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"Fermented Eggplant Peel Extracts Enhance Skin Health and Anti-Aging through the Gut-Skin Axis"

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1. Introduction

In recent years, the gut-skin axis has attracted growing attention as a key pathway through which the gut microbiota exerts influence on skin physiology. It is increasingly recognized that microbial metabolites, such as short-chain fatty acids and polyphenol-derived compounds, can modulate systemic inflammation, oxidative stress, and skin barrier integrity through immune and metabolic signaling pathways[1,2]. This bidirectional communication highlights new opportunities for skin health improvement by targeting gut microbiota or utilizing gut-relevant interventions.

Fermentation is one such strategy, known to enhance the bioavailability and functionality of plant-derived bioactives. During microbial fermentation, complex phytochemicals can be broken down into more absorbable and biologically active forms, thus amplifying their physiological effects [3,4]. In the context of dermatological applications, fermented botanical extracts have demonstrated potential for anti-inflammatory, antioxidant, and skin-repairing properties.

Eggplant (Solanum melongena) is a nutrient-rich vegetable widely consumed in many parts of the world. Its peel, often discarded as food waste, contains a high concentration of polyphenols, flavonoids, and chlorogenic acid—compounds known for their antioxidant and anti-inflammatory effects [5]. However, the functional utilization of eggplant peel in skin care applications remains largely unexplored.

In this study, we investigated the effects of fermented eggplant peel extracts (BEPs) on skin health and aging-related biomarkers. Specifically, we aimed to evaluate their antioxidant capacity, anti-inflammatory activity, and their influence on skin barrier–related gene expression in keratinocytes. By integrating the concept of the gut-skin axis, this research provides insight into the cosmetic potential of a fermented botanical ingredient derived from food waste, contributing to both skin health innovation and sustainability.

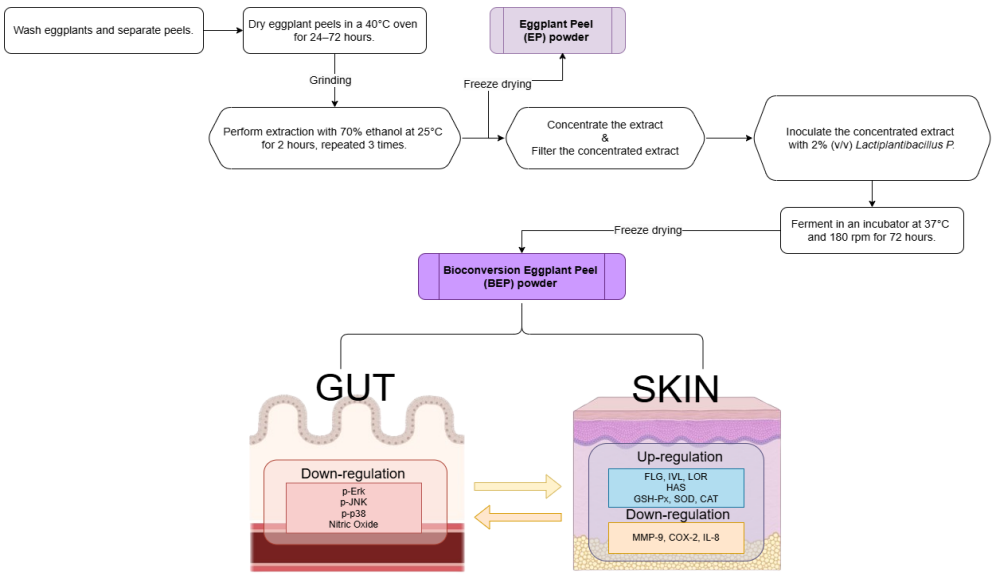

Figure 1. Schematic overview of the preparation and functional mechanism of bioconverted eggplant peel extract (BEP).
Eggplant peels were extracted with 70% ethanol and fermented with *Lactiplantibacillus plantarum* to yield BEP powder. The extract was shown to exert dual effects through the gut-skin axis: inhibiting inflammatory markers (p-ERK, p-JNK, p-p38, NO) in the gut, and enhancing barrier function and antioxidant responses (FLG, IVL, LOR, HAS, GSH-Px, SOD, CAT) while suppressing inflammation (MMP-9, COX-2, IL-8) in the skin.

