JTL 15 (1) JUNE 2026
Page: 59-69

Contents list available at Jurnal Teknologi Laboratorium

JURNAL TEKNOLOGI LABORATORIUM

Journal Homepage: www.teknolabjournal.com
ISSN 2580-0191(Online) I ISSN 2338 – 5634(Print)

Original Research

OPEN ACCESS

Effect of topical soy extract cream on TNF-α and VEGF expression in a sub-chronic UVB-induced skin injury model in BALB/c mice

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Abstract: Excessive ultraviolet B (UVB) radiation induces skin injury through oxidative stress and inflammatory signaling, characterized by increased tumor necrosis factor-alpha (TNF-α) and dysregulation of vascular endothelial growth factor (VEGF). Soy-derived isoflavones possess antioxidant and anti-inflammatory properties and have been proposed as potential natural photoprotective agents. This study aimed to evaluate the effects of topical soy extract cream on TNF-α and VEGF expression in a sub-chronic UVB-induced skin injury model. An in vivo experimental study with a post-test-only control group design was conducted using 30 BALB/c mice randomly allocated into five groups: healthy control, UVB-exposed untreated control, UVB-exposed treated with vitamin E cream, UVB-exposed treated with 10% soy extract cream, and UVB-exposed treated with 20% soy extract cream (n = 6 per group). Mice were exposed to UVB radiation at 1 minimal erythema dose (MED) for 8 minutes per session, ten sessions over 14 days. On day 15, dorsal skin tissues were harvested and analyzed for TNF-α and VEGF levels using enzyme-linked immunosorbent assay. Statistical analyses were performed using one-way ANOVA for TNF-α and Kruskal–Wallis test for VEGF. Sub-chronic UVB exposure significantly increased TNF-α levels compared with healthy controls. Topical application of soy extract cream significantly reduced TNF-α levels at both 10% (627 ± 44 pg/mL) and 20% (551 ± 130 pg/mL) compared with the UVB-exposed untreated group (916 ± 134 pg/mL) ($p < 0.05$). In parallel, VEGF levels were significantly elevated in the 10% (313.90 ± 101.39 pg/mL) and 20% (722.00 ± 57.67 pg/mL) treatment groups compared with the untreated UVB group (145.04 ± 26.57 pg/mL) ($p < 0.05$). These findings demonstrate that topical soy extract cream attenuates UVB-induced inflammation while enhancing angiogenic signaling, suggesting its potential as a natural photoprotective formulation for mitigating sub-chronic UVB-induced skin damage.

Keywords: Ultraviolet B radiation; Soy isoflavones; TNF-α; VEGF; Photoprotection

INTRODUCTION

Ultraviolet B (UVB) radiation is a major environmental factor contributing to skin damage, photoaging, inflammation, and carcinogenesis through oxidative stress and inflammatory signaling pathways. UVB exposure induces the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and dysregulates angiogenic factors including vascular endothelial growth factor (VEGF), which play key roles in inflammation, tissue remodeling, and wound healing following skin injury. These molecular disruptions contribute to epidermal hyperplasia, erythema, and the breakdown of dermal structural integrity observed in UVB-damaged skin.[1]

Indonesia is a tropical country located on the equator with an intensity of sun exposure throughout the year. Excessive ultraviolet radiation from sunlight can

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DOI: 10.29238/teknolabjournal.v15i1.619
Received 19 August 2025; Received in revised form 07 November 2025; Accepted 11 January 2026

cause health problems. UVB rays have a wavelength of 280-320 nm which can penetrate the epidermal layer to the stratum papillary dermis resulting in inflammation (sunburn), photoaging, photocarcinogenesis, and immunosuppression. UVB rays produce reactive oxygen species (ROS) that cause DNA damage and activate pro-inflammatory cytokines, one of which is tumor necrosis factor-α (TNFα). TNFα is a response to tissue damage.[2] Sunburn causes dilatation of blood vessels and damages the endothelial cells of blood vessels thereby reducing the ability of cells to obtain oxygen (hypoxia). Vascular Endothelial Growth Factor (VEGF) plays an important role in increasing blood vessel permeability and promoting angiogenesis. Angiogenesis is the process of forming new blood vessels from existing blood vessels that act as an initial response to skin damage due to exposure to UVB rays.[2]

