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Effect of Turmeric Ethanol Extract *(Curcuma Longa Linn)* on IL-6, IL-10 Levels and Skin Moisture

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Ultraviolet B (UVB) radiation is known to induce skin damage, including erythema, roughness, sagging, wrinkles, and reduced skin moisture, contributing to premature aging. Turmeric (*Curcuma longa Linn.*) contains curcumin, an active compound with potent anti-inflammatory properties. This study investigated the effect of turmeric ethanol extract on IL-6 and IL-10 levels, as well as skin moisture, in UVB-exposed rats. A total of 24 Wistar rats were randomly divided into four groups: healthy controls (K1), UVB-exposed without treatment (K2), UVB-exposed treated with turmeric ethanol extract at 100 mg/kg BW (K3), and 200 mg/kg BW (K4). The extract was administered orally for 14 days. IL-6 and IL-10 levels were measured using ELISA, and skin moisture was assessed macroscopically. Statistical analysis was performed using one-way ANOVA. Rats in groups K2, K3, and K4 exhibited very dry skin, redness, visible wrinkles, and peeling following UVB exposure. IL-6 levels were significantly lower in treated groups, with the lowest levels observed in K4 (1.85 ± 0.24 ng/L), compared to K1 (4.36 ± 0.75 ng/L) and K2 (4.46 ± 0.74 ng/L) ($p = 0.000$). IL-10 levels increased in the treated groups, notably in K3 (376.48 ± 78.24 pg/mL) and K4 (351.06 ± 78.24 pg/mL), compared to K1 (285.34 ± 45.54 pg/mL) and K2 (306.89 ± 45.54 pg/mL) ($p = 0.001$). These findings suggest that oral administration of turmeric ethanol extract modulates inflammatory responses by reducing IL-6 and enhancing IL-10 in UVB-exposed skin, although significant dryness persists.

Keywords: Turmeric Ethanol Extract, IL-6, IL-10, UVB, Skin Moisture

INTRODUCTION

Exposure to Ultraviolet B (UVB) rays on the skin can cause *photoaging* where the skin becomes erythema, rough, saggy, wrinkled, less shiny and increases the risk of skin diseases can eventually lead to a decrease in skin moisture and premature aging (Gromkowska-Kępka et al., 2021).UV-B radiation can increase *reactive oxygen species* (ROS) which causes oxidative destructive stress, impairs cell structure and function, mediates inflammation, reduces collagen and elastic fibers(Banerjee & Leptin, 2014; Salminen et al., 2022). As a result, cell structure and function experience an increase in pro-inflammatory cytokines, such as TNF-α, IL-1, IL-6 so that anti-inflammatory cytokines will appear, one of which is IL-10(Ansary et al., 2021; Omer et al., 2019). This inflammatory reaction plays a significant role in the decrease in skin moisture, which can lead to dry and rough skin conditions (Roy & Oktarlina, 2018).

Turmeric (*Curcuma longa Linn.*) contains several active substances, namely, *curcumin*, dihydrocurcumin, desmethoxycurcumin, axary oil, and fat.(Wolnicka-Glubisz & Wisniewska-Becker, 2023) Turmeric has long been the focus of research in traditional medicine thanks to its curcumin content which has significant anti-inflammatory and antioxidant properties. Although a number of studies have examined curcumin's potential in managing a variety of inflammatory conditions, its effects on cytokine profiles, particularly interleukin-6 (IL-6) and interleukin-10 (IL-10), as well as simultaneous skin moisture levels still require further research (Mohammad et al., 2023).

According to the U.S. National Health Interview Survey in 2010 and the National Sun Survey (Canada) in 2006, 37% of adults reported at least one sunburn per year during the summer. Research conducted on 720 respondents, found that the face is a part of the body that is prioritized to be protected (Daulay, 2023). In Indonesia, as many as 57.3% focus on UV exposure or sunlight. Thus, in Indonesia, which has two seasons, sunburn is often found. The prevalence of dry skin or xerosis in Indonesia is 50%-80%. Meanwhile, in some other countries such as Brazil, Australia, Turkey, and others, it is 35% - 70% (Fauziyyah et al., 2023).

Research on curcumin compounds in turmeric that have the potential to increase interleukin-10 (IL-10) after high-intensity exercise showed that administration of curcumin at a dose of 400 mg can increase IL-10 levels (Bafirman et al., 2024). Research on the effect of curcumin gel on inflammatory biomarkers and anti-inflammatory in experimentally induced periodontitis in rats: biochemical and immunological studies exert anti-inflammatory effects after 6 weeks of use (Mohammad et al., 2023).
The effects of curcumin can suppress inflammatory reactions, increase the proliferation of fibroblasts, the formation of granulating tissue and collagen deposition in mice with wounds (Threskeia et al., 2023).