2. Materials and Methods

2.1. Preparation of Eggplant Peel Extracts (EPs) and Fermented Extracts (BEPs)

Fresh eggplants (*Solanum melongena*) were thoroughly washed, and their peels were manually separated. The peels were dried using a food dehydrator (or drying oven) at 40°C for 24–72 hours, then ground into fine powder. The powdered sample was extracted three times with 70% ethanol at 25°C for 2 hours (1:10, w/v), and the combined extracts were filtered and concentrated under reduced pressure. The concentrated extract was divided into two portions. One was freeze-dried directly to produce the non-fermented eggplant peel extract powder (EP). The other portion was used for fermentation by inoculating with *Lactiplantibacillus plantarum* (2% v/v) and incubated at 37°C and 180 rpm for 72 hours. After fermentation, the extract was freeze-dried to obtain the bioconverted eggplant peel extract powder (BEP).

2.2. Antioxidant Activity

Total phenolic and flavonoid contents were determined by the Folin–Ciocalteu method and aluminum chloride colorimetric assay, respectively. Antioxidant activity was assessed via DPPH and ABTS radical scavenging assays, as well as ferric reducing antioxidant power (FRAP) assays. DNA protection was evaluated through hydroxyl radical-induced plasmid DNA cleavage assay.

2.3. Cell Culture

RAW 264.7 murine macrophages and HaCaT human keratinocytes were purchased from ATCC and cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10%

fetal bovine serum (FBS) and 1% penicillin-streptomycin under standard conditions (37°C, 5% CO_2).

2.4. Cell Viability and Inflammatory Response

Cell viability was assessed using the MTT assay after treatment with EP or BEP at various concentrations (50–1000 μg/mL) for 24 hours. Nitric oxide (NO) production in RAW 264.7 cells was measured using the Griess reagent following stimulation with LPS and treatment with test samples.

2.5. Quantitative Real-Time PCR

HaCaT cells were treated with EP and BEP extracts, and total RNA was extracted using TRIzol reagent. RNA was reverse-transcribed into cDNA, and quantitative PCR was conducted using SYBR Green Master Mix. The relative mRNA expression of skin barrier markers (FLG, IVL, LOR), hyaluronic acid synthases (HAS1, HAS2, HAS3), antioxidant enzymes (GSH-Px, SOD), and inflammatory genes (COX-2, IL-8, MMP9) was analyzed using the ΔΔCt method and normalized to GAPDH.

2.6. Western Blot Analysis

Protein expression of MAPK pathway components (p-Erk, p-JNK, p-p38) in RAW 264.7 cells was assessed. Cells were lysed, and proteins were separated by SDS-PAGE and transferred to PVDF membranes. After blocking, membranes were incubated with specific primary antibodies, followed by HRP-conjugated secondary antibodies. Bands were visualized using an enhanced chemiluminescence system.

2.7. Statistical Analysis

All data are presented as mean ± standard deviation (SD) from at least three independent experiments. Statistical significance was determined by one-way ANOVA followed by Tukey's post hoc test. A p-value < 0.05 was considered statistically significant.

3. Results

1.1. Polyphenolic Composition and Antioxidant Activities of EP and BEP Extracts

To evaluate the functional potential of fermented eggplant peel extracts, we first quantified their total phenolic and flavonoid contents (Table 1). The non-fermented extract (EP) exhibited a phenolic content of 364.6 ± 3.4 mg gallic acid equivalents (GAE)/g extract, whereas fermentation for 72 hours (BEP72) resulted in a slightly decreased but still considerable level (346.1 ± 2.6 mg GAE/g extract). Interestingly, the total flavonoid content increased following fermentation, with BEP72 showing the highest level among the groups (491.0 ± 1.4 mg catechin equivalents [CE]/g extract), suggesting that microbial bioconversion may enhance the release or transformation of flavonoid compounds.

Table 1. Total phenolic acid and Flavonoid content. All data are expressed as mean±standard deviation (n=3) GA: gallic acid equivalent, CE: catechin equivalent, EP: *Solanum melongena* (Eggplant) peel

extract, EP-I: *Solanum melongena* (Eggplant) peel extract for incubator, BEP48: 48h fermented *Solanum melongena* (Eggplant) peel extract., BEP72: 72h fermented *Solanum melongena* (Eggplant) peel extract.