Skin damage caused by UVB rays can be addressed with the use of cosmeceuticals, combining cosmetic and therapeutic benefits for the skin. Cosmeceuticals are made from synthetic and organic ingredients that provide protective and repairing benefits to the skin, promoting a healthy appearance. Cosmeceuticals containing synthetic ingredients can cause side effects such as skin irritation, contact allergies, dryness, thinning of the skin, and increased sensitivity to UV light.[3] Cosmeceuticals generally use semi-solid preparations, namely creams, because the texture is light, not sticky, easy to apply to the skin, easy to absorb into the skin, and as a local drug delivery.[4]

In recent years, natural cosmeceuticals containing plant-derived bioactive compounds have gained interest as photoprotective agents due to their antioxidant, anti-inflammatory, and multifunctional biological properties. Isoflavones a major class of phytoestrogens abundant in soybean (Glycine max) have demonstrated protective effects against UV-induced photoaging and inflammatory responses in both in vitro and in vivo models. Topical application of soybean isoflavones has shown photoprotective outcomes by reducing sunburn cell formation and erythema in skin models exposed to UV irradiation.[5] Additionally, isoflavones, such as genistein and daidzein, have been reported to mitigate UVB-induced oxidative stress and inflammation via modulation of cellular signaling pathways involved in DNA repair and inflammatory processes.[1]

Natural ingredients are currently being developed based on the great interest of the public and are relatively safe for the skin. The development of natural ingredients today has reached the use of soybeans. Soybeans have bioactive components, one of which is isoflavones, which have effectiveness as photoprotection, antioxidant, anti-inflammatory, anticarcinogen and anti-aging.[6] According to research, oral administration of soy extract 100 mg/kgBB/day which has bioactive isoflavones is proven to be antioxidant and inhibits the production of pro-inflammatory cytokines such as TNFα.[7] Another study proved that oral administration of a combination of soy extract at a dose of 10 mg and Phaleria macrocarpa at a dose of 0.14 mg/day can reduce the production of TNFα and VEGF.[8]

This study is expected to prove the benefits of photoprotection, antioxidants, and anti-inflammatory so that it can reduce the incidence of skin disorders due to a history of high sun exposure. Epidemiologically, skin damage due to exposure to UVB rays often occur in fitzpatrick I-III skin types.[9] Studies in Australia and New Zealand showed that 1,400 of the 2,095 subjects experienced photoaging, most of which 83% experienced heavy photoaging. In Indonesia, especially in Jakarta, research showed that 78 out of 136 subjects aged 18-21 years experienced premature aging due to sun exposure and other studies showed that sunburn due to UV can still occur even with the use of sunscreen.[10,11]

Cream itself is a semi-solid preparation form that is applied by rubbing, having one or more dissolved or dispersed medicinal ingredients in a suitable base or base material. Cream preparations themselves can help provide an oily, shiny, moisturizing effect and can be easily spread evenly. The advantages of cream

preparations themselves can be seen from the ability of the preparation to spread well on the skin, easy to wash with water, because the slow evaporation of water with the skin so that it provides a cooling effect on the area where it is applied, especially the skin.[12] Previous research has shown that soybean ethanol extract gel at concentrations of 2%, 4%, and 6% has SPF values of 13.82, 13.96, and 14.54, respectively. These values fall within the maximum protection category.

However, despite growing evidence supporting the photoprotective potential of soy-derived compounds, there remain important limitations in the current literature. Most prior investigations have focused on systemic administration or general oxidative biomarkers rather than the specific molecular mediators of inflammation and angiogenesis such as TNF-α and VEGF following sub-chronic UVB exposure. Moreover, although topical phytoestrogen-based formulations have shown promising results in reducing general photodamage, little attention has been paid to their effects on inflammatory cytokines and angiogenic factor expression in controlled in vivo models of repeated UVB exposure.[13] This gap is particularly notable because inflammatory and angiogenic pathways are central to the pathophysiology of UVB-induced skin injury and its resolution.

Importantly, studies of topical isoflavonoids have demonstrated inhibition of UVB-induced increases in pro-inflammatory cytokines like TNF-α in mice, suggesting therapeutic potential; however, comprehensive evaluation of both inflammatory and angiogenic responses especially VEGF modulation remains limited.[14] Furthermore, the dose-dependent effects of soy extract creams on these biomarkers have not been clearly established in sub-chronic UVB models, underscoring a critical research gap in understanding the mechanisms underlying natural photoprotective agents.

