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The Effect of Cucumber (*Cucumis sativus*) Extract Cream on VEGF and IL-10 in Xerotic Rats

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Abstract: Xerosis cutis is a chronic dry skin condition aggravated by impaired skin barrier function and increased transepidermal water loss (TEWL). Decreased levels of interleukin-10 (IL-10) and vascular endothelial growth factor (VEGF) contribute to prolonged inflammation and hinder tissue regeneration. Cucumber (*Cucumis sativus*) contains flavonoids and vitamin C, which possess anti-inflammatory and angiogenic properties, making it a promising candidate for natural topical therapy. This study aimed to determine the effect of cucumber extract cream on IL-10 and VEGF levels in the skin of female Wistar rats with grade II xerosis cutis induced by acetone and ethanol. This experimental research employed a post-test only control group design. A total of 30 Wistar rats were randomly divided into five groups: normal control, negative control, positive control (10% ceramide cream), and two treatment groups receiving cucumber extract cream at concentrations of 3% and 5%. Following the induction of xerosis, the respective creams were applied topically for 14 consecutive days. Results showed that administration of 5% cucumber extract cream significantly increased VEGF levels (715.75 ± 152.65 ng/L) and IL-10 levels (200.35 ± 43.49 pg/mL) compared to the negative control (VEGF 494.29 ± 95.05 ng/L; IL-10 120.62 ± 22.11 pg/mL, $p<0.05$). The 3% cucumber extract cream also elevated VEGF (522.96 ± 115.48 ng/L) and IL-10 (197.86 ± 31.32 pg/mL), though less effectively than the 5% formulation. Meanwhile, the group treated with ceramide 10% cream showed increases in VEGF (694.87 ± 180.52 ng/L) and IL-10 (140.85 ± 32.42 pg/mL), indicating that cucumber extract at 5% comparable to ceramide therapy. In conclusion, cucumber extract cream, particularly at 5% concentration, significantly enhances IL-10 and VEGF levels in the skin of xerosis cutis model rats. These findings indicate its potential as an effective natural topical therapy for reducing inflammation and promoting skin regeneration in xerosis cutis caused by chemical exposure.
Keywords: Anti-inflammatory; cucumber; interleukin-10; xerosis cutis.

INTRODUCTION

Xerosis cutis, or chronic dry skin, is a common dermatological disorder characterized by disruption of the skin barrier and increased transepidermal water loss (TEWL). (Torshina, 2024) Current approaches for treating xerosis cutis predominantly involve moisturizers, which effectively increase skin hydration; however, some products can cause irritation or prove less effective at improving skin barrier function. (Augustin et al., 2019) Therefore, safer, more innovative, and molecular-based therapeutic alternatives are needed, including new ways to utilize natural base ingredients with anti-inflammatory and regenerative properties, such as cucumber (*Cucumis sativus*). Cucumber s one such natural agent, selected for its high vitamin

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C and flavonoid content, which act as antioxidants, aid collagen synthesis, and accelerate skin regeneration. Additionally, cucumbers' anti-inflammatory properties help balance skin pH and soothe irritation, and their topical application has been shown to improve hydration and restore skin barrier function. (Insanu et al., 2021; Sahu & Sahu, 2015)

The prevalence of xerosis cutis in Indonesia ranges from 50% to 80%. While several other countries, such as Brazil, Australia, and Turkey, report a prevalence of 35%-70%. (Kusumaningrum & Widayati, 2017) Extrinsic factors such as UV exposure, pollution, detergents, and irritant chemicals like acetone and ethanol can damage epidermal lipids and natural moisturizing factor (NMF), Intrinsic factors such as aging, genetic disorders, and epidermal lipid deficiency further exacerbate water loss and could impair skin regeneration. The Overall Dry Skin Score (ODS) classification by EEMCO categorizes xerosis cutis on a scale of 0-4. The most severe condition is characterized by extremely dry, scaly skin that is prone to cracking. (Augustin et al., 2019; Gimenez-Arnau, 2014)