Sample	Total Phenolic (GAE per g of extract)	Total Flavonoid (CE per g of extract)
EP	364.6 ± 3.4	455.0 ± 0.3
EP-I	337.0 ± 0.9	475.8 ± 1.5
BEP48	338.7 ± 1.9	460.8 ± 1.6
BEP72	346.1 ± 2.6	491.0 ± 1.4

Antioxidant activities of the extracts were assessed through DPPH and ABTS radical scavenging assays, as well as ferric reducing antioxidant power (FRAP) and DNA protective activity (Figure 2). All extracts, including EP, EP-I (incubated control), BEP48, and BEP72, demonstrated strong DPPH and ABTS scavenging effects at all tested concentrations (0.25–4 mg/mL), comparable to ascorbic acid (AA). In particular, BEP72 showed marginally higher scavenging activity across assays, although the differences were not statistically significant. In the reducing power assay, a concentration-dependent increase in absorbance was observed in all samples, with BEP72 demonstrating the most potent electron-donating capacity among the fermented groups.

Additionally, the DNA protection assay confirmed the antioxidant efficacy of BEP72. Exposure of plasmid DNA to hydroxyl radicals induced strand breaks, resulting in a shift from supercoiled to nicked or linear forms. Treatment with BEP72 effectively preserved the supercoiled form, indicating superior DNA protective ability compared to EP and BEP48.

Collectively, these results suggest that fermentation maintains or enhances the antioxidant potential of eggplant peel extracts, likely by modulating the bioavailability of phenolic and flavonoid constituents. Among all groups, BEP72 exhibited the most favorable antioxidant profile.

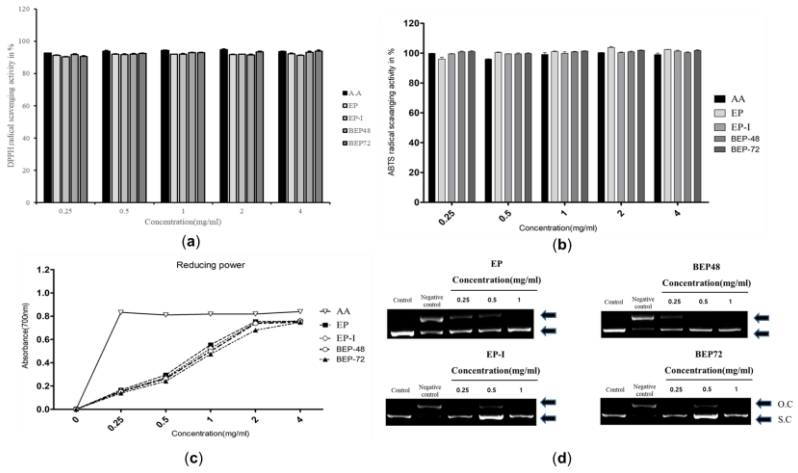

Figure 2. Antioxidant activity and DNA protection effects of fermented eggplant peel extracts (BEPs). (a) DPPH radical scavenging activity of EP and BEP samples at various concentrations (0.25–4 mg/mL), compared to ascorbic acid (AA) as a positive control. (b) ABTS radical scavenging activity of

each sample at different concentrations. (c) Reducing power measured at 700 nm showing dose-dependent antioxidant capacity of EP and BEP samples. (d) DNA protective effect against hydroxyl radical-induced oxidative damage assessed via agarose gel electrophoresis. The upper bands represent intact supercoiled plasmid DNA, while lower bands indicate nicked or linearized forms. BEP72 showed superior DNA protection compared to EP and BEP48.

1.2. Effects of EP and BEP Extracts on Cell Viability and NO Production in RAW 264.7 Macrophages

To assess the cytocompatibility of the eggplant peel extracts, RAW 264.7 macrophages were treated with EP, EP-I, BEP48, or BEP72 at concentrations ranging from 10 to 1000 μg/mL for 24 hours, followed by MTT assay analysis (Figure 3A). All tested extracts exhibited minimal cytotoxicity up to 500 μg/mL. Notably, BEP72-treated cells showed slightly higher viability across the concentration range, indicating that fermentation may improve biocompatibility. At the highest concentration (1000 μg/mL), a slight decrease in viability was observed for all groups, although cell survival remained above 80%, suggesting overall safety for topical application.