Although various topical antioxidants and phytoestrogen-based formulations have been investigated for their photoprotective effects, most studies have focused on either general oxidative stress markers or clinical outcomes, with limited attention to inflammatory–angiogenic balance at the molecular level. In particular, evidence regarding the simultaneous modulation of pro-inflammatory cytokines such as TNF-α and angiogenic factors such as VEGF following sub-chronic UVB exposure remains scarce.[15] Moreover, despite the known bioactivity of soy-derived isoflavones, in vivo studies evaluating topical soy extract cream in controlled UVB-induced skin damage models are still limited, and comparative dose-dependent effects have not been clearly established, this study aimed to evaluate whether topical soy extract cream at 10% and 20% concentrations can modulate TNF-α and VEGF expression as inflammatory and angiogenic markers in UVB-induced skin injury.

MATERIAL AND METHOD

Study Design and Ethical Approval

This study was an in vivo experimental study employing a post-test-only control group design. All experimental procedures involving animals were conducted in accordance with internationally accepted guidelines for laboratory animal care and use. Ethical approval for this study was obtained from the Faculty of Medicine, Sultan Agung Islamic University, Semarang with No. 229/VII/2024/KomisiBioetik.

The results of phytochemical screening of soybean extracts showed flavonoid and phenol content. The results of measuring the total flavonoid content of soybean extracts were 64.12±78% (w/w) and the total phenol content of soybean extracts was 7.75±1.03% (w/w). Previous research has shown that the results of measuring the flavonoid content produced by Anjasmoro soybean varieties were 0.060±0.050% (w/w).[16] Other research has proven that Wild Soybean (Glycine soja) has a total flavonoid content of 219.51±5.18% (w/w) and a total phenolic content of 41.53±1.25% (w/w).[17] This research is in line with previous research that the total flavonoid content is higher than the total phenolic content.

Experimental Animals

Thirty healthy male BALB/c mice (8–10 weeks old, body weight 20–25 g) were obtained from Animal Model Research Center SCCR Indonesia dengan No 003/AMRC-SCCR/VI/2024. The mice were housed under standard laboratory conditions (temperature 22–25 °C, relative humidity 50–60%, 12-h light/dark cycle) with ad libitum access to standard chow and water. Animals were acclimatized for seven days prior to the experiment.

Experimental Groups and Study Workflow

Following acclimatization, mice were randomly allocated into five experimental groups (n = 6 per group):
K1 (Normal control): No UVB exposure, no topical treatment
K2 (UVB control): UVB exposure without topical treatment
K3 (Positive control): UVB exposure with topical vitamin E cream
K4 (Treatment I): UVB exposure with 10% soy extract cream
K5 (Treatment II): UVB exposure with 20% soy extract cream
The overall experimental workflow, including group allocation, UVB exposure schedule, topical treatment application, and outcome assessment, is summarized schematically in Figure 1