Interleukin-10 (IL-10) and Vascular Endothelial Growth Factor (VEGF) are considered critical keys in the inflammatory processes associated with xerosis cutis. IL-10 functions as an anti-inflammatory cytokine that suppresses pro-inflammatory mediators such as TNF-α and IL-6, while VEGF increases angiogenesis and the supply of oxygen and nutrients, accelerating skin regeneration,on other hand IL-10 is secreted by regulatory T cells, macrophages, monocytes, dendritic cells, and other immune cells, acting centrally in maintaining immune homeostasis and preventing excessive tissue-damaging inflammation (Saraiva et al., 2020) all the while VEGF predominantly found in the epidermis and dermis, is produced by keratinocytes, fibroblasts, and macrophages in response to hypoxia or injury, and plays a key role in wound healing by inducing endothelial proliferation and vascular permeability (Belvedere et al., 2022). Among its isoforms, VEGF-A is most widely studied, acting via VEGFR-2 to activate downstream signaling pathways, such as PI3K/AKT and ERK1/2, that regulate cell proliferation, migration, and survival (Chen et al., 2024). Exposure to extrinsic substances that damage the skin barrier can lead to excessive production of Reactive Oxygen Species (ROS). ROS triggers oxidative stress and cell damage, exacerbates inflammation, and inhibits tissue regeneration. An imbalance between IL-10 and VEGF, driven by increased ROS, leads to uncontrolled inflammation and impaired skin regeneration. (Johnson et al., 2020; Stanca Melincovici et al., 2018; Wise et al., 2020)

Previous research has indicated the potential of cucumber extract to suppress inflammation and increase IL-10 levels. A study by Bernardini et al. (2018) reported that the aqueous/ethanol extract of cucumber can inhibit lipopolysaccharide (LPS)-induced inflammation in endothelial cells, increase IL-10 levels, and reduce inflammatory angiogenesis. However, this study was limited to cellular models and has not yet evaluated its effects on skin barrier disorders such as xerosis cutis induced by extrinsic factors. Xerosis cutis caused by extrinsic factors is characterized by impaired skin homeostasis, increased levels of inflammatory mediators, and an imbalance between IL-10 and VEGF. Therefore, highlights the need for further evaluation of the potential of cucumber extract as an anti-inflammatory and immunomodulatory agent in this condition. (Bernardini et al., 2018)

Another study by Wise et al. (2020b) found that a combination of VEGF-E and IL-10 from the Orf virus accelerated wound healing in female Wistar rats. VEGF-E promotes angiogenesis without excessive inflammation, while viral IL-10 (ovIL-10) suppresses pro-inflammatory cytokines. These two proteins were obtained by

recombination in HEK293-EBNA cells, purified, and administered subcutaneously. This combination improves re-epithelialization, endothelial cell density, and reduces fibrosis. However, this research is still limited to recombinant proteins and has not explored the potential of natural ingredients like cucumber. (Wise et al., 2020)

Various studies have shown that cucumber (*Cucumis sativus*) extract possesses antioxidant, anti-inflammatory, and angiogenic properties, supporting skin hydration, barrier function, and wound healing. Amani et al. (Amani et al., 2024) reported that the antioxidant and anti-inflammatory activity of cucumber extract was comparable to synthetic standards, while Jadhav et al. (Jadhav et al., 2024) demonstrated the stability and non-irritating nature of cucumber-based facial gel formulations. Bernardini et al. (2018) also confirmed that cucumber extract increased IL-10 levels and inhibited pro-inflammatory angiogenesis.

Collectively, these studies suggest that cucumber extract has the potential to modulate IL-10 and VEGF, which play a key role in inflammation and skin regeneration (Bernardini et al., 2018; Wise et al., 2020). An imbalance in these two proteins due to extrinsic factors, such as exposure to alcohol, detergents, and pollution, can impair skin regeneration and exacerbate inflammation (Lacy & Ziemer, 2020). However, most existing research has been limited to in vitro or non-skin models and has not specifically examined xerosis cutis induced by extrinsic factors such as acetone, ethanol, detergents, or environmental pollutants. This leaves an important gap, as xerosis cutis caused by barrier-disrupting agents is highly prevalent yet poorly studied in relation to natural topical therapies. To date, studies comprehensively evaluating whether cucumber extract cream can restore the balance between IL-10 and VEGF in an in vivo model of xerosis cutis remain limited.

This study aims to fill that gap by testing the effects of cucumber extract cream (3% and 5%) on IL-10 and VEGF expression in Wistar rats with chemically induced xerosis cutis. The results are expected to contribute to the development of natural ingredient-based topical therapies as agents to reduce inflammation and improve the skin barrier due to environmental factors, as well as support skin hydration, barrier restoration, and tissue regeneration.