To evaluate anti-inflammatory potential, we measured nitric oxide (NO) production in LPS-stimulated RAW 264.7 cells following treatment with the extracts (Figure 3B). As expected, LPS stimulation significantly increased NO levels compared to the untreated control group. EP and EP-I moderately suppressed NO production in a dose-dependent manner. In contrast, BEP48 and particularly BEP72 exhibited a pronounced inhibitory effect, with BEP72 achieving the greatest NO reduction at both 50 and 100 μg/mL. The reduction in NO by BEP72 was statistically significant compared to both the LPS-only group and the non-fermented counterparts ($p < 0.01$).

These findings suggest that fermentation enhances the anti-inflammatory efficacy of eggplant peel extracts, potentially by generating or enriching bioactive metabolites capable of modulating inflammatory signaling pathways such as iNOS-mediated NO production.

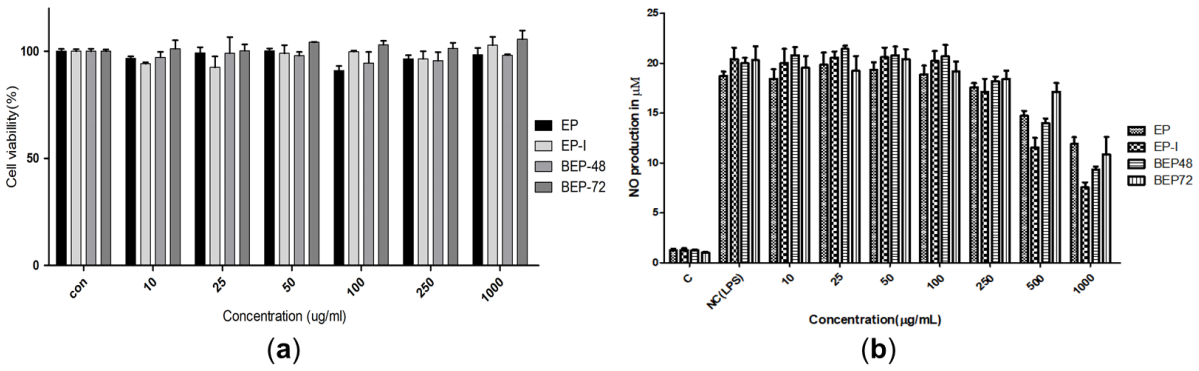

Figure 3. Cell viability and anti-inflammatory effects of EPs and BEPs in RAW 264.7 macrophages. (a) Cell viability of RAW 264.7 cells treated with EP, EPI, BEP48, and BEP72 at concentrations ranging from 10 to 1000 μg/mL for 24 hours, assessed using the MTT assay. Untreated cells served as the control (Con). (b) Nitric oxide (NO) production in LPS-stimulated RAW 264.7 cells following treatment

with EPs and BEPs. Cells were pre-treated with the samples for 1 hour, then stimulated with LPS (100 ng/mL) for 24 hours. NO levels were measured using the Griess assay. NC (LPS) indicates the negative control group treated with LPS only. All data are presented as mean ± standard deviation (n = 6).

1.*3 Suppression of MAPK Signaling Pathways by BEP Extracts in LPS-Stimulated RAW 264.7 Cells*

To further elucidate the anti-inflammatory mechanism of BEP extracts, we investigated their effects on the phosphorylation of mitogen-activated protein kinases (MAPKs), including ERK, JNK, and p38, in LPS-stimulated RAW 264.7 cells using Western blot analysis (Figure 4). Phosphorylation of all three MAPK proteins was markedly upregulated following LPS treatment, consistent with canonical inflammatory activation pathways.

Treatment with EP and EP-I led to a partial reduction in the phosphorylation levels of ERK, JNK, and p38. However, BEP extracts—particularly BEP72—resulted in a more pronounced suppression of all three phospho-MAPKs. Densitometric analysis confirmed that BEP72 significantly reduced the p-ERK/ERK, p-JNK/JNK, and p-p38/p38 ratios when compared to both the LPS group and non-fermented EP samples (**$p < 0.001$).

