

RESEARCH ARTICLE

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The Effects of Kombucha Extract Cream in Modulating EGF and IL-10 Levels in Xerosis-Like Model

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Background: Xerosis leading to chronic pruritus and increased inflammation. Current treatment like urea, may induce itching, burning and stinging sensations in some patients. Kombucha extract exhibits antioxidant, anti-inflammatory, and moisturizing properties; however, evidence on the effects of green tea kombucha extract cream on IL-10 and EGF in xerosis remains limited. This study investigates the effects of kombucha extract cream on epidermal growth factor (EGF) and interleukin-10 (IL-10) represent epidermal generation and inflammation resolution in xerosis-like rat model.

Materials and methods: Experimental study employed 30 male Wistar rats divided into five groups, consisting of healthy control (G1), negative control (cream base) (G2), positive control (5% urea cream) (G3), treatment groups receiving 10% (G4) and 20% (G5) kombucha extract cream. Xerosis induction by applying 5% SLS for nine days, topical treatments were applied for seven days. EGF and IL-10 levels were measured from skin tissue using ELISA. EGF data analyzed using One-Way ANOVA and post hoc Tamhane. IL-10 data were analyzed using Kruskal-Wallis and Mann-Whitney ($p < 0.05$).

Results: The highest mean EGF levels were observed in G4 (665.96 ± 17.74 ng/L) and the lowest in G3 (573.88 ± 25.09 ng/L). One-Way ANOVA revealed a significant difference in EGF levels across groups ($p = 0.006$). Regarding IL-10 levels, the highest mean was found in G1 (201.41 ± 20.41 pg/mL) and the lowest in G4 (181.60 ± 3.42 pg/mL). The Kruskal-Wallis showed a significant difference in IL-10 levels across treatment groups ($p = 0.013$).

Conclusion: Topical 10% kombucha extract cream increased EGF levels and modulated IL-10 in a xerosis-like rat model, highlighting its potential as a topical agent to enhance the skin repair process in xerotic conditions.

Keywords: *skin barrier repair, EGF, IL-10, topical antioxidant, Wistar rats, sodium lauryl sulfate*

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Introduction

Xerosis remains a significant dermatological condition, affecting up to 85% of adults globally and 53% of dermatological cases in Indonesia.¹⁻³ Beyond surface dryness, severe pruritus triggers chronic scratching, which increases the risk of dermatitis, skin desquamation, and fissures. These conditions are susceptible to secondary infection and potentially reduce quality of life.⁴ The primary triggers of xerosis are often associated with frequent skin contact with common household substances, particularly essential products such as soaps, detergents, and solvents.^{5,6} Current management relies on moisturizers, with urea-based creams as the first-line therapy. However, urea lacks of antioxidant and anti-inflammatory effects and may cause irritation with long-term use. Consequently, there is a necessity for alternative natural therapies that provide antioxidant and anti-inflammatory benefits alongside better tolerability.^{7,8}

At the molecular level, xerosis impairs epidermal regeneration by reducing EGF activity. EGF binds to the epidermal growth factor receptor (EGFR), stimulating the proliferation, migration, and differentiation of keratinocyte and fibroblast to accelerate re-epithelialization and tissue repair. Beyond impaired repair, xerosis-induced inflammation is mediated through NF- κ B activation. IL-10 acts as a key counter-regulatory anti-inflammatory cytokine to maintain immune homeostasis.^{9,10}