MATERIALS AND METHODS

This in vivo study employed a post-test-only control group design to evaluate the effect of cucumber (*Cucumis sativus*) extract cream on VEGF and IL-10 levels in a rat model of grade II xerosis cutis. The research design used a completely randomized design (CRD) with five groups: one normal control group (K1), one negative control (K2) with xerosis but no treatment, one positive control (K3) treated with 10% ceramide cream, and two treatment groups receiving cucumber extract cream at concentrations of 3% (K4) and 5% (K5). These groups were established to assess the topical formulation’s impact on skin hydration, barrier function, and inflammation resolution.

The independent variable in this study was the concentration of cucumber extract cream administered topically in two formulations: 3% and 5%. The dependent variables included skin levels of vascular endothelial growth factor (VEGF) and interleukin-10 (IL-10), measured in pg/mL using ELISA, and skin hydration, assessed visually using the Overall Dry Skin Score (ODS). To minimize external influence, environmental variables such as laboratory temperature and humidity were strictly controlled, while Skin hydration and barrier integrity were evaluated visually using a scoring scale (0–4) adapted from clinical dry skin assessment tools.

Thirty healthy female Wistar rats (*Rattus norvegicus*), aged 10–12 weeks and weighing 200-250 grams, were used in the experiment. Female rats were specifically selected to ensure hormonal consistency, as hormonal fluctuations, particularly testosterone and estrogen, can influence skin physiology, immune response, and healing. All animals were confirmed to be healthy and free of dermatological disorders prior to the study and were sourced from the Indonesian Biological Laboratory (IBL) and Sultan Agung Islamic University, Semarang. The animals underwent a 7-day acclimatization period before treatment.

Simple random sampling was used to assign the 30 rats into five equal groups, with six rats per group. The grouping included one healthy control and four groups with induced xerosis, ensuring an unbiased distribution of samples. Healthy rats within the specified weight range met the inclusion criteria, while those with visible signs of illness or skin conditions met the exclusion criteria. Rats that died or developed secondary skin issues during the study were excluded as dropouts.

A range of laboratory equipment was used, including ELISA readers, centrifuges, micropipettes, digital microscopes, hot plate stirrers, and cryotubes. Materials included acetone, ethanol, standard rat feed, cucumber extract, ceramide base cream, and ELISA kits with specific antibodies for VEGF and IL-10 detection. The cucumber extract was sourced from PT. Menjangan Sakti, and the cream base was obtained from PT. Derma Elok Farma is manufactured in accordance with cosmetic-grade specifications.

Before the experiment, the dorsal skin of each rat was shaved with an electric clipper to induce xerosis. Grade II xerosis was induced by applying a 1:1 mixture of 70% acetone and ethanol with sterile cotton to a 3×3 cm skin area twice daily for seven consecutive days. The induction was considered successful once the skin showed moderate dryness, scaling, and pale appearance; meanwhile, the cucumber extract cream was prepared by blending the extract (3% or 5% w/w) into the cream base. The formulation process involved gentle heating (40–50°C) and stirring to ensure homogeneity. Once mixed, the cream was cooled, packed into sterile cosmetic jars, and stored in a dry, cool environment away from sunlight. The final cream was tested for pH (5.5–7.0), viscosity, spreadability, adhesion, and stability.

Once xerosis was successfully induced, treatment began. Throughout the treatment phase, the skin condition was monitored daily using a calibrated digital microscope (magnification 50x–200x) to assess hydration, texture, and inflammation. Images were captured under standardized lighting and distance, coded for each subject, and stored in high resolution for documentation and further analysis.

At the end of the 14-day treatment period, on day 15, skin tissue samples were collected and processed for VEGF and IL-10 analysis using ELISA. These biomarkers were quantified to determine the anti-inflammatory and pro-regenerative effects of cucumber extract cream in a chemically induced xerosis cutis model.

Ethical Clearance

This study used animal models and was conducted in accordance with institutional and national guidelines for the ethical treatment of laboratory animals. Prior to the experiment, the research protocol was reviewed and approved by the Ethics Committee of the Faculty of Medicine, Sultan Agung Islamic University, Semarang, No. 220/V/2015/KOMISI BOITIK, and conducted at the IBL Clinical Laboratory in Semarang from May to July 2025. All procedures were designed to ensure animal welfare, including appropriate handling, housing conditions, and humane treatment. Tissue sampling was performed under anesthesia to minimize pain and distress.