These findings indicate that fermentation amplifies the anti-inflammatory potential of eggplant peel extract by targeting upstream inflammatory signaling pathways. Specifically, BEP72 appears to inhibit LPS-induced activation of MAPK cascades, thereby reducing downstream expression of inflammatory mediators such as NO, IL-8, and COX-2 as observed in subsequent assays.

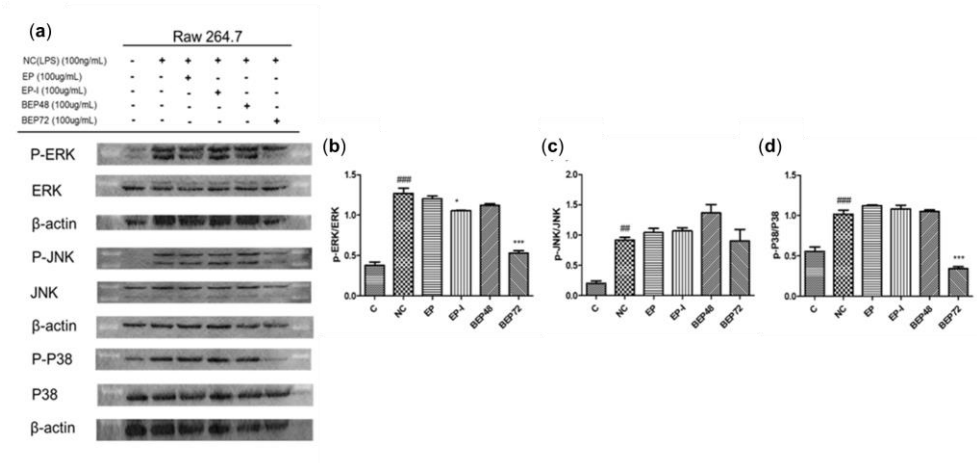

Figure 4. EPs and BEPs inhibit the phosphorylation levels of ERK, p38 and JNK in LPS-induced Raw 264.7. Specifically, BEP-72 samples demonstrate the best efficacy compared to other samples. (A) Relative the phosphorylation ERK, p38 and JNK levels. (B) Relative the phospho-ERK level was compared with total-ERK. (C) Relative the phospho-JNK level was compared with total-JNK. (D) Relative the phospho-p38 level was compared with total-p-p38. ***p< 0.0001 indicate a significant difference compared to the only LPS-induced groups.

1.4. Modulation of Skin Barrier, Antioxidant, Moisturization, and Inflammatory Gene Expression in HaCaT Cells

BEP treatment markedly influenced the expression of multiple gene groups involved in skin defense mechanisms. As shown in Figure 5, mRNA levels of the barrier-associated proteins *filaggrin (FLG)*, *involucrin (IVL)*, and *loricrin (LOR)* were significantly elevated in HaCaT keratinocytes compared to EP. These structural proteins are essential for forming a robust epidermal barrier and preventing transepidermal water loss. Their upregulation by BEP suggests improved barrier integrity and protection against environmental insults.

Simultaneously, antioxidant defense genes—*superoxide dismutase (SOD)*, *catalase (CAT)*, and *glutathione peroxidase (GSH-Px)*—were also upregulated, with *SOD* and *GSH-Px* showing particularly strong induction. This pattern indicates that BEP enhances intrinsic ROS-scavenging capacity, which may contribute to the observed protective effects on skin barrier components. The concurrent regulation of both skin structure and oxidative stress markers implies a synergistic mechanism in maintaining epidermal homeostasis.