Kombucha is a natural fermented beverage produced through the fermentation of tea by a symbiotic culture of bacteria and yeast (SCOBY). Recently, kombucha trends have shifted from beverages to skincare products. Kombucha contains various bioactive compounds, including organic acids, polyphenols, flavonoids, B-complex vitamins, and exopolysaccharides. These components exhibit antioxidant and anti-inflammatory activities, as well as moisturizing properties.^{11,12} Previous studies have demonstrated that green tea-based kombucha (*Camellia sinensis*) contains high levels of catechins, particularly epigallocatechin gallate (EGCG), which support anti-inflammatory activity and promote epidermal regeneration.¹³ Furthermore, a study published in 2025 reported that a coffee-derived kombucha extract moisturizer was effective in improving dry skin conditions.¹⁴ Nevertheless, study investigating the effects of green tea kombucha extract cream on the modulation of the anti-inflammatory cytokine IL-10 and the epidermal regeneration biomarker EGF in xerosis management remains

limited. This study addresses a critical gap by evaluating the effects of greentea kombucha extract cream on EGF and IL-10 in a xerosis-like model.

Materials and methods

Experimental Design

The research subjects were male Wistar rats with body weights ranging from 180 to 220 g. Thirty healthy rats meeting the inclusion criteria were randomly allocated into five groups using a simple randomization method. The sample size for the three control and two treatment groups followed Federer's formula, which suggested a minimum of five rats per group, with one additional reserve per group to anticipate potential dropouts. Exclusion criteria included rats with morphological abnormalities, and any rats that died during the experimental period were considered dropouts.

The groups were defined as follows: group 1 (G1) consisted of healthy rats group without xerosis induction or treatment; group 2 (G2) the negative control, received xerosis-like induction and was treated with cream base only; group 3 (G3) the positive control, received xerosis-like induction and was treated with 5% urea cream; group 4 (G4) received xerosis-like induction and was treated with 10% kombucha extract cream; while group 5 (G5) received xerosis-like induction and was treated with 20% kombucha extract cream.

Kombucha Extract Cream Preparation

Kombucha cream concentrations were selected based on prior studies, where a 10% concentration demonstrated optimal skin repair results. This was adopted as the baseline dose for the current study, with a double concentration (20%) included as a comparative dose. The green tea kombucha extract used in this study was obtained in powdered form from PT. Provital Group and was standardized for its key active compounds to ensure consistency. According to the certificate of analysis (Batch No. LSM250305), the extract contained 4.3% polyphenols and 7.9 mg/kg acetic acid, which are the primary constituents responsible for its antioxidant and anti-inflammatory properties.

The 10% cream was prepared by mixing 10 g of kombucha extract with 90 g of cream base, while the 20% cream was formulated by mixing 20 g of kombucha extract with 80 g of cream base. Both formulations were homogenized and stored in sterile containers at 4°C. The cream base was formulated as an oil-in-water (O/W)

emulsion. This was prepared by melting 58 g stearic acid as the lipid phase in a water bath, adding 500 mg borax as a stabilizing agent, and then gradually mixing 6 mL TEA as an emulsifier, 40 mL glycerin as a humectant, and 100 mL distilled water until a stable 200 g cream was formed. The final pH of the formulation was 6,4 which was adjusted to the physiological skin range (pH 4,5-6,5).

SLS-Induced Xerosis-Like Model and Administration of Kombucha Extract Cream

A 5% SLS solution was prepared by dissolving 25 g of 100% SLS powder (Sigma Aldrich) in 500 mL distilled water and homogenizing the mixture with a magnetic stirrer, the solution was then stored in a tightly closed container. The experiment began with an acclimatization phase for 14 days. The xerosis-like rat model was induced by initially shaving 4x4 cm area on dorsal region before the rats were divided into groups. A sterile gauze was immersed in a prepared 5% SLS solution and applied evenly over the shaved dorsal area to induce skin barrier disruption and xerosis-like conditions.

The procedure was performed twice daily for nine days, as this duration had previously been shown to consistently induce a clinical presentation of xerosis-like rat model. Xerosis-like lesions were validated using USB Digital Microscope and quantified using the Overall Dry Skin (ODS) score, which assessed skin dryness, roughness, scaling, fissures, and erythema prior to treatment initiation. Topical treatment was administered to the xerosis-like area twice daily for seven consecutive days, starting on day 10. Each topical formulation (0.3 mL) was applied evenly and gently spread over the 4×4 cm xerosis-like area to ensure uniform coverage.