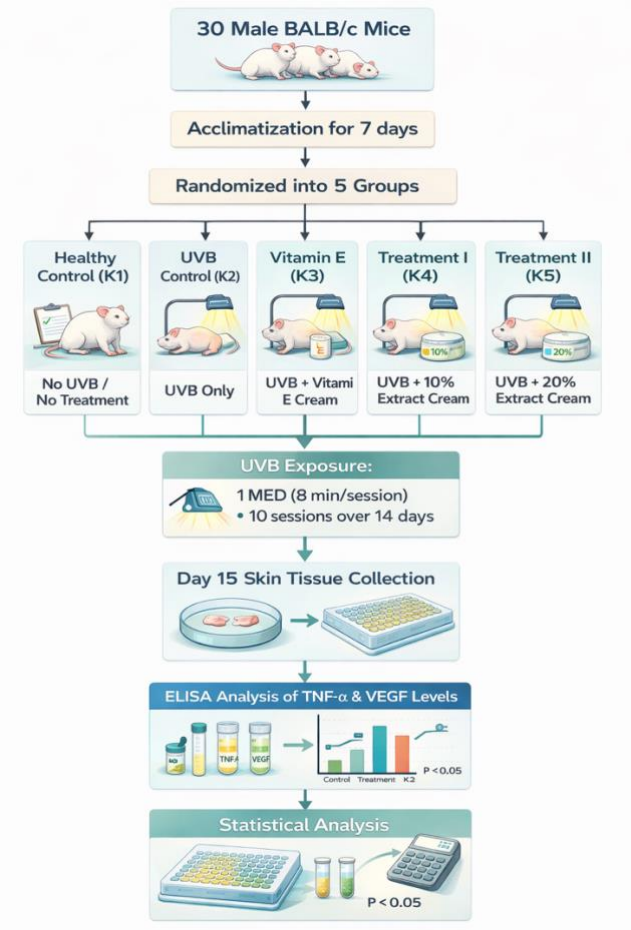

Figure 1. Experimental workflow for soy extract study

Preparation of Soy Extract

Soybean seeds that have been dried in the oven and have a moisture content of <5% are floured using a flouring machine into soybean simplicia. The simpliasia is then soaked in a 70% ethanol solution and stirred for 48 hours for

the maceration process and precipitated for 12 hours. The extract that has dissolved in alcohol is taken and then filtered using filter paper. The filtering results are put into an evaporator flask to separate the ethanol and extract. Evaporation is carried out at a temperature of 60°C using *a vacuum pump* and *chiller*. Once separated, the extracts are taken and stored in a temperature of 2-8° for mixing with a cream base.

Formulation of Soy Extract Cream

Soy extract cream was formulated using a standard oil-in-water cream base. The concentrated soy extract was incorporated into the cream base to obtain final concentrations of 10% (w/w) and 20% (w/w). A commercially available vitamin E cream was used as a positive control. All formulations were prepared under aseptic conditions and stored in opaque containers at room temperature.

UVB Exposure Protocol

Mice in groups K2–K5 were exposed to UVB radiation using a UVB lamp with a peak emission between 280–320 nm. The dorsal skin area was shaved 24 hours prior to the first exposure. UVB exposure was administered at 1 minimal erythema dose (MED) for 8 minutes per session**,** ten sessions over a 14-day period (sub-chronic exposure model). During irradiation, mice were restrained in custom-designed holders to ensure uniform exposure while protecting non-target areas.

Topical Treatment Application

Topical treatments were applied once daily to the dorsal skin area throughout the UVB exposure period. Creams were gently applied in a standardized amount (approximately [insert amount, e.g., 0.1 g]) using sterile applicators. Treatment was administered approximately 30 minutes prior to each UVB exposure session.

Skin Tissue Collection

On day 15, all animals were euthanized humanely using approved anesthetic protocols. Dorsal skin tissue samples were excised, rinsed with cold phosphate-buffered saline (PBS), and stored at −80 °C until further analysis.

Measurement of TNF-α and VEGF Levels

Skin tissue samples were homogenized in cold PBS and centrifuged to obtain supernatants. Levels of TNF-α and VEGF were quantified using commercially available enzyme-linked immunosorbent assay (ELISA) kits, according to the manufacturer's instructions. Absorbance was measured using a microplate reader, and cytokine concentrations were calculated from standard curves.

Data Analysis

TNFα and VEGF level data in BALB/c mice will be descriptive tested using a ratio data scale. Normality analysis was carried out using *the Shapiro-Wilk* test and homogeneity using *the Levene's Test*. The results of the TNFα level analysis showed normal ($p>0.05$) and homogeneous ($p>0.05$) data distribution, so the One-Way ANOVA test was performed. There was a significant difference ($p<0.05$) among all study groups after the One-Way ANOVA test, the Post *Hoc LSD* test will be used to determine the significance of the differences between the study groups. The significance value of $p<0.05$ showed a significant difference between the study groups.

The results of the analysis of VEGF levels showed abnormal ($p<0.05$) and inhomogeneous ($p<0.05$) data distribution, the *Kruskal-Wallis* test was performed. There was a significant difference ($p<0.05$) in all study groups after *the Kruskal-*

Wallis test, the Mann-Whitney *test was performed* to determine the significance of the differences between the study groups. The significance value of p<0.05 showed a significant difference between the study groups.

