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J.Biomed.Transl.Res
ISSN: 2503-2178

JOURNAL OF BIOMEDICINE AND TRANSLATIONAL RESEARCH

Available online at JBTR website: https://jbtr.fk.undip.ac.id

Original Research Article

Anti-Inflammatory and Photoprotective Potential of *Clitoria ternatea* Extract in Mitigating UV-B-Induced IL-1β Elevation

Galih Sari Damayanti[1*], Febryan FadhFanyresnantio[2], Narendra Lintang Mahadewa[3], Rizki Noval Nursyafillah[1], Alfa Sofia Fany[1]

[1]*Department of Dermatology, Venereology, and Aesthetics, Faculty of Medicine, Universitas Diponegoro, Indonesia*
[2]*Department of Medicine, Faculty of Medicine, Universitas Diponegoro, Universitas Yarsi, Indonesia*

Article Info
History
Received: 26 Jan 2026
Accepted: 3 Apr 2026
Available: 30 April 2026

Abstract

Background: Global climate change has escalated ultraviolet-B (UV-B) radiation exposure, a potent inducer of reactive oxygen species (ROS) that triggers skin photoaging. Interleukin-1β (IL-1β) acts as a primary initiator in the inflammatory cascade following UV-B exposure, making it a strategic biomarker for evaluating anti-photoaging interventions. *Clitoria ternatea* (butterfly pea) contains bioactive phytochemicals like flavonoids and anthocyanins with known antioxidant and anti-inflammatory properties.

Objective: This study evaluates the effects of *C. ternatea* extract cream on serum IL-1β levels in UV-B-induced Wistar rats.

Methods: A true experimental study with a post-test-only control group design was conducted on 32 male Wistar rats for 30 days. Rats were divided into four groups: negative control (base cream) and treatment groups receiving 2.5%, 5%, and 10% *C. ternatea* extract cream. UV-B induction was applied for 30 minutes, three times per week. Serum IL-1β was quantified using an ELISA kit and analyzed using One-Way ANOVA followed by a Post-Hoc LSD test.

Results: Significant differences were observed among groups ($p < 0.001$). The 2.5% and 5% extract groups showed the lowest IL-1β levels (17.36 ± 2.67 pg/mL and 25.48 ± 8.48 pg/mL, respectively) compared to the control (51.14 ± 7.66 pg/mL). Interestingly, the 10% concentration did not show a significant reduction ($p = 0.260$), suggesting a potential saturation effect at higher doses.

Conclusion: *C. ternatea* extract cream, particularly at 2.5% and 5% concentrations, effectively mitigates UV-B-induced IL-1β elevation. Its anti-inflammatory properties make it a promising candidate for photoprotective skincare.

Keywords: *Clitoria ternatea extract; IL-1β modulation; anti-photoaging; photoprotective agents; herbal skincare.*
Permalink/ DOI: https://doi.org/10.14710/jbtr.v12i1.31148

INTRODUCTION

Climate change, a major global health threat this century, has increased solar radiation accumulation, contributing significantly to global warming. The earth's average surface temperature has risen by approximately 1.15°C since 1880, marking the point at which greenhouse gases began accumulating in the earth's atmosphere. This increase in temperature and subsequent environmental changes pose substantial health risks, particularly affecting the skin, the body's first line of defense against external factors. Dermatologists are critical in addressing and mitigating the adverse effects of solar radiation exposure, offering education, treatment, and comprehensive interventions to safeguard skin health.[1]

*Corresponding author:
E-mail: galih.derm@gmail.com
(Galih Sari Damayanti)

The skin serves a vital protective role as the body's outermost organ. Aging, a complex biological process, affects all organ systems and is characterized by declining functional capacity and resilience to physical, biological, and chemical stressors. Environmental factors significantly contribute to premature skin aging, commonly referred to as photoaging, where ultraviolet (UV) radiation from sunlight triggers the formation of reactive oxygen species (ROS). ROS leads to increased pro-inflammatory activity within the skin, escalating the production of inflammatory mediators like IL-1, IL-6, IL-8, and TNF-α, associated with skin damage and accelerated aging. Among these, IL-1β acts as a primary initiator in the inflammatory cascade following UV-B exposure, driving the subsequent release of other cytokines and matrix metalloproteinases (MMPs). Therefore, targeting IL-1β offers a strategic approach to halt the initial stages of photoaging.[2]