The increasing prevalence of skin damage due to sun exposure is driving the search for safe and effective photoprotective agents. Curcumin, the polyphenol compound in turmeric, has shown potential as a skin-protective agent. This study aimed to test the effect of turmeric extract on IL-6, IL-10 levels and skin moisture levels in mice exposed to UV-B rays.

METHODS

This experimental study employed a post-test only control group design and was conducted in June 2024 at the Integrated Biomedical Laboratory (IBL), Faculty of Medicine, Sultan Agung Islamic University (UNISSULA), Semarang. The study used 24 healthy male Wistar rats aged 2–3 months and weighing 200–250 grams. Prior to treatment, the animals were acclimatized for seven days under standard laboratory conditions. The subjects were randomly assigned into four groups (n=6 per group): the healthy control group (K1) received no treatment and was maintained on a standard diet; the negative control group (K2) was exposed to UVB radiation without turmeric extract; the first treatment group (K3) received turmeric ethanol extract (EEK) orally at a dose of 100 mg/kg body weight and was exposed to UVB; and the second treatment group (K4) received EEK at 200 mg/kg body weight and was also exposed to UVB.

UVB irradiation was delivered using a TL20W/12 RS UVB lamp (Philips, Germany) with a peak emission at 312 nm. The dose of UVB radiation was standardized at 0.5 J/cm² for 10 minutes per day for 14 consecutive days, applied to the shaved dorsal area of each rat at a distance of 20 cm from the source. This UVB dose and duration were selected based on previous studies that induced photoaging and inflammatory responses in a safe and controlled manner. The turmeric extract was prepared by macerating dried *Curcuma longa* rhizomes in 96% ethanol, and the chosen doses (100 and 200 mg/kg) were based on prior research demonstrating effective anti-inflammatory and antioxidant activity.(Agung et al., 2018; Cavinato et al., 2017)

At the end of the 14-day treatment, blood samples were collected via cardiac puncture under anesthesia to analyze serum IL-6 and IL-10 levels using ELISA. Skin hydration was assessed macroscopically and quantitatively using a skin analyzer.(Çetin et al., 2018) The collected data were cleaned, tabulated, and subjected to statistical analysis. Data normality was evaluated using the Shapiro-Wilk test, and homogeneity of variance was tested with Levene's test. If both assumptions were met, one-way ANOVA was used to determine differences among groups. All statistical analyses were performed using SPSS for Windows with a significance level set at $\alpha = 0.05$.

RESULTS AND DISCUSSION

Phytochemical analysis revealed that the average flavonoid content in turmeric ethanol extract was 24.035 mg/mL at a concentration of 50 ppm, while the phenolic content reached 77.105 mg/mL at a concentration of 500 ppm. These bioactive compounds support the antioxidant and anti-inflammatory potential of turmeric extract.

Skin moisture measurement using the Aramo Skin Analyzer showed that the rat groups exposed to UVB radiation (K2, K3, and K4) experienced a reduction in skin hydration. Skin moisture was categorized as follows: very dry (≤33%), dry (34-37%), normal (38-42%), and moist (43-46%). On day 1, most subjects were classified as having dry or normal skin, but over time particularly by day 14 most rats in the treatment groups exhibited very dry skin conditions.

Table 1
Results Of Measuring The Humidity Level of Rats

Group	Measurement Day			
	Day 1	**Day 3**	**Day 7**	**Day 14**
Healthy mice (K1)	2K,3N	2K,,3N	2SK,1K, 2N	2SK,1K,1N, 1L
Negative Control (K2)	1K,4N	3SK,1K, 1N	5SK	5SK
EEK 100mg/kg BB (K3)	1K,3N, 1L	3SK,3K	5SK	5SK
EEK 200mg/kg BB (K3)	1K,4N	4SK,1K	5SK	5SK

Table 1 shows rat subjects with dry skin conditions in the K1 (2 heads), K2 (1 head), K3 (1 head), and K4 (1 head) groups. Only 1 rat subject in the K3 group had moist skin, the rest had normal skin conditions on day 1. Figure 1 shows an example of a rat skin condition:

Day 7 UVB exposure causes the skin of mice to experience dryness, redness, wrinkles, and peeling. The subjects in the K1 group had various skin conditions, while the subjects in the K2, K3, and K4 groups experienced very dry skin.

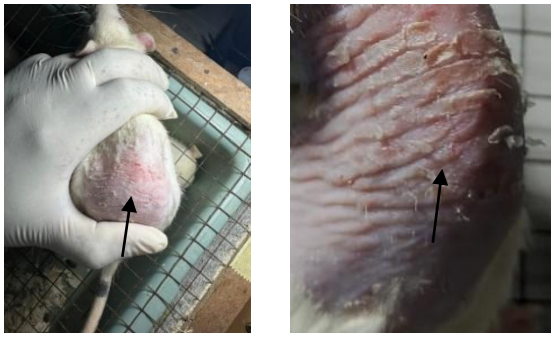

Figure 2. Macroscopic Skin of Rats Exposed to UVB on Day 7 with Very Dry Skin Moisture Conditions.