RESULTS AND DISCUSSION

This study was to determine the effect of soybean extract cream on TNFα and VEGF levels on the skin of female BALB/c mice exposed to sub-chronic UVB rays. In vivo experimental research was conducted at the SCCR Indonesia Semarang Laboratory. The research sample amounted to 30 mice divided into 5 groups, consisting of 6 BALB/c mice per group. The research group consisted of a healthy group without treatment (K1), a negative control group (K2) exposed to UVB rays, kelompok kontrol positif (K3) yang exposed to UVB rays and given vitamin E cream, treatment group 1 (K4) exposed to UVB rays and given a 10% dose of soybean extract cream, and treatment group 2 (K5) exposed to UVB rays and given a 20% dose of soybean extract cream. The back of a shaved mouse was exposed to UVB rays five times a week for fourteen days. The examination was carried out on the fifteenth day using a sample of skin tissue using the ELISA method to measure TNF-α and VEGF levels. The results of TNF-α level examination by the ELISA method using mouse skin tissue samples, data are presented in table 1.

Table 1. TNF-α levels in dorsal skin tissue of BALB/c mice following sub-chronic UVB exposure and topical treatment

Group	TNF-α (pg/mL), Mean ± SD
K1 (Normal control)	162.8 ± 74[a]
K2 (UVB control)	1215 ± 178[b]
K3 (Vitamin E)	916 ± 134[c]
K4 (Soy extract 10%)	627 ± 44[d]
K5 (Soy extract 20%)	551 ± 130[d]

Data were normally distributed (Shapiro–Wilk test, $p > 0.05$) and homogeneous (Levene's test, $p = 0.108$). One-way ANOVA revealed a significant difference among groups ($p < 0.001$). Values with different superscript letters indicate significant differences based on LSD post hoc test ($p < 0.05$).

Based on table 1, it was found that the K2 group had the highest TNF-α levels (1215 ± 178 pg/mL) and K1 had the lowest TNF-α levels (162.8 ± 74 pg/mL). K4 with a dose of 10% and K5 with a dose of 20% showed a decrease in TNF-α levels compared to the K3 group. The results of the Post Hoc LSD test of TNF-α levels showed that there was a significant difference (p<0.05) in each group when compared to the K1 group. The K4 and K5 groups given soy extract cream showed significant differences compared to the K2 and K3 groups (p<0.05). The results of the analysis between K4 and K5 showed that there was no significant difference (p>0.05).

Table 2. VEGF levels in dorsal skin tissue of BALB/c mice following sub-chronic UVB exposure and topical treatment

Group	VEGF (pg/mL), Mean ± SD
K1 (Normal control)	52.14 ± 37.71[a]
K2 (UVB control)	46.90 ± 11.30[a]
K3 (Vitamin E)	145.04 ± 26.57[b]
K4 (Soy extract 10%)	313.90 ± 101.39[c]
K5 (Soy extract 20%)	722.40 ± 57.67[d]

Data were not normally distributed (Shapiro–Wilk test, $p < 0.05$ in K1) and were not homogeneous (Levene's test, $p = 0.045$). Therefore, differences among groups were analysed using the Kruskal–Wallis test, which showed a significant difference ($p < 0.001$). Values with different superscript letters indicate significant differences based on Mann–Whitney post hoc test ($p < 0.05$).

Based on the results of the analysis, it was found that group 5 had the highest VEGF levels (722.60 ±57.67 pg/mL) and K2 had the lowest VEGF levels

(46.90 ±11.29 pg/mL). K4 with a dose of 10% and K5 with a dose of 20% showed an increase in VEGF levels compared to the K3 group.

The Mann-Whitney test results on VEGF levels showed that groups K4 and K5 given soy extract cream had a significant difference compared to groups K1, K2, and K3 ($p<0.05$). This indicates that K4 at a dose of 10% and K5 at a dose of 20% significantly affected VEGF levels.