Clinically, the most common signs of skin aging include wrinkles, sagging, dullness, and uneven pigmentation. As healthy, youthful skin gradually gives way to these signs of aging, individuals often experience concerns that affect their quality of life, both physically and psychologically. The visible effects of photoaging emphasize the importance of finding effective skin-protective measures, especially those that target and mitigate the root inflammatory and oxidative processes triggered by UV exposure.[3]

In recent years, using natural ingredients has been recognized as a promising source of bioactive compounds, increasingly explored by the pharmaceutical and cosmetic industries. One such natural ingredient, *Clitoria ternatea* or butterfly pea, is widely available in Indonesia and has garnered attention for its potential benefits in the cosmetic field. Traditionally used in Ayurvedic medicine to enhance memory, reduce stress, and provide sedative effects, the butterfly pea is known for its high antioxidant, antibacterial, and anti-inflammatory activity. Its bioactive phytochemicals, including ternatin, anthocyanins, and phenolic compounds like quercetin and kaempferol derivatives, contribute to its potential as a natural anti-aging agent.[4]

This study investigates the effects of *C. ternatea* extract cream on serum Interleukin-1β (IL-1β) levels in UV-B-induced Wistar rats. This research aims to evaluate the anti-inflammatory and photoprotective effects of *C. ternatea*, particularly its efficacy in reducing IL-1β as a marker of photoaging.

MATERIALS AND METHODS

Preparation of *Clitoria ternatea* Extract

Fresh *C. ternatea* flowers were harvested from a flower farm in Ngawi, ensuring they were in optimal condition with their characteristic blue color. The flowers were then dried at 40°C over three days to produce dry simplicia. The dried flowers were further processed in the Integrated Chemistry Laboratory at UNDIP using a maceration method with 96% ethanol, repeated three times to maximize extraction. The filtrate was separated using a Buchner funnel and collected in a beaker. The collected filtrate was concentrated using an evaporator set at 40°C.

Flavonoid Content Analysis Using UV-Vis Spectrophotometry

The *C. ternatea* extract, prepared at a concentration of 3000 ppm in 96% ethanol, was incubated for several hours at 25°C before analysis. The extract's absorbance was measured using a UV-Vis spectrophotometer at a wavelength of 420 nm to determine flavonoid content, expressed in mg of quercetin equivalents per gram (mg QE/g), with quercetin serving as the standard.

Formulation of *Clitoria ternatea* Extract Cream

Based on research by Purnamasari (2023), 2.5% and 5% concentrations showed similar effects. These lower concentrations were retained in this study to serve as a validated baseline within the same experimental conditions, while introducing a higher concentration at 10% to determine the specific dose-response curve and identify potential saturation points of the bioactive compounds. The cream formulations were prepared at the UNDIP Faculty of Pharmacy using Synchro® base cream, a well-tolerated and commercially available cosmetic base with an established safety profile, enriched with ingredients such as calendula oil, sweet almond oil, beeswax, hypericum extract, fatty acid esters, vitamins B complex, A, C, E, H, biological extracts, amino acids, potassium, magnesium, glutamine, arginine, and lysine. *C. ternatea* extract was incorporated into the base at varying concentrations of 2.5%, 5%, and 10%. To control for the potential confounding effects of antioxidants naturally present in the Synchro® base, the exact same base cream was applied to the negative control group (K), ensuring that any significant reduction in IL-1β could be directly attributed to the addition of the C. ternatea extract.

Animal Treatment

Thirty-two healthy male Wistar rats (Rattus norvegicus), aged 8-12 weeks and weighing between 150-200 grams, were included in this study. Rats exhibiting any signs of illness, skin abnormalities, or macroscopic anatomical defects were excluded. The animals were acclimatized for seven days, provided with food and water ad libitum, and maintained in a temperature-controlled environment (25-28°C) with a 12-hour light cycle (6:00 AM - 6:00 PM). The rats' dorsal hair was shaved to create a 2x2 cm area for application. On the eighth day, the rats were randomly assigned into four groups (Table 1).

The sample size was determined using Federer's formula (n-1)(t-1)/15. With four experimental groups (t=4), the minimum required sample size was 6 rats per group. This minimum requirement also complies with the WHO Research Guidelines for Evaluating the Safety and Efficacy of Herbal Medicines. To account for potential dropouts or mortality during the 30-day intervention period, the sample size was increased, resulting in 8 rats per group (a total of 32 rats). The rats were assigned to their

respective groups using a simple random sampling technique by drawing lots.