Tissue Collection and Biomarker Analysis

The 7-day topical treatment duration was established based on preliminary pilot studies, which demonstrated that a one-week application of kombucha cream was sufficient to induce significant recovery in the xerosis-like rat model. This timing was chosen to capture the active phase of epidermal repair and observe the transition from acute irritation to the resolution of inflammation, specifically regarding the levels of EGF and IL-10.

Following the 7-day treatment period, EGF and IL-10 levels were measured using the ELISA method. The rats were anesthetized with an intraperitoneal injection of ketamine (75 mg/kg body weight) followed by euthanasia via cervical

dislocation. Skin tissue samples (0.5 g per sample) were excised from the xerotic lesion sites and rinsed in PBS prior to homogenization. ELISA was performed using specific kits for EGF (Cat. No: MBS824918, MyBioSource, California, US) and IL-10 (Cat. No: MBS702776, MyBioSource, California, US) in accordance with the manufacturer's instructions.

Data Analysis

Statistical analysis was performed using SPSS for Windows, version 25.0. EGF and IL-10 levels were expressed as mean±standard deviation. The normality of the data distribution was assessed with the Shapiro–Wilk test, and the homogeneity of variance was evaluated using Levene's test. Since the EGF data followed a normal distribution but exhibited non-homogenous variances, a one-way ANOVA was employed to determine overall differences among groups, followed by Tamhane's T2 post hoc test for pairwise comparisons. IL-10 data were non-normally distributed with non-homogenous variances, the Kruskal-Wallis test was used to analyze differences among groups. Following a significant Kruskal-Wallis result, the Mann-Whitney test was performed to identify specific differences between groups. A significance threshold of $p < 0.05$ was applied for all analyses.

Results

Induction of Xerosis-Like Condition Using 5% SLS

The xerosis-like rat model was validated macroscopically prior to treatment initiation. Macroscopic observations of skin dryness, roughness, scaling, fissures, and erythema were captured using a USB Digital Microscope. To provide an objective assessment, these characteristics were evaluated using the ODS scoring system, ranging from 0 (absent) to 4 (severe). The grades were defined as follows: 0 (normal, hydrated skin), 1 (faint scaling, roughness, and dull appearance), 2 (small and occasional large scales with slight roughness), 3 (uniformly distributed scales, definite roughness, and possible erythema or fissures), and 4 (large scales, advanced roughness, erythema, and eczematous changes). The skin condition before induction (Day 0) and after induction (Day 9) is illustrated (Figure 1). On Day 0, all groups exhibited relatively homogeneous and smooth dorsal skin surfaces without scaling, fissures, or erythema, providing a baseline for comparison. On Day 9, G1 (healthy

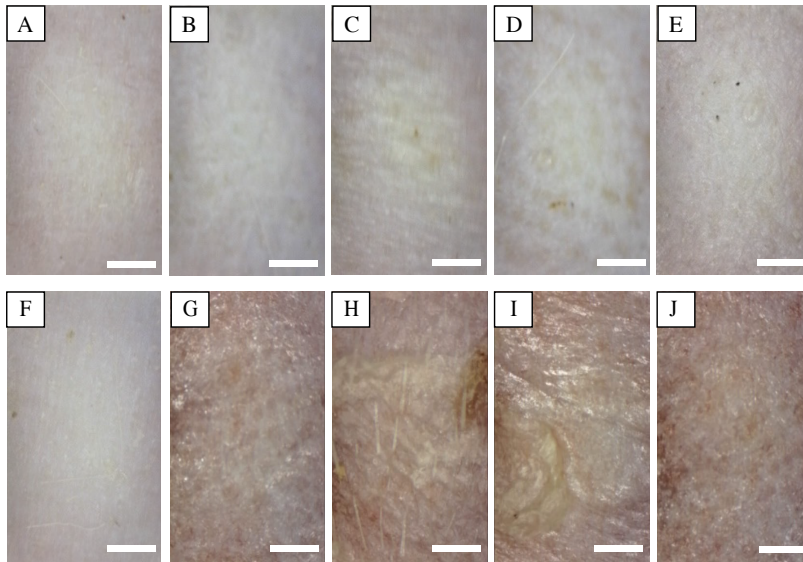


Figure 1. Macroscopic validation of 5% SLS induce in xerosis-like models.

