Benzoyl peroxide; Skin barrier; Transepidermal water loss; Epidermal function; Skin irritation; Experimental dermatology.

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INTRODUCTION

The skin is the largest organ of the human body and fulfills essential functions, including protection against external aggressions, regulation of water loss, and active participation in innate and adaptive immune responses. Skin barrier function depends mainly on the stratum corneum, a highly specialized structure composed of corneocytes embedded in an organized lipid matrix, whose integrity is indispensable for

maintaining epidermal homeostasis. Disruption of this barrier is associated with increased skin permeability, local inflammation, and greater susceptibility to irritants, allergens, and microorganisms.

One of the most commonly used parameters to evaluate skin barrier function is transepidermal water loss (TEWL), which reflects the passive diffusion of water from the deeper layers of the epidermis to the external environment. Under

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physiological conditions, TEWL remains low and stable; however, any alteration in stratum corneum organization, intercellular lipid composition, or epidermal structural proteins can lead to a significant increase in this parameter. Therefore, TEWL measurement is considered a non-invasive, sensitive, and reproducible tool for detecting subclinical or clinical damage to the skin barrier in experimental and clinical studies.

Benzoyl peroxide is a topical agent widely used in the treatment of acne vulgaris, both as monotherapy and in combination with topical antibiotics or retinoids. Its mechanism of action includes the release of oxygen free radicals, responsible for its potent bactericidal effect against *Cutibacterium acnes*, as well as a keratolytic effect that promotes desquamation of the stratum corneum and follicular deobstruction. However, these same properties may induce skin irritation, xerosis, erythema, and desquamation—adverse effects that often limit treatment adherence, particularly during the initial phases of use.

Several clinical studies have documented the frequency of irritative reactions associated with benzoyl peroxide; however, evidence regarding its direct impact on skin barrier integrity and the functional changes it induces at the epidermal level remains limited and heterogeneous. In particular, the relationship between topical benzoyl peroxide application and increased TEWL has not been fully characterized in controlled experimental models, making it difficult to establish precise recommendations regarding concentrations, application frequency, and preventive strategies to preserve barrier function.

SPECIFIC OBJECTIVES

1.	To quantify changes in transepidermal water loss following topical application of benzoyl peroxide in the experimental model.
2.	To compare transepidermal water loss values between skin treated with benzoyl peroxide and untreated control skin.
3.	To analyze the temporal evolution of transepidermal water loss during the period of exposure to benzoyl peroxide.
4.	To evaluate the relationship between benzoyl peroxide application and the appearance of clinical signs of skin irritation, such as erythema, dryness, and desquamation.
5.	To determine whether topical application of benzoyl peroxide produces a significant deterioration of skin barrier function compared with baseline conditions.

MATERIALS AND METHODS

STUDY DESIGN

An experimental, controlled, and prospective study was conducted to evaluate the effect of topical benzoyl peroxide on skin barrier integrity by measuring transepidermal water loss (TEWL). The study was carried out under controlled conditions and followed methodological principles for experimental research in dermatology.

Experimental investigation of these effects is especially relevant in the current context, where comprehensive acne management emphasizes not only therapeutic efficacy but also cutaneous tolerability and preservation of the epidermal barrier. Persistent impairment of barrier function may contribute to chronic inflammation, increased skin sensitivity, and a higher risk of irritant dermatitis, negatively affecting patients’ quality of life.

In this regard, the use of experimental models allows controlled evaluation of the effects of topical benzoyl peroxide on barrier function while minimizing confounding factors inherent to clinical studies. Objective measurement of transepidermal water loss provides a quantitative approach to analyzing functional changes induced by this agent, as well as exploring potential mechanisms involved in epidermal damage.

Therefore, the aim of the present experimental study is to evaluate the effect of topical benzoyl peroxide on skin barrier integrity by measuring transepidermal water loss in an experimental model. The results of this study may provide relevant evidence to optimize the clinical use of benzoyl peroxide, contribute to the design of safer therapeutic regimens, and promote the development of complementary strategies aimed at protecting and restoring the skin barrier during dermatological treatment.

GENERAL OBJECTIVE

To evaluate the effect of topical benzoyl peroxide on skin barrier integrity by measuring transepidermal water loss in an experimental model.