UV Radiation Exposure and Intervention

UV-B irradiation was administered using a calibrated artificial UV-B lamp positioned within a covered enclosure to restrict movement. The lamp was placed at a 20 cm distance from the rats. UV-B exposure was carried out thrice per week for 30 days, starting at 6:00 AM, with a 30-minute duration per session. In each group (K, P1, P2, and P3), the cream was applied twice daily, 20 minutes before UV exposure and four hours post-exposure. After 30 days, blood samples were collected for serum analysis. Subsequently, for tissue sampling and termination, the rats were anesthetized via intraperitoneal injection of ketamine (35 mg/kg BW) and xylazine (5 mg/kg BW), adhering to modern animal welfare and ethical standards.

The UV source utilized was a Blue Light Philips TL 20W/52 lamp. While precise dosimetric measurements in mJ/cm² were not recorded due to equipment limitations, the exposure intensity was standardized across all experimental groups by maintaining a strict, fixed distance of 20 cm for a 30-minute duration per session.

Statistical Analysis

Data analysis was performed using SPSS software. The normality of the data distribution for serum IL-1β levels was evaluated using the Shapiro-Wilk test. Following the confirmation of normal distribution ($p > 0.05$) and homogeneity of variance via Levene's test, a One-Way Analysis of Variance (ANOVA) was conducted. A Post-Hoc Least Significant Difference (LSD) test was subsequently used to identify specific differences between the experimental groups. A p-value of < 0.05 was considered statistically significant.

Ethical Clearance

This research protocol was reviewed and approved by the Health Research Ethics Committee (KEPK) of the Faculty of Medicine, Diponegoro University, under Ethical Clearance No. 045/EC-H/KEPK/FK-UNDIP/V/2024. The ethical approval is valid for research conducted in the Animal Laboratory of the Faculty of Medicine, Diponegoro University, from May 21st, 2024, until May 21st, 2025. All animal experiments were performed in accordance with institutional guidelines for the care and use of laboratory animals.

RESULTS

TFC, TPC, and antioxidant activity

The total flavonoid content (TFC) was 12.80 ± 0.11 mg QE/g, indicating a substantial presence of flavonoids in the extract. The total phenolic content (TPC) of *C. ternatea* extract was 20.76 ± 0.62 mg GAE/g, reflecting a high phenolic content in the extract. The IC50 value, which represents the concentration required to inhibit 50% of DPPH radicals, was found to be 437.74 µg/mL. This IC50 value indicates moderate antioxidant activity. The antioxidant activity observed could be attributed to the high levels of flavonoids and phenolic compounds present in the extract, which are known to contribute to ROS neutralization and anti-inflammatory effects.

Serum IL-1β levels

Male Wistar rats were fasted for 6–8 hours prior to blood collection. Blood samples (5 mL) were obtained from the orbital sinus and stored in vacutainer tubes without anticoagulant. Serum IL-1β concentrations were quantified using a Rat IL-1β ELISA kit at the GAKI Laboratory, Central Laboratory of FK UNDIP.

As shown in **Figure 1**, serum IL-1β levels were markedly reduced in rats treated with C. ternatea extract cream at concentrations of 2.5% (P1) and 5% (P2) compared to the control group following UV-B exposure. Statistical analysis revealed significant differences among the experimental groups ($p < 0.001$). Post hoc comparisons demonstrated that both P1 and P2 groups exhibited significantly lower IL-1β levels than the control group ($p < 0.001$).

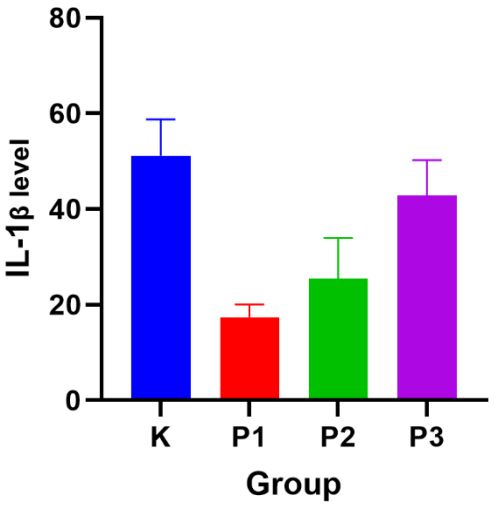

Figure 1. IL-1β levels in serum across experimental groups following UV-B exposure. Each bar represents the mean of IL-1 β levels ± SD. The IL-1β levels were significantly reduced in groups P1 and P2 compared to the control group (K), indicating a dose-dependent anti-inflammatory effect of *C. ternatea* extract at lower concentrations. K=negative control, P1=2.5% *C. ternatea* extract cream), P2=5% *C. ternatea* extract cream, P3=10% *C. ternatea* extract cream