A–E: baseline skin condition at Day 0 for all groups. F–J: macroscopic appearance at Day 9 following 5% SLS application, showing successful xerosis induction prior to treatment across all groups. White bar: 2 cm.

group) maintained a skin appearance consistent with the baseline, appearing smooth and without visible scales. In contrast, evident changes were observed in G2, G3, G4, and G5, which showed prominent scaling, rough and dry skin, and localized erythema. These clinical signs were graded as ODS scores of 2 or 3. Based on the ODS scoring system, these clinical manifestation confirms that 5% SLS induction for nine days successfully generated xerosis-like skin changes.

Macroscopic Recovery of Skin Appearance in Response to Kombucha Extract Cream Treatment

A macroscopic evaluation was conducted to observe the skin surface conditions following the 7-day topical treatment period in the xerosis-like rat model (Figure 2). The negative control (G2) displayed marked erythema and scaling, while the treatment groups (G3–G5) showed smoother skin surfaces with minimal scales. This suggests that the 7-day application of base cream alone was insufficient to restore xerotic skin. In contrast, the groups treated with kombucha extract cream demonstrated significant morphological improvement, with the skin surface closely resembling the baseline characteristics of the G1 group.

Upregulation of EGF Level Following Treatment with Kombucha Extract Cream

In alignment with the observed macroscopic improvements, topical administration of the kombucha-extract cream led

to an increase in EGF. Changes in EGF levels indicate regenerative signaling in response to barrier disruption and serve as indicators of the efficacy of topical intervention (Figure 3, Table 1). The EGF levels in the G2 were higher than G1 (641.24 ± 52.35 ng/L vs. 618.43 ± 62.62 ng/L), G3 (573.88 ± 25.09 ng/L), and G5 (602.63 ± 18.00 ng/L). In contrast, EGF levels in G2 were lower than those in G4 (641.24 ± 52.35 ng/L vs. 665.96 ± 17.74 ng/L). Among all treatment groups, G4 (10% kombucha extract cream) demonstrated the highest mean of EGF levels while G3 demonstrated the lowest.

The Shapiro-Wilk and Levene's test indicated that the data were normally distributed but exhibit non-homogenous variance. One-Way ANOVA revealed significant differences in EGF levels among groups ($p=0.006$), suggesting that the kombucha extract cream significantly influences EGF levels in the xerosis-like rat model. A Post Hoc Tamhane analysis was performed due to the lack of variance homogeneity (Table 2). The results revealed significant differences between G3 and G4 ($p=0.001$) as well as between G4 and G5 ($p=0.001$). However, no significant difference was observed between G2 and G1 ($p=0.999$), indicating that the induction results did not fully meet the baseline expectations. Furthermore, the differences between G2 and G4 ($p=0.977$) and between G2 and G5 ($p=0.771$) were not statistically significant, suggesting that EGF levels in xerosis-like rat model did not differ substantially from those in groups treated with 10% and 20% kombucha extract cream.