Flavonoid Content Analysis

The flavonoid content, particularly fisetin, in the cucumber (*Cucumis sativus*) extract was determined using either UV-Vis spectrophotometry or High-Performance Liquid Chromatography (HPLC). For the UV-Vis method, the extract was dissolved in methanol and reacted with aluminum chloride ($AlCl_3$) to form a flavonoid–$AlCl_3$ complex, which exhibits maximum absorbance at approximately 430 nm. The absorbance values were compared to a fisetin standard curve to quantify flavonoid levels. (Abriyani et al., 2024; Dzakwan & Priyanto, 2019)

Alternatively, HPLC analysis was performed for higher precision. The extract solution was injected onto a reverse-phase C18 column, using a gradient of water (acidified with formic acid) and methanol or acetonitrile. The fisetin retention time was determined by comparison with known standards, and its concentration was calculated from a calibration curve. Results were expressed as mg of fisetin per gram of dried extract. (Abriyani et al., 2024; Dzakwan & Priyanto, 2019)

VEGF and IL-10 Analysis

The concentrations of Vascular Endothelial Growth Factor (VEGF) and *Interleukin*-10 (IL-10) in skin tissue were measured using the Enzyme-Linked Immunosorbent Assay (ELISA) method. Skin samples were collected from treated Wistar rats and homogenized in lysis buffer containing phosphate-buffered saline (PBS) and protease inhibitors to preserve protein integrity.

The homogenates were centrifuged at 10,000 × g for 15–20 minutes at 4 °C to obtain the supernatant, which contained soluble proteins. ELISA plates were pre-coated with primary antibodies specific to VEGF and IL-10. Sample supernatants and standard solutions were added to the wells, followed by incubation at room temperature or 37 °C, as specified in the kit protocol.

After incubation, TMB (3,3′,5,5′ tetramethylbenzidine) substrate was added to initiate color development. The intensity of the resulting color, proportional to VEGF or IL-10 concentration, was measured at 450 nm using a microplate reader. Sample concentrations were determined by comparison to a standard curve. These data were used to evaluate the anti-inflammatory and pro-regenerative effects of cucumber extract cream in a grade II xerosis cutis model (Invitrogen Corporation, n.d).

Data Analysis

The collected data were edited, processed, and tabulated prior to statistical evaluation. To ensure appropriate statistical methods were applied, the normality of the data distribution was assessed using the Shapiro-Wilk test, and homogeneity of variance was evaluated using Levene's test.

Based on the results of these preliminary tests, the data analysis was carried out accordingly. The VEGF level data met the assumptions of normality and homogeneity, thus permitting the use of parametric analysis. *A one-way analysis of variance* (ANOVA) was employed to determine significant differences among all experimental groups, followed by a Least Significant Difference (LSD) post hoc test to identify specific intergroup differences.

In contrast, the IL-10 level data did not follow a normal distribution and were not homogeneous. Therefore, a non-parametric approach was used. The *Kruskal-Wallis* test was applied to evaluate differences across all groups, with subsequent pairwise comparisons conducted using the *Mann-Whitney* U test. A significance level of $p < 0.05$ was set for all statistical tests to determine meaningful differences in biomarker expression between treatment groups.

RESULTS AND DISCUSSION

Quantification of Flavonoid and Ascorbic Acid Content in Cucumber Extract

Measurements of total flavonoid levels showed a very strong correlation between quercetin concentration and absorbance values. The absorbance of the cucumber extract was measured three times at concentrations of 10,000 ppm, with values of 0.331, 0.346, and 0.326, with an average absorbance of 0.334. Based on the curve equation, the total flavonoid content in the extract was 20.9 mg/L, equivalent to 0.0021 mg QE/g extract. Meanwhile, the vitamin C content in the cucumber extract was found to be 9.588 ppm. After a 1,000-fold dilution, the vitamin C content in the original sample was 95.88%. This indicates that the cucumber extract contains high levels of vitamin C, which has the potential to act as a powerful antioxidant.

However, compared to other studies, the flavonoid content obtained in this extract is lower. For instance, Shah et al. (2024) reported that cucumber peel extracted with 50% ethanol contained 1.20 mg QE/g for the regular variant and 2.20 mg QE/g for the Japanese variant (Mu'azzam Shah et al., 2024) . This difference may be attributed to the use of whole fruit in our study rather than peel alone, as well as the choice of extraction solvent, since polarity strongly influences flavonoid yield.