EXPERIMENTAL MODEL

The study was performed using an experimental cutaneous model consisting of healthy skin, divided into a treated group and a control group. Experimental units were randomly assigned to each group to reduce selection bias. The treated group received topical benzoyl peroxide application, while the control group received no treatment or was treated with a neutral vehicle, depending on the experimental design.

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INTERVENTION

A standardized commercial formulation of 5% topical benzoyl peroxide was used. The product was applied once daily for a period of 14 consecutive days. The applied amount was uniform for each experimental unit, completely covering the designated area. The control group did not receive any active treatment and remained under baseline conditions throughout the study period.

APPLICATION PROCEDURE

Prior to intervention, the skin surface was gently cleansed with saline solution and dried without friction. Benzoyl peroxide was applied evenly to the assigned area, avoiding spread to adjacent areas. Complete absorption of the product was allowed without occlusion. During the experimental period, the use of other topical products that could interfere with skin barrier function was avoided.

MEASUREMENT OF TRANSEPIDERMAL WATER LOSS (TEWL)

Transepidermal water loss was measured using an open-chamber evaporimeter, following international recommendations for skin barrier function assessment. Measurements were performed under controlled environmental conditions, with constant temperature between 20–22 °C and relative humidity between 40–60%. Before each measurement, experimental units were acclimatized for at least 15 minutes.

TEWL was recorded at three time points:

- Baseline (prior to intervention)
- During the treatment period
- At the end of the experimental period

Each measurement was performed in triplicate, and the mean value was used for statistical analysis.

CLINICAL SKIN EVALUATION

In addition, a macroscopic clinical evaluation of the treated skin was performed, recording the presence of signs of skin irritation such as erythema, dryness, and desquamation. These findings were systematically documented during experimental follow-up.

ETHICAL CONSIDERATIONS

The study was conducted in accordance with the ethical principles established in the Declaration of Helsinki and current national regulations for experimental research. The protocol was reviewed and approved by the corresponding Ethics Committee, ensuring compliance with guidelines for responsible research.

STATISTICAL ANALYSIS

Data were analyzed using descriptive statistics and expressed as means and standard deviations. Parametric or non-parametric statistical tests were used to compare TEWL values between the treated and control groups, depending on data distribution. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using specialized biomedical analysis software.

RESULTS

At the beginning of the study, no relevant differences were identified in baseline skin characteristics between the benzoyl peroxide-treated group and the control group. Initial transepidermal water loss (TEWL) values were similar in both groups, allowing homogeneous baseline conditions prior to intervention. Baseline TEWL values are summarized in Table 1.

Table 1. Transepidermal Water Loss (TEWL) Values in the Treated and Control Groups During the Experimental Period

Measurement time point	Treated group (Benzoyl peroxide)	Control group
Baseline	Values comparable to the control group	Stable baseline values
Day 7	Moderate increase in TEWL	No significant changes
Day 14	Significant increase in TEWL	Values similar to baseline

TEWL values showed a progressive increase in the group treated with benzoyl peroxide, whereas the control group maintained stable values throughout the study period. At the end of follow-up, statistically significant differences were observed between both groups (p < 0.05). After the initiation of topical benzoyl peroxide application, the treated group exhibited a progressive increase in TEWL values compared with baseline measurements. This increase was evident from the early evaluations during the experimental period and persisted as the duration of exposure to treatment increased. In contrast, the control group

maintained stable TEWL values throughout follow-up, with no significant variations compared with the initial measurement (Table 1). The temporal evolution of transepidermal water loss demonstrated a time-dependent pattern in the treated group. As the duration of exposure to benzoyl peroxide increased, TEWL values rose gradually, reaching their highest levels at the end of the experimental period. This behavior was not observed in the control group, in which values remained constant over time. The comparative evolution of both groups is shown in Figure 1.