Detailed quantitative values are presented in **Table 1**, which shows that the P1 group had the lowest mean IL-1β concentration (17.36 ± 2.67 pg/mL), representing approximately a 66% reduction compared to the control group (51.14 ± 7.66 pg/mL). In contrast, the 10% extract group (P3) did not differ significantly from the control group ($p = 0.260$), indicating a reduced anti-inflammatory effect at higher extract concentrations. Furthermore, comparison between treatment groups **(Table 1)** revealed that P1 exhibited

Table 1. Average IL-1β serum levels

Group	Treatment	IL-1β (mean ± SD)	p-value
K	Base cream + UV-B exposure 3x/week	51.14 ± 7.66	-
P1	2.5% extract + UV-B exposure 3x/week	17.36 ± 2.67	<0.001*
P2	5% extract + UV-B exposure 3x/week	25.48 ± 8.48	<0.001*
P3	10% extract + UV-B exposure 3x/week	42.84 ± 7.39	0.260

significantly lower IL-1β levels than both P2 and P3, suggesting that the optimal anti-inflammatory response occurred at lower extract concentrations.

DISCUSSION

The study findings highlight the potential of *C. ternatea* extract as an effective anti-inflammatory agent against UV-B-induced skin inflammation mediated IL-1β serum. Our result indicates that the topical of *C. ternatea* extract cream at concentrations of 2.5 and 5% significantly reduced IL-1β serum levels compared to the control group. Thus, the findings support the hypothesis of bioactive compounds in *C. ternatea*, such as flavonoids and anthocyanics has the ability to mitigate UV-induced inflammatory responses.[5,6] These bioactive compounds are well-documented for their antioxidant properties. They are essential in neutralizing reactive oxygen species (ROS), reducing oxidative stress, and limiting subsequent inflammatory signaling pathways triggered by UV exposure.[6-9]

The observed reduction in IL-1β levels in the treatment groups is consistent with the known mechanisms by which flavonoids exert their anti-inflammatory effects. Flavonoids play a key role in the inhibition of pro-inflammatory pathways, such as the NF-κB and MAPK signaling pathways, often activated by oxidative stress.[5,10–12] By suppressing these pathways, *C. ternatea* extract likely reduces the transcription of pro-inflammatory cytokines like IL-1β, thus minimizing cellular damage and inflammatory responses associated with photoaging. Interestingly, the 10% concentration group did not demonstrate the same level of efficacy as the lower concentrations, suggesting that there may be an optimal concentration threshold for the bioavailability and effectiveness of *C. ternatea* compounds in topical applications. In addition, this finding aligns with similar studies where increased concentration did not significantly enhance outcomes, possibly due to saturation effects or antagonist reactions among phytochemicals.[13–15]

The ability of *C. ternatea* to lower IL-1β levels positions itself as a promising ingredient in dermatological formulations aimed at preventing and mitigating photoaging. UV-B radiation is a potent primary factor in skin aging and inflammatory skin conditions,[16–18] natural, plant-based agents like *C. ternatea* offer safer, sustainable alternative compared to synthetic compounds.[19,20] Its rich flavonoid and anthocyanin content contributes to anti-inflammatory effects and promotes skin health by enhancing photoprotection. Therefore, this study contributes to the growing body of evidence supporting *C. ternatea's* role in dermatology and suggests further exploration into optimal formulation and concentration for maximizing its protective effects.

This study has several limitations, including the reliance on a single biomarker (IL-1β) and the use of an animal model with a post-test-only design, which limits direct extrapolation to clinical human settings. Future studies should incorporate baseline measurements and broader cytokine panels.

CONCLUSION

Our findings demonstrate that *C. ternatea* extract cream, particularly at lower concentrations of 2.5% and 5%, effectively mitigates UV-B-induced IL-1β elevation compared to higher doses. The extract holds promise for future dermatological use, especially in products designed to prevent or reduce skin aging caused by environmental factors. Further research is recommended to explore optimal formulations and long-term efficacy in clinical applications. This could solidify its role as a safe, effective alternative in cosmetics and dermatology.

ACKNOWLEDGMENTS

We would like to thank the Department of Dermatology, Venereology, and Aesthetic Diponegoro University, Semarang for their support and motivation.

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