TNF-α levels in the negative control group showed higher values than in the healthy controls. This is in line with previous research that in vivo exposure to UVB rays will increase TNF-α.[18] Exposure to UVB rays produces ROS and activates the NF-kB pathway which triggers the transcription of TNF-α genes thereby increasing the production and secretion of TNF-α by skin cells and immune cells.[19] Exposure to UVB rays can also result in DNA damage that causes cytochrome C activation by mitochondria that leads to apoptosis. Apoptosis will then cause terbentuknya DAMP that triggers inflammation and increases pro-inflammation, such as TNF-α.[2]

Based on the results of the study, the 10% and 20% doses of soy extract cream groups showed lower TNF-α levels compared to the control group. Previous studies have reported that soy extract contains isoflavones which are high in antioxidants and as anti-inflammatory, which play a role in protecting skin cells from exposure to UVB rays, suppressing the activation of NF-kB and MAPK, so that it can reduce TNF-α production.[20] The content of active substances in soybeans plays a role in reducing the inflammatory response in the skin due to exposure to UVB rays. The results of this study are strengthened by the results of previous studies showing that oral administration of soy extract of 100 mg/kg/day has been proven to inhibit TNF-α production.[7]

The TNF-α levels in the 20% dose of soy extract cream group were not significantly different compared to the 10% dose of soy extract cream group. This is influenced by several factors, namely tolerance to certain doses, where the body has a limited capacity to metabolize active compounds, so that an increase in the dose of 20% is still less than optimal to reduce the inflammatory response even though it has affected growth factors. Another factor is the bioavailability of active compounds which is limited to high doses, but this study did not test the bioavailability of soy extract.[21] The results of this study are in line with previous research that the use of higher doses has been shown to be optimal to reduce TNF-α, such as in studies with oral administration of 350 mg/KgBB of soybean extract more optimally reduced TNF-α production compared to doses of 300 mg/KgBB and 250 mg/KgBB.[18]

VEGF levels in the negative group were not significantly different compared to the healthy group, because on the fourteenth day in a physiological state it was already in a proliferation phase characterized by high VEGF levels. Angiogenesis is the formation of new existing blood vessels and increases vascular permeability so that more oxygen and nutrients are needed for skin regeneration, thereby increasing the production of elastin and collagen. The fourteenth day also occurs when the granulation phase is well formed, characterized by active fibrolast cells and new blood vessels.[22,23]

Sub-chronic UVB exposure resulted in a pronounced inflammatory response in the skin of BALB/c mice, as evidenced by markedly elevated TNF-α levels in the UVB-exposed untreated group compared with healthy controls. This finding confirms that repeated UVB irradiation induces a sustained pro-inflammatory microenvironment in the skin, consistent with activation of oxidative stress pathways and NF-κB–mediated cytokine transcription.[24] The magnitude of TNF-α elevation observed in the negative control group indicates that sub-chronic UVB exposure produces not merely transient inflammation, but a biologically relevant inflammatory burden capable of disrupting skin homeostasis.[25]

Topical application of soy extract cream at both 10% and 20% concentrations resulted in a substantial reduction of TNF-α levels compared with the UVB-exposed untreated group. Importantly, this reduction was not only

statistically significant but also quantitatively meaningful, indicating a strong anti-inflammatory effect of soy-derived bioactive compounds. The comparable magnitude of TNF-α suppression observed in the 10% and 20% treatment groups suggests that the anti-inflammatory response may approach a plateau within this concentration range, where increasing the dose does not proportionally enhance cytokine inhibition. This phenomenon may reflect saturation of cellular signaling pathways or limited cutaneous bioavailability of isoflavones at higher concentrations.[26]

From a mechanistic perspective, the observed reduction in TNF-α is consistent with the known ability of soy isoflavones, particularly genistein and daidzein, to attenuate UVB-induced oxidative stress and inhibit activation of NF-κB and MAPK signaling pathways. By limiting these pathways, soy extract cream likely reduces transcriptional activation of pro-inflammatory cytokines, thereby mitigating sustained inflammatory signaling in UVB-damaged skin. The magnitude of TNF-α reduction observed in this study supports the interpretation that topical soy extract exerts a biologically meaningful modulation of inflammatory responses rather than a marginal or incidental effect.[1] In parallel with the reduction in inflammatory markers, soy extract cream significantly increased VEGF levels in UVB-exposed skin, particularly at the 20% concentration.

The observed elevation of VEGF represents a marked enhancement of angiogenic signaling relative to UVB-exposed untreated controls, suggesting that soy extract not only suppresses inflammation but also promotes tissue repair mechanisms.[27] VEGF plays a critical role in angiogenesis, vascular permeability, and nutrient delivery, all of which are essential for effective skin regeneration following UV-induced injury. The magnitude of VEGF increase observed in the higher-dose treatment group indicates a robust pro-angiogenic response that is likely to contribute to improved tissue remodeling.