By contrast, the vitamin C concentration in this extract (~95.9 mg/L) is consistent with values reported in previous analyses of cucumber fruit, which ranged between 10.17 and 12.05 mg per 100 g fresh weight (Onyenweaku & Kesa, 2024) . The relatively high concentration obtained here suggests efficient recovery of ascorbic acid, which is significant because vitamin C is a potent antioxidant, supports collagen synthesis, and enhances angiogenesis via VEGF upregulation. These mechanisms may synergize with flavonoids, even at modest levels, to contribute to the observed therapeutic effects in xerosis cutis.

Macroscopic Validation of the Skin Tissue of the Model

Observations in the K2 group, which had been topical induction with 70% acetone and ethanol (1:1) for seven days, revealed significant changes in skin morphology. The skin surface showed small to moderate scaling, with a rough texture and a pale white discoloration. These characteristics correspond to an ODS score of category 2. This indicates that moderate xerosis cutis has developed. This pathological condition was used as a basis to evaluate the effectiveness of cucumber extract cream in improving clinical and molecular skin parameters.

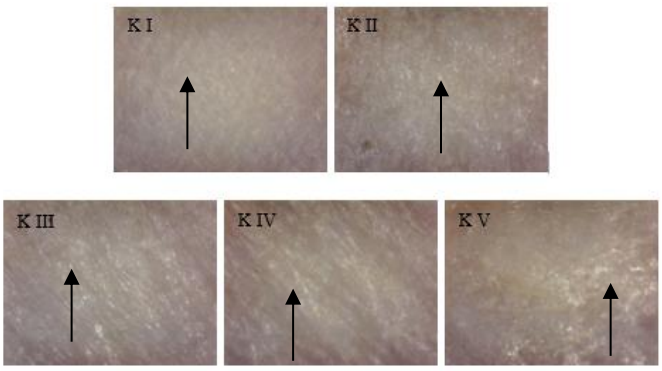

Figure 1. Macroscopic View of the Rat Skin on Day 1 of Treatment in Each Experimental Group; The normal control (K1) showed smooth, moist skin without abnormalities, while the negative control (KII) displayed roughness and scaling at the arrow-marked site. The ceramide 10% group (KIII) also showed dull skin with scaling, whereas the cucumber extract 3% (KIV) and 5% (KV) groups exhibited

rough texture and discoloration. Arrows indicate areas of macroscopic abnormalities (roughness, scaling, and discoloration) resulting from xerosis induction.

Observations on the first day of treatment showed the healthy control group (K1) exhibited a smooth, moist skin surface with no macroscopic abnormalities, indicating a normal skin condition. In contrast, the treatment groups K2, K3, K4, and K5 demonstrated visual changes consistent with Grade II xerosis cutis. The skin surface in this group displayed roughness, fine to moderate scales, and a duller or paler coloration. The differences between group K1 and the other groups confirmed the initial success of the induction procedure in producing a model of xerosis cutis suitable for testing topical therapy in treatment groups K2, K3, K4, and K5.

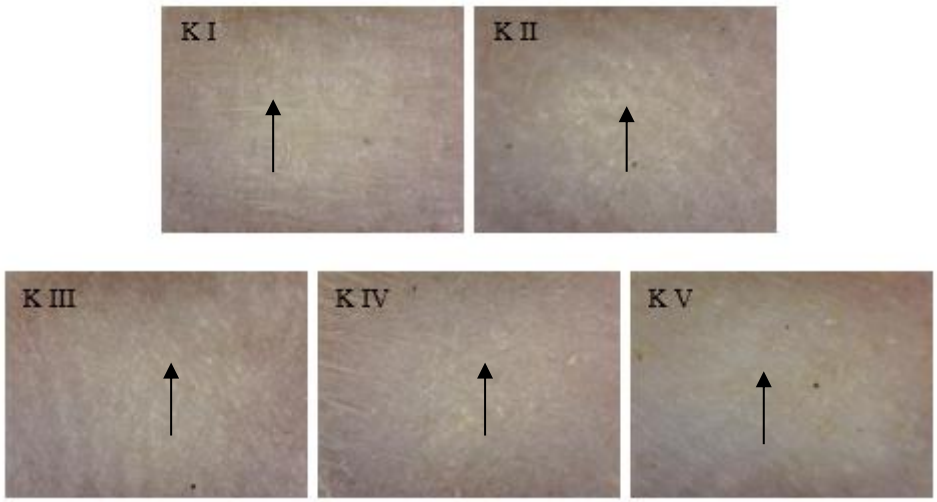

Figure 2. Macroscopic View of Rat Skin on Day 14 of Treatment in Each Experimental Group; The normal control (KI) maintained smooth skin without abnormalities, while the negative control (K II) still showed mild roughness and discoloration at the arrow-marked site. The ceramide 10% group (K III) and cucumber extract 5% group (K V) demonstrated the best recovery, with smoother skin and minimal scaling. The cucumber extract 3% group (K IV) also improved but less than K III and K V. Arrows indicate areas of residual abnormalities or recovery.