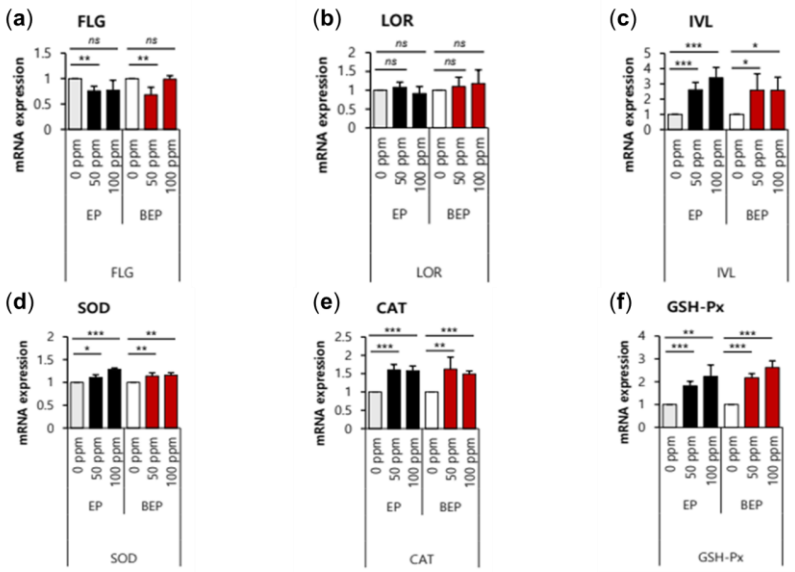

Figure 4. Effects of EP and BEP treatment on the expression of skin barrier and antioxidant-related genes in HaCaT cells. HaCaT keratinocytes were treated with EP or BEP at 50 or 100 ppm for 24 hours. Gene expression levels of (A) filaggrin (FLG), (B) loricrin (LOR), (C) involucrin (IVL), (D) superoxide dismutase (SOD), (E) catalase (CAT), and (F) glutathione peroxidase (GSH-Px) were analyzed by quantitative RT-PCR and normalized to GAPDH. BEP treatment significantly upregulated FLG, IVL, and all antioxidant-related genes (SOD, CAT, GSH-Px), with GSH-Px showing the most pronounced effect. No significant change was observed in LOR expression. Data are presented as mean ± SD (n = 3). Statistical significance: *p < 0.05, **p < 0.01, ***p < 0.001, ns = not significant.

Gene expression related to hyaluronic acid synthesis was then examined to assess moisturizing potential (Figure 6A–C). All three HAS isoforms (*HAS1*, *HAS2*, *HAS3*) were significantly upregulated by BEP, with *HAS3* showing the most prominent effect. These enzymes are

directly responsible for producing hyaluronic acid, a critical molecule for skin hydration and elasticity.

The anti-inflammatory potential of BEP was further confirmed by reduced expression of *COX-2*, *MMP-9*, and *IL-8* (Figure 6D–F). These markers are typically elevated during skin irritation and chronic inflammation; their downregulation indicates effective suppression of inflammatory responses by BEP treatment.

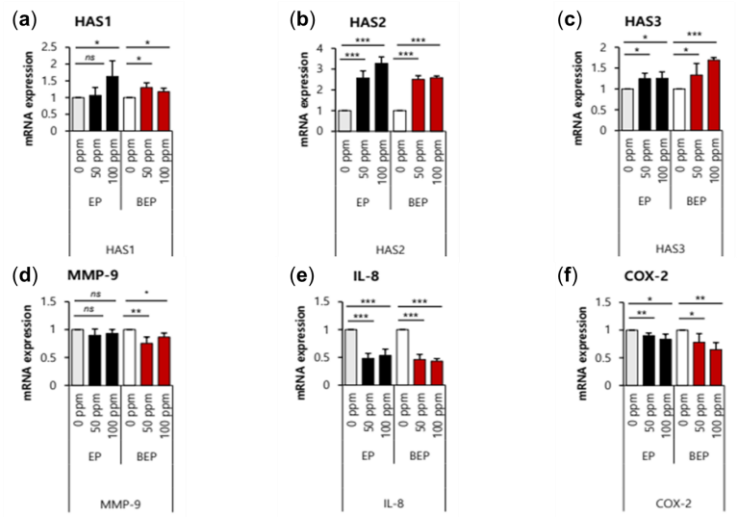

Figure 6. Effects of EP and BEP treatment on hyaluronic acid synthase (HAS) and inflammation-related gene expression in HaCaT cells. HaCaT keratinocytes were treated with EP or BEP at concentrations of 50 or 100 ppm for 24 hours. Expression levels of (A) hyaluronic acid synthase 1 (HAS1), (B) HAS2, and (C) HAS3 were evaluated to assess hydration-related effects, while (D) matrix metalloproteinase-9 (MMP-9), (E) interleukin-8 (IL-8), and (F) cyclooxygenase-2 (COX-2) were assessed to determine anti-inflammatory activity. qRT-PCR was performed and data were normalized to GAPDH. BEP-treated groups showed significant upregulation of HAS genes, particularly HAS2 and HAS3, and significantly reduced expression of MMP-9, IL-8, and COX-2, indicating both moisturizing and anti-inflammatory effects. Data are presented as mean ± SD (n = 3). Statistical significance: *p < 0.05, **p < 0.01, ***p < 0.001; ns = not significant.