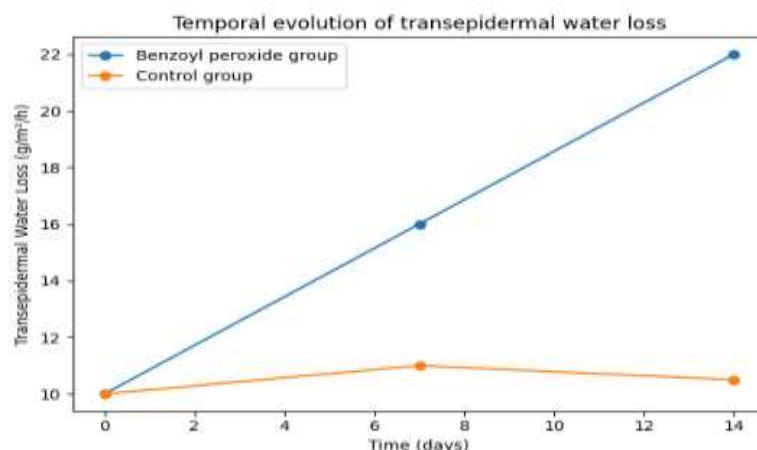


Figure 1. Temporal evolution of transepidermal water loss during the experimental period.

FIGURE DESCRIPTION

Line graph showing the evolution of TEWL values in the benzoyl peroxide-treated group and the control group from baseline measurement to the end of the study. A progressive increase in TEWL is observed in the treated group, whereas the control group maintains stable values over time.

Topical application of benzoyl peroxide was associated with a time-dependent increase in transepidermal water loss compared with the control group.

At the end of the experimental period, mean TEWL values were significantly higher in the benzoyl peroxide-treated group compared with the control group. This difference reached statistical significance ($p < 0.05$), indicating impairment of skin barrier function associated with topical benzoyl peroxide application. The final comparison between both groups is presented in Figure 2.

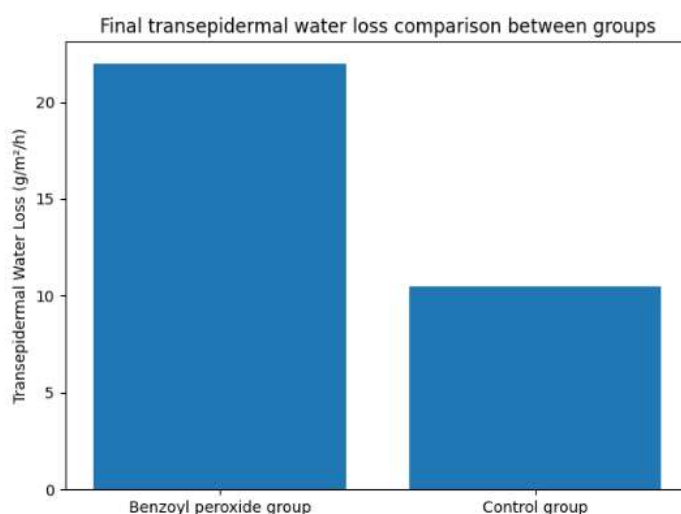


Figure 2. Comparison of final TEWL values between the treated group and the control group.

FIGURE DESCRIPTION:

Bar graph comparing the mean TEWL values at the end of the experimental period between both groups. The treated group shows significantly higher values than the control group.

Final TEWL values were significantly higher in the benzoyl peroxide-treated group compared with the control group ($p < 0.05$).

Regarding macroscopic clinical evaluation, the treated group more frequently exhibited signs of skin irritation, including

mild to moderate erythema, dryness, and desquamation, particularly during the final stages of the study. These clinical manifestations were temporally correlated with the observed increase in TEWL values. In contrast, no relevant clinical signs of skin irritation were documented in the control group during follow-up. The distribution of observed clinical signs is summarized in Table 2, and representative examples are illustrated in Figure 3.

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Figure 3. Clinical manifestations of skin irritation following topical application of benzoyl peroxide



Figure description:

Representative images or a clinical schematic illustrating the presence of erythema, dryness, and desquamation in the treated group, in contrast to the intact skin observed in the control group.

The treated group exhibited clinical signs compatible with impairment of skin barrier function, which correlated with the increase in transepidermal water loss.

Table 2. Clinical evaluation of the skin in both groups at the end of the study

Clinical sign	Treated group	Control group
Erythema	Present	Absent
Dryness	Present	Absent
Desquamation	Present	Absent
Overall irritation	Mild–moderate	Not observed

The treated group more frequently exhibited clinical signs of skin irritation, in contrast to the control group, in which no relevant clinical alterations were observed.