The absence of a significant difference in VEGF levels between healthy controls and UVB-exposed untreated mice may reflect the timing of tissue sampling during the proliferative phase of skin repair, when angiogenic activity is physiologically elevated. However, the substantially higher VEGF levels observed in soy-treated groups suggest that soy extract amplifies this endogenous repair response beyond baseline levels. This enhancement may facilitate more efficient vascular remodeling and collagen synthesis, thereby supporting structural recovery of UVB-damaged skin. Taken together, the simultaneous suppression of TNF-α and enhancement of VEGF expression observed in this study indicates that soy extract cream acts as a dual modulator of inflammation and angiogenesis in sub-chronic UVB-induced skin injury. Rather than exerting a unidirectional effect, soy extract appears to rebalance the inflammatory–angiogenic axis by attenuating excessive inflammatory signaling while promoting reparative processes. This coordinated modulation is particularly relevant in the context of UVB-induced skin damage, where persistent inflammation can impair effective healing if not counterbalanced by angiogenic and regenerative mechanisms.[28]

Although increasing the soy extract concentration from 10% to 20% did not further reduce TNF-α levels, the greater VEGF response observed at the higher dose suggests a dose-dependent enhancement of angiogenic signaling. This differential dose response underscores the importance of evaluating multiple biological endpoints when assessing photoprotective agents, as anti-inflammatory and pro-repair effects may not scale identically with dosage.[29,30] Future studies evaluating effect size estimates and bioavailability parameters would further clarify the optimal concentration range for maximizing therapeutic benefit.

Overall, the findings of this study demonstrate that topical soy extract cream produces quantitatively meaningful modulation of key inflammatory and angiogenic biomarkers following sub-chronic UVB exposure. These results strengthen the biological plausibility of soy extract as a natural photoprotective

agent and support its potential application in cosmeceutical formulations aimed at mitigating UVB-induced skin damage.

This study has several limitations. First, the evaluation of skin responses was limited to biochemical markers, namely TNF-α and VEGF levels, without histopathological confirmation. The absence of microscopic analysis, such as epidermal thickness measurement or assessment of dermal angiogenesis, limits the ability to directly correlate molecular changes with structural skin alterations following UVB exposure. Second, although the soy extract cream was applied topically, no assessment of skin barrier function or penetration efficiency was performed. Parameters such as transepidermal water loss or dermal penetration depth were not evaluated, which restricts conclusions regarding the extent of topical absorption and local distribution of bioactive compounds. Third, this study did not include bioavailability analysis of soy-derived isoflavones in skin tissue. As a result, the relationship between applied dose, local tissue concentration, and biological response could not be fully established. Future studies incorporating pharmacokinetic or tissue distribution analyses would provide a more comprehensive understanding of dose–response relationships.

Finally, the relatively small sample size per experimental group may limit the generalizability of the findings, although statistically significant differences were observed. Larger sample sizes and complementary outcome measures are warranted to strengthen the robustness of these results. Despite these limitations, the present study provides valuable in vivo evidence supporting the anti-inflammatory and pro-angiogenic effects of topical soy extract cream in a sub-chronic UVB exposure model.

CONCLUSION

These research demonstrate that topical soy extract cream significantly reduced TNF-α and VEGF levels in UVB-exposed skin, indicating attenuation of both inflammatory and angiogenic responses. The dose-dependent effect observed, particularly at 20% concentration, suggests that soy extract may function as a dual anti-inflammatory and anti-angiogenic agent. Collectively, these results support its potential as a natural photoprotective formulation against UVB-induced skin damage.

AUTHORS' CONTRIBUTIONS

Nurul Setyani prepares samples, designs protocols, implements protocols, and writes manuscripts. Titiek Sumarawati and Atina Hussaana reviewed and supervised the script. All authors have read and agreed to the final manuscript.

ACKNOWLEDGEMENT

We would like to thank the Head of the Semarang Stem Cell Cancer and Research (SCCR) Laboratory for all his support for this research.

FUNDING INFORMATION

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

DATA AVAILABILITY STATEMENT

The utilized data to contribute to this investigation are available from the corresponding author on reasonable request.

DISCLOSURE STATEMENT

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the

authors. The data is the result of the author's research and has never been published in other journals.

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