4. Discussion

This study demonstrates that fermented eggplant peel extract (BEP), obtained through microbial bioconversion using *Lactiplantibacillus plantarum*, exhibits multifunctional properties relevant to skin health, including enhanced antioxidant capacity, anti-inflammatory effects, and the regulation of genes related to skin barrier integrity and moisturization.

The fermentation process led to subtle changes in the phytochemical profile of the extract, as evidenced by the increased flavonoid content and maintained phenolic levels. These biochemical changes correlated with improved antioxidant activities in DPPH, ABTS, and reducing power assays. Notably, BEP72 exhibited the highest antioxidant efficacy and was also the most effective in protecting DNA from oxidative stress. These results are consistent with prior

reports showing that microbial fermentation can release or transform phenolic compounds into more bioactive forms, thus enhancing their radical-scavenging potential [3,4].

In LPS-stimulated RAW 264.7 cells, BEP significantly suppressed nitric oxide production and inhibited the phosphorylation of MAPK pathway components (p-ERK, p-JNK, p-p38). This downregulation of pro-inflammatory signaling suggests that the fermented extract exerts systemic anti-inflammatory effects, likely attributable to its enriched polyphenolic metabolites. Similar findings have been reported with other fermented plant extracts, where lactic acid bacteria-mediated transformation increases bioactivity by producing small phenolic acids or flavonoid derivatives with higher cellular permeability and reactivity [6].

In HaCaT keratinocytes, BEP promoted the expression of skin barrier-related genes (*FLG*, *IVL*, *LOR*), while also enhancing endogenous antioxidant defense via upregulation of *SOD*, *CAT*, and *GSH-Px*. These results indicate that BEP not only supports structural reinforcement of the stratum corneum but also protects epidermal cells from oxidative damage. In addition, BEP significantly increased the expression of *HAS1–3*, key enzymes involved in hyaluronic acid synthesis, suggesting improved skin hydration capacity. Concurrently, the extract downregulated *COX-2*, *MMP-9*, and *IL-8*, which are well-known pro-inflammatory mediators associated with skin aging and chronic irritation.

Taken together, these findings provide compelling evidence that BEP exerts its beneficial effects through multiple mechanisms, acting both on the gut-associated inflammatory axis and directly on epidermal cells. The concept of the gut-skin axis is increasingly recognized in dermatological research, and our results support the idea that dietary or topically applied fermented phytochemicals may modulate systemic and local skin health simultaneously [2,7].

While the in vitro findings are promising, further studies involving ex vivo human skin models or in vivo assessments are warranted to confirm the observed effects in more physiologically relevant systems. Additionally, metabolomic profiling could help elucidate specific fermentation-derived metabolites responsible for the enhanced bioactivities.

In conclusion, this study presents fermented eggplant peel extract as a sustainable and bioactive ingredient with potential applications in skin care formulations targeting hydration, barrier repair, inflammation, and oxidative stress. Its multifunctional profile positions it as a novel candidate for cosmetic and dermatological products focused on well-aging and skin resilience.

5. Conclusion

This study highlights the potential of fermented eggplant peel extract (BEP) as a multifunctional bioactive ingredient for skin health. Compared to non-fermented extracts, BEP demonstrated enhanced antioxidant activity, superior anti-inflammatory effects through MAPK pathway inhibition, and the upregulation of genes involved in skin barrier function, moisturization, and oxidative stress defense in HaCaT cells. These biological effects suggest that BEP not only

reinforces the skin's structural and biochemical defenses but also contributes to anti-aging through comprehensive skin protection. The fermentation process using Lactiplantibacillus plantarum thus adds functional value to eggplant peel, an underutilized by-product, offering a sustainable and efficacious solution for cosmetic applications focused on well-aging and skin resilience.

6. Acknowledgments

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7. References

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