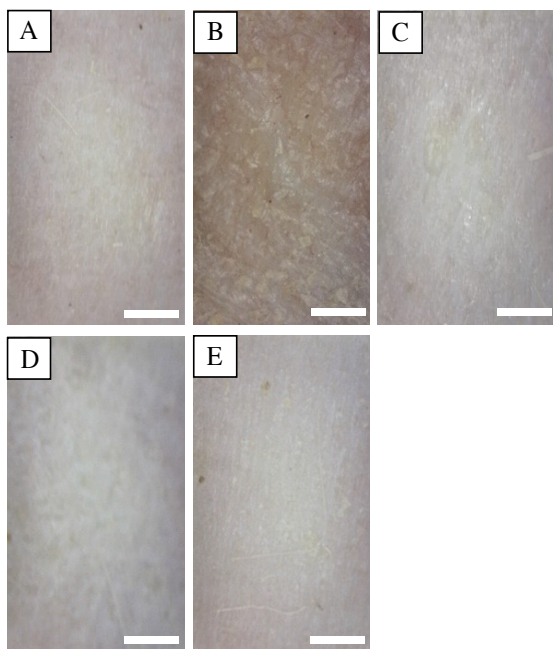


Figure 2. Macroscopic observation following 7-days of topical treatment. A: healthy rats; B: negative control, received cream base; C: positive control, received 5% urea cream; D: received 10% kombucha extract cream; E: received 20% kombucha extract cream. White bar: 2 cm.

Decreased of IL-10 Levels Following Kombucha Extract Cream Treatment

IL-10 is an anti-inflammatory biomarker measured in skin tissue to evaluate local immune responses among xerosis-like rat model groups following topical treatment. Descriptive analysis showed that IL-10 levels in G2 were lower than those in G1 (190.41 ± 3.89 pg/mL vs. 201.41 ± 20.41 pg/mL). Interestingly, IL-10 levels in G2 were found to be higher than those in the urea-treated group (G3: 189.69 ± 6.99 pg/mL) and the groups treated with kombucha extract cream, specifically G4 (181.60 ± 3.42 pg/mL) and G5 (182.37 ± 3.19 pg/mL) (Figure 4, Table 3).

Data normality was met in groups G1–G4 but not G5, thus, the data were considered non-normally distributed. Furthermore, Levene's test ($p=0.001$) indicated non-homogenous variances. The Kruskal-Wallis analysis confirmed significant differences among the groups ($p=0.013$). Mann-Whitney tests were then used to determine

which group pairs differed significantly while maintaining statistical validity. The Mann-Whitney analysis revealed no significant difference in IL-10 levels between G2 and G1 ($p=0.423$), indicating that the healthy group and negative control group exhibited comparable IL-10 levels (Table 4). However, significant differences were observed between G2 and the kombucha-treated groups, G4 ($p=0.010$) and G5 ($p=0.006$). The application of 10% and 20% of kombucha extract cream resulted in significantly lower IL-10 levels compared to the cream base. The lower IL-10 levels observed in kombucha-treated groups likely reflect an earlier resolution of inflammation rather than ongoing inflammatory activity. Furthermore, significant differences were observed between G3 and G4 ($p=0.025$) as well as between G3 and G5 ($p=0.030$), suggesting that the kombucha extract cream induced a distinct immunomodulatory effect compared to the urea cream. No significant difference was found between the two kombucha concentrations, G4 and G5 ($p=0.337$).

Discussion

Xerosis induction using 5% SLS for nine days effectively established a xerosis-like rat model, as confirmed

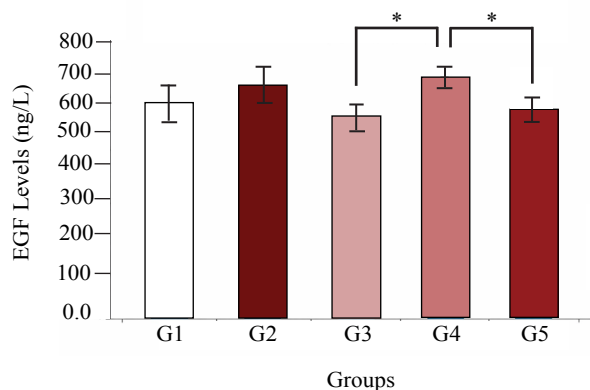


Figure 2. Comparison of mean EGF levels among groups following 7-day post treatment. G1: healthy rats); G2: negative control, received cream base; G3: positive control, received 5% urea cream; G4: received 10% kombucha extract cream; G5: received 20% kombucha extract cream.