By day 14, all treatment groups showed varying degrees of improvement. The K1 (healthy control), maintained normal physiological conditions, while K2 (xerosis without treatment) continued to show slightly rough skin with a slightly paler coloration. indicating persistent dryness, in contrast with the groups who received topical treatment, showed signs of marked improvement. Specifically, in K3 (10% ceramide cream) and K5 (5% cucumber extract cream), both groups demonstrated significant recovery, with visually smoother skin texture and markedly reduced scaling, bringing the skin closer to normal skin condition.

The persistence of roughness and paleness in the untreated xerosis group (K2), in contrast to the marked recovery observed in the ceramide (K3) and 5% cucumber extract (K5) groups, underscores the restorative effects of both treatments on skin barrier function. Ceramide-based moisturizers are known to replenish stratum corneum lipids, effectively reducing transepidermal water loss (TEWL) and restoring barrier integrity (e.g., formulations with ceramides 1, 3, and 6-II demonstrate controlled release and prolonged hydration) (Danby et al., 2020; Wang et al., 2024). Clinically,

ceramide regimens have been shown to significantly improve xerosis symptoms and overall skin quality of life within four weeks (Abbad-Jaime de Aragon et al., 2025)

Therefore, the similar degree of improvement in K5 compared to K3 implies that a 5% cucumber extract cream can perform comparably to ceramide therapy in restoring skin structure and appearance in chemically induced xerosis. The less pronounced, but still meaningful recovery in K4 (3% cucumber) supports a dose-dependent efficacy. Taken together, these results highlight cucumber extract's potential as a natural, accessible alternative to ceramide-based treatments for xerotic skin, particularly in contexts where synthetic lipids are inaccessible or undesirable.

It is shown that cucumber extract, which is rich in ascorbic acid and antioxidants, has demonstrated hydrating, soothing, anti-inflammatory, and skin-brightening properties in dermatological applications(Murad & Nyc, 2016). Its benefits likely stem from supporting barrier repair via antioxidant activity, modulating inflammation, and reducing TEWL through ingredients such as phytosterols.

Analysis of VEGF and IL-10 Levels in Rat Skin Tissue Across Treatment Groups

The mean levels of Vascular Endothelial Growth Factor (VEGF) and *Interleukin*-10 (IL-10) in rat skin tissue were analyzed using the Enzyme-Linked Immunosorbent Assay (ELISA) method. The results are summarized in Table 1, with visual representations provided in Figures 3 and 4.

Table 1. Mean VEGF (ng/L) and IL-10 (pg/mL) Levels in Each Group

Variable	**Group**					**p**
	K1 Mean±SD	K2 Mean ±SD	K3 Mean±SD	K4 Mean±SD	K5 Mean±SD	
Levels VEGF (ng/L)	515.42 ± 116.72	494.29 ± 95.05	694.87 ± 180.52	522.96 ± 115.48	715.75 ± 152.65	
Saphiro wilk	0. 314	0.275	0.621	0.894	0.994	
Levene's Test						0.456
One Way Anova						0.016
Levels IL-10 (pg/mL)	115.45 ± 26.77	120.62 ± 22.11	140,85 ± 32.42	197,86 ± 31.32	200.35 ± 43.49	
Saphiro wilk	0.197	0.991	0.888	0.623	0.031	
Levene's Test						0.668
Kruskal Wallis						0.001

Note:
Uji Saphiro Wilk (p > 0,05) = normal
Levene's Test (p > 0,05) = homogen
One Way Anova (p<0,05) = significant
Kruskal Wallis (p<0,05) = significant

VEGF levels were highest in the group treated with 5% cucumber extract cream (K5), reaching 715.75 ± 152.65 ng/L. This was followed by the 10% ceramide cream group (K3) at 694.87 ± 180.52 ng/L, and the 3% cucumber extract group (K4) at 522.96 ± 115.48 ng/L. The normal control (K1) measured 515.42 ± 116.72 ng/L, while the untreated xerosis model (K2) showed the lowest level at 494.29 ± 95.05 ng/L.