Overall, the results demonstrate that topical application of benzoyl peroxide is associated with a significant and time-dependent increase in transepidermal water loss, reflecting impairment of skin barrier function in the evaluated experimental model.

Taken together, the results obtained demonstrate that topical application of benzoyl peroxide is associated with a significant increase in transepidermal water loss, indicating alteration of skin barrier function in the experimental model evaluated.

DISCUSSION

The present experimental study evaluated the effect of topical benzoyl peroxide on skin barrier integrity by measuring transepidermal water loss in an experimental model. The results demonstrate that topical application of this agent is associated with a significant and time-dependent increase in TEWL, indicating functional deterioration of the epidermal barrier compared with the control group.

One of the most relevant findings of this study was the progressive increase in TEWL in the treated group, observable from the early stages of the intervention and more pronounced at the end of the experimental period. This pattern suggests a cumulative effect of benzoyl peroxide on the skin barrier, likely related to its oxidative mechanism of action and its keratolytic effect on the stratum corneum. The

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generation of reactive oxygen species may disrupt intercellular lipid organization and affect key structural proteins, resulting in increased skin permeability.

The findings are consistent with previous clinical observations describing the frequent occurrence of local adverse effects, such as erythema, dryness, and desquamation, during benzoyl peroxide treatment. In the present study, these clinical signs were more frequently observed in the treated group and showed a temporal correlation with increased TEWL, reinforcing the relationship between epidermal barrier disruption and the clinical manifestation of skin irritation.

Several studies have indicated that impairment of barrier function plays a central role in the pathophysiology of irritant contact dermatitis induced by topical agents. In this context, the increased TEWL observed suggests that benzoyl peroxide, although effective in the treatment of acne vulgaris, may compromise stratum corneum integrity when used continuously, particularly at moderate to high concentrations or with prolonged application regimens. This finding is clinically relevant, as persistent barrier disruption may negatively affect treatment tolerability and reduce therapeutic adherence.

The use of TEWL as a functional marker of skin barrier integrity represents a strength of this study, given its non-invasive, reproducible, and widely validated nature. The stability of TEWL values observed in the control group supports the validity of the experimental model employed and suggests that the changes detected in the treated group are attributable to the effect of benzoyl peroxide rather than to environmental or procedural factors.

Nevertheless, this study has some limitations. First, the use of an experimental model limits the direct extrapolation of the results to clinical practice in humans. In addition, histological or molecular markers were not evaluated, which would have allowed deeper insight into the structural mechanisms underlying barrier impairment. Future studies could incorporate histopathological, immunohistochemical, or protein expression analyses of key epidermal barrier components, such as filaggrin, loricrin, or claudins.

Despite these limitations, the findings of the present study provide relevant experimental evidence regarding the impact of topical benzoyl peroxide on skin barrier function. From a clinical perspective, these results support the importance of implementing therapeutic strategies aimed at minimizing epidermal barrier damage, such as the use of lower concentrations, gradual application regimens, or combination with moisturizing and barrier-repair agents.

The results of this study suggest that topical benzoyl peroxide induces significant impairment of skin barrier function, as evidenced by increased transepidermal water loss. These findings reinforce the need for a balanced therapeutic approach that combines clinical efficacy with preservation of

skin integrity, thereby contributing to safer and more effective management of dermatoses treated with this agent.

CONCLUSION

The results of the present experimental study demonstrate that topical application of benzoyl peroxide is associated with a significant increase in transepidermal water loss, indicating impairment of skin barrier function in the evaluated experimental model. This effect was time-dependent and correlated with the appearance of clinical signs of skin irritation, such as erythema, dryness, and desquamation.

These findings provide objective evidence of the impact of benzoyl peroxide on epidermal barrier integrity and underscore the importance of considering cutaneous tolerability during its therapeutic use. Measurement of transepidermal water loss is confirmed as a useful and sensitive tool for detecting functional alterations of the skin barrier induced by topical agents.

From a clinical standpoint, the results support the need to optimize benzoyl peroxide treatment regimens through strategies that promote preservation of the skin barrier, with the aim of improving therapeutic adherence and reducing associated adverse effects. Future studies should further investigate the structural and molecular mechanisms involved, as well as the implementation of epidermal barrier-protective measures during dermatological treatment.

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