Table 1. EGF levels, Shapiro–Wilk, Levene, and One-Way ANOVA results.

Parameter	G1	G2	G3	G4	G5	p Value
	Healthy	Negative Control	Positive Control	(10% Kombucha)	(20% Kombucha)	
Mean	618.43	641.24	573.88	665.96	602.63	
SD	62.62	52.35	25.09	17.74	18.00	
Shapiro-Wilk	0.125	0.779	0.956	0.085	0.356	
Levene test						0.000
One-Way ANOVA						0.006

- Shapiro–Wilk >0.05 indicates normal distribution
- Levene test p>0.05 indicates homogeneity (not met here)
- One-Way ANOVA p<0.05 indicates significant differences between groups

by macroscopic skin evaluation with a USB Digital Microscope. On day 0 (pre-induction), the rat dorsal skin appeared normal, smooth, and hydrated, identical to G1 (healthy control) group on Day 9. Conversely, groups G2-G5 exhibited classical xerosis features after topical 5% SLS application, including roughness, dullness, white scaling and erythema. These observations were consistent with established models of SLS-induced irritation models.¹⁵ SLS disrupts stratum corneum lipids and structural proteins, which increases TEWL, reduces hydration, and accelerates dry scale formation. This disruption induces an epidermal barrier damage, localized immune activation, and a cascade of pro-inflammatory cytokines (IL-1 α , IL-6, TNF- α).¹⁶

Treatment with 10% and 20% kombucha cream aimed to restore barrier function and skin hydration. Preliminary findings indicate that kombucha cream improved xerosis

more effectively than the base cream, evidenced by reduced inflammatory cell infiltration and minimal epidermal desquamation.¹⁷ ELISA analysis demonstrated significant differences in EGF levels between G3 (positive control) and G4 (10% kombucha), as well as G4 and G5 (20% kombucha). Interestingly, G4 exhibited the highest EGF levels, suggesting that 10% kombucha cream provides optimal stimulation of EGF for epidermal regeneration.^{18,19}

EGF is essential for re-epithelialization, because it promotes proliferation and migration of keratinocyte and

Table 2. Post Hoc Tamhane Test results after treatment on EGF levels.

Group	G2	G3	G4	G5
G1	0.999	0.809	0.739	1.000
G2	–	0.218	0.977	0.771
G3		–	<0.001*	0.390
G4			–	<0.001*
G5				–

*Significant at p<0.05

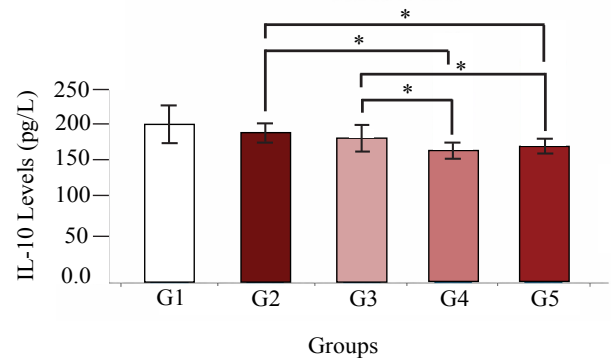


Figure 4. Comparison of mean EGF levels among groups following 7-day post treatment. G1: healthy rats; G2: negative control, received cream base; G3: positive control, received 5% urea cream; G4: received 10% kombucha extract cream; G5: received 20% kombucha extract cream.

Table 3. IL-10 levels, Shapiro–Wilk, Levene, and One-Way ANOVA results.