The Shapiro-Wilk test indicated a normal distribution in all groups (p > 0.05), and Levene's test confirmed homogeneity of variance (p = 0.456). These results permitted the use of One-Way ANOVA, which revealed a statistically significant difference in VEGF levels across the groups (p = 0.016).

Further analysis using the LSD *post hoc* test showed that the VEGF level in K5 was significantly higher than in the healthy control group (K1) (p = 0.017), suggesting that the 5% cucumber extract cream not only restored VEGF expression but also enhanced it beyond normal physiological levels. A significant difference was also observed between the untreated group (K2) and both K3 (p = 0.017) and K5 (p = 0.009), indicating that both treatments effectively reversed VEGF suppression caused by xerosis cutis. Additionally, VEGF levels in K3 differed significantly from both K1 (p = 0.031) and K4 (p = 0.038), while K5 showed higher levels than K4 (p = 0.021), reinforcing the dose-dependent effectiveness of cucumber extract in promoting angiogenesis.

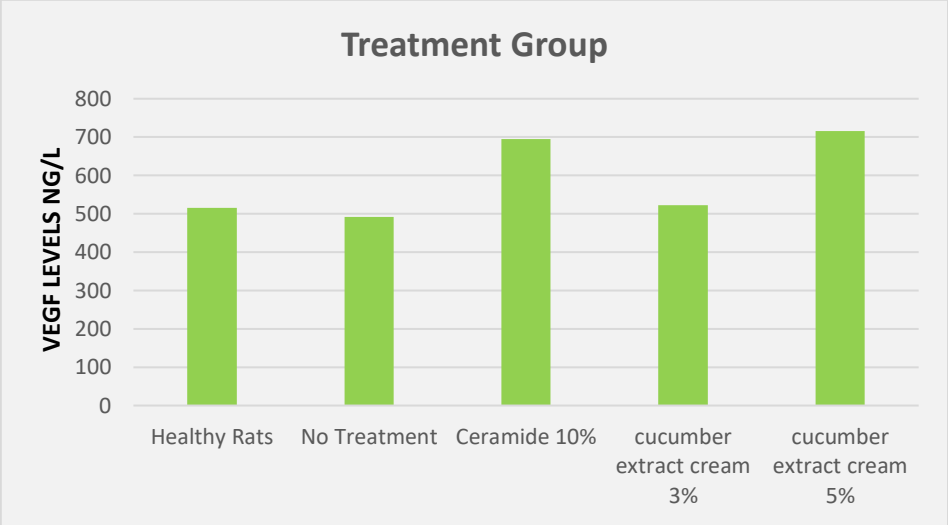

Figure 3. Mean VEGF Levels in Each Treatment Group

IL-10 levels followed a similar pattern. The highest mean IL-10 concentration was found in the K5 group (200.35 ± 43.49 pg/mL), followed closely by K4 (197.86 ± 31.32 pg/mL), with K3 at 140.85 ± 32.42 pg/mL, K2 at 120.62 ± 22.11 pg/mL, and K1 at 115.45 ± 26.77 pg/mL. However, the Shapiro-Wilk test revealed that the K5 group did not meet the normality assumption (p = 0.031), so the Kruskal-Wallis test was applied, which showed a statistically significant difference among all groups (p = 0.001).

Pairwise comparisons using the Mann-Whitney U test indicated that IL-10 levels in both K4 and K5 were significantly higher than those in the healthy control group (K1) (p = 0.006 and p = 0.004, respectively), as well as the untreated group (K2) (p = 0.004 for both). These results confirm that cucumber extract cream—particularly at 5% concentration—can significantly elevate IL-10 expression compared to both untreated and healthy skin.

Moreover, both cucumber extract treatment groups (K4 and K5) also showed significantly higher IL-10 levels than the ceramide cream group (K3), with *p-values* of 0.020 and 0.025, respectively. This suggests that cucumber extract may offer superior immunomodulatory benefits compared to standard ceramide-based topical therapy. These findings support the potential of cucumber extract cream, especially at 5%, not only to restore but also to enhance anti-inflammatory cytokine production, positioning it as a strong candidate for the topical treatment of xerosis cutis.