Parameter	G1	G2	G3	G4	G5	<i>p</i> Value
	Healthy	Negative Control	Positive Control	10%Kombucha	20%Kombucha	
Mean	201.41	190.41	189.69	181.60	182.37	
SD	20.41	3.89	6.99	3.42	3.19	
Shapiro-Wilk	0.297	0.650	0.141	0.403	0.000	
Levene test						0.000
Kruskal-Wallis						0.013

- Shapiro–Wilk $p > 0.05$ indicates normal distribution

- Levene test $p > 0.05$ indicates homogeneity (not met here)

- One-Way ANOVA $p < 0.05$ indicates significant differences between groups

fibroblast, while enhancing barrier protein synthesis, and reduces TEWL. The lower EGF levels observed in G3 may reflect passive hydration that lacks active anti-inflammatory stimulation. Unlike urea, which primarily acts as a humectant and keratolytic agent without intrinsic antioxidant or anti-inflammatory properties, kombucha extract provides a multifaceted biological effect. These include oxidative stress modulation and cytokine regulation, which likely contribute to superior epidermal regeneration.²⁰ The significant increase in EGF levels with 10% kombucha extract cream suggests a potent stimulation of the epidermal regenerative process. This effect shares mechanistic similarities with the regenerative pathways observed in Mesenchymal Stem Cell (MSCs)-mediated tissue repair, particularly through the upregulation of such as EGF.^{21,22} Notably, the 10% cream

produced higher EGF levels than 20%, indicating a potential optimal dose, excessive concentration may induce feedback inhibition, thereby reducing EGF stimulation.²³

Conversely, IL-10 levels were lower in G4 and G5 compared to G2 and G3. This finding must be interpreted through the dynamic nature of cytokine signaling. While IL-10 is recognized for its anti-inflammatory properties, its expression reflects the magnitude and duration of inflammatory stimuli rather than constitutive anti-inflammatory activity. Therefore, the reduced IL-10 levels in the kombucha-treated groups may indicate an earlier resolution of inflammation, rather than insufficient anti-inflammatory signaling. In contrast, the higher IL-10 levels in G2 likely represent a prolonged compensatory response to persistent inflammatory stress. These results were similar to previous studies suggesting that successful regenerative therapy can downregulate inflammatory markers upon the completion of the active repair phase.²⁴⁻²⁶ Overall, kombucha extract creams effectively modulated cytokine dynamics, promoted barrier repair, and enhanced regenerative EGF signaling. This suggests their potential as therapeutic moisturizers that accelerate comprehensive skin recovery.

Table 4. Mann-Whitney test results after treatment on IL-10 levels.

Group	G2	G3	G4	G5
G1	0.423	0.522	0.055	0.078
G2	–	1.000	0.010*	0.006*
G3		–	0.025*	0.030*
G4			–	0.337
G5				–

*Significant at $p < 0.05$

Conclusion

Topical application of 10% kombucha extract cream demonstrated the highest EGF levels compared to both the control group and the 20% kombucha cream groups, confirming its efficacy in enhancing epidermal regeneration.

Additionally, kombucha extract cream significantly modulated IL-10 levels, with both 10% and 20% treatments resulting in lower IL-10 levels compared to negative controls, reflect an earlier resolution of inflammation rather than ongoing inflammatory activity. Overall, these findings demonstrate that kombucha extract cream effectively modulates EGF and IL-10 levels, highlighting its potential as a topical agent to enhance the skin repair process in xerotic conditions.

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Authors' Contributions

WSP, SPM and STZ were involved in the research design and conception. WSP perform the data acquisition and data analysis. WSP, SPM, STZ were responsible for the result interpretation and manuscript preparation. WSP also designed the figures and/or tables. All authors (WSP, SPM, and STZ) contributed to the critical revision of the manuscript.

Ethical Statement

Ethical clearance for this research was officially granted by the Ethics Committee of the Faculty of Medicine's Ethics Committee at Sultan Agung Islamic University (557/XI/2025/Komisi Bioetik).

Conflict of Interest

The authors declare no conflict of interest.

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