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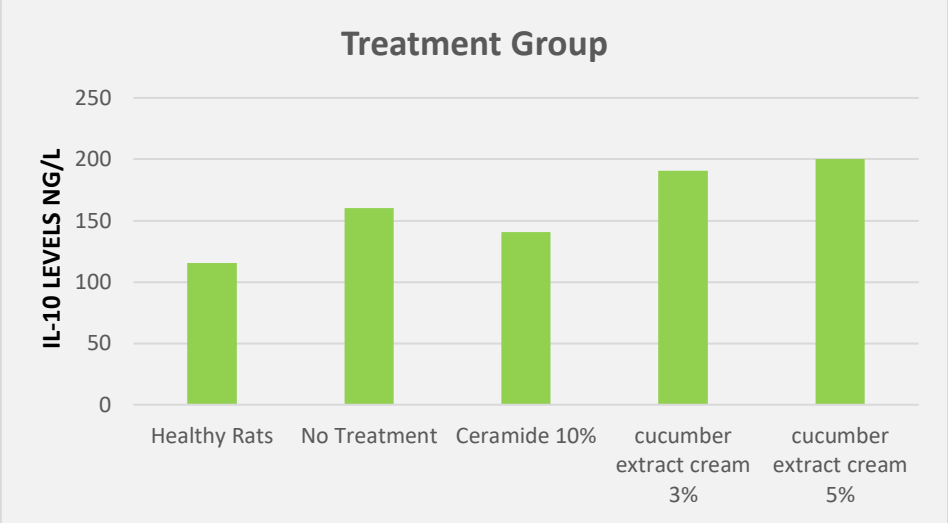

Figure 4. Mean IL-10 Levels in Each Treatment Group

Together, the statistical results and biological responses presented here indicate that cucumber extract cream, particularly at 5%, significantly improves both angiogenic and anti-inflammatory markers in skin affected by xerosis cutis. These improvements are dose-dependent and, in some cases, exceed those of conventional ceramide-based treatments. This highlights the potential of cucumber extract as a natural, effective, and safer alternative for managing moderate skin barrier dysfunction.

A comparable relationship between VEGF and anti-inflammatory factors such as IL-10 in promoting skin repair has been demonstrated in murine wound models. For instance, recombinant VEGF-E combined with viral IL-10 produced more robust vascularization and scar reduction than either agent alone, highlighting a synergistic effect in skin regeneration. (Wise et al., 2020b)

Mechanistically, cucumber extract contains flavonoids and vitamin C, known for their antioxidative and immunomodulatory properties. These phytochemicals may stimulate endogenous VEGF production and shift macrophage polarization toward the M2 (healing) phenotype, thereby elevating IL-10 while reducing oxidative stress—paralleling pathways documented for other botanical extracts (Michalak, 2023)

Nevertheless. This study provides important insights into the potential of cucumber extract cream for the treatment of xerosis cutis, but several limitations should be acknowledged. First, the treatment duration was relatively short (14 days), which may not reflect long-term efficacy or safety. Chronic xerosis often requires extended management, and longer studies are needed to confirm sustained benefits. Second, the use of a rat model limits generalizability to humans, as differences in skin physiology and immune response may affect outcomes (Danby et al., 2020). Third, the sample size (six rats per group) was modest, reducing statistical power and potentially overlooking subtle effects. Fourth, only macroscopic and molecular markers (IL-10 and VEGF) were assessed; histopathological evaluations and broader cytokine profiling could provide a more comprehensive understanding of skin barrier recovery. Lastly, this study used a single extract preparation method and two concentrations (3% and 5%); different formulations or delivery systems (e.g., gels, nanocarriers) might alter bioavailability and effectiveness (Jadhav et al., 2024). Future research should include larger cohorts, extended treatment periods, histological assessments, and human clinical trials to validate cucumber extract as a natural alternative to ceramide-based therapy.

CONCLUSION

The application of 5% cucumber (*Cucumis sativus*) extract cream demonstrated significant therapeutic potential in improving skin hydration, barrier function, and molecular markers of inflammation and angiogenesis in a Wistar rat model of grade II xerosis cutis. Compared to the 10% ceramide cream, the cucumber extract formulation showed equal or superior effects in elevating VEGF and IL-10 levels, suggesting its dual structural and biological benefits. These findings support the efficacy of cucumber extract cream as a natural topical agent for the management of moderate xerosis cutis. However, it must be emphasized that this research is still at the preclinical stage using an animal model. Further studies are recommended with extended induction and treatment durations, as well as histopathological assessments, to observe deeper and more sustained molecular changes. Caution should be exercised in generalizing these findings to human applications, given species-specific differences in skin physiology and immune responses. Nonetheless, cucumber extract cream holds promise for future clinical development as a plant-based alternative in skin barrier therapy.

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CONFLICT OF INTEREST

The author affirms that there are no conflicts of interest associated with the publication of this research.

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