Exposure to UVB for 14 days caused very dry skin in the K1 and K2, K3, and K4 rat groups. The skin of the mice experienced redness, wrinkles, and peeling after UVB exposure.

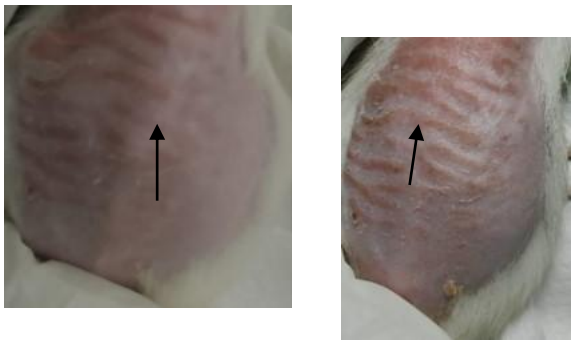

Figure 3. Macroscopic Skin of Mice Exposed to UVB on Day 14 with Very Dry Skin Moisture Conditions

The results of IL-6 level analysis using the ELISA method obtained the following results:

Table 2
Results of IL-6 Level Research

Group	Group K1	K2	K3	K4	*p value*
Mean	4.36	4.46	3.76	1.86	
Std. Dev	0.75	0.74	0.59	0.24	
Saphiro Wilk	0.422*	0.290*	0.078*	0.0747*	
Levene's Test					0.285*
One Way Anova					0.000*

Information:
*Uji *Saphiro Wilk* (p > 0.05 = normal)
**Levene's Test* (p > 0.05 = homogen)
**One Way Anova* (p <0.05 = signifikan)

Based on the results presented in Table 2 and Figure 4, the mean IL-6 level in the healthy rat group (K1) was 4.36 ± 0.75 ng/L, while the negative control group (K2) had a mean value of 4.46 ± 0.74 ng/L. The group receiving turmeric ethanol extract (EEK) at a dose of 100 mg/kg body weight (K3) had an average IL-6 level of 3.76 ± 0.59 ng/L, and the group receiving a dose of 200 mg/kg body weight (K4) showed the lowest mean value of 1.86 ± 0.24 ng/L. The distribution and variance of IL-6 levels were assessed using the Shapiro-Wilk and Levene's tests, which showed that the data were normally distributed (p > 0.05) and exhibited homogeneous variance (p = 0.285; p > 0.05). Since the data met the assumptions of normality and homogeneity, further analysis was conducted using a one-way ANOVA test.

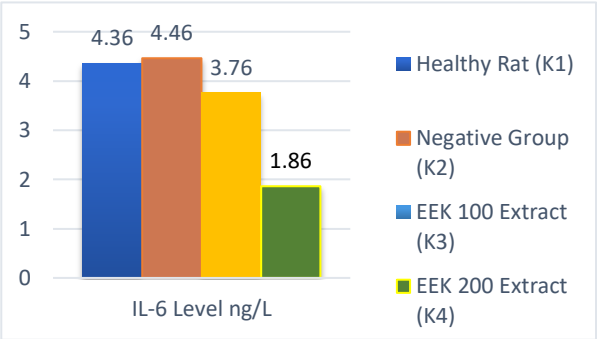

Figure 4. Mean IL-6 Levels Between Treatment Groups

Statistical analysis with the One Way Anova test obtained a significant value, namely p=0.000 (p<0.05) so that it was concluded that there was a significant difference in the average IL-6 level between the treatment groups.

The results of IL-10 level analysis using the ELISA method obtained the following results:

Table 3
Results of IL-10 Level Research

Group	Group K1	K2	K3	K4	*p value*
Mean	285.34	306.89	435.52	376.48	
Std. Dev	37.76	45.54	32.96	78.24	
Saphiro Wilk	0.740*	0.910*	0.629*	0.358*	
Levene's Test					0.548*
One Way Anova					0.001*

Information:
*Uji *Saphiro Wilk* (p > 0.05 = normal)
**Levene's Test* (p > 0.05 = homogen)
**One Way Anova* (p <0.05 = signifikan)

Based on the results presented in Table 3 and Figure 5, the mean IL-10 level in the healthy rat group (K1) was 285.34 ± 37.76 pg/mL, while the negative control group (K2) showed a mean value of 306.89 ± 45.54 pg/mL. The group administered turmeric ethanol extract (EEK) at a dose of 100 mg/kg body weight (K3) had the highest mean IL-10 level of 435.52 ± 32.96 pg/mL, whereas the group receiving 200 mg/kg body weight (K4) had a mean value of 376.48 ± 78.24 pg/mL. The distribution and variance of IL-10 levels were assessed using the Shapiro-Wilk and

Levene's tests, which confirmed that the data were normally distributed ($p > 0.05$) and had homogeneous variance ($p = 0.548$; $p > 0.05$). Since the assumptions of normality and homogeneity were met, a one-way ANOVA test was conducted for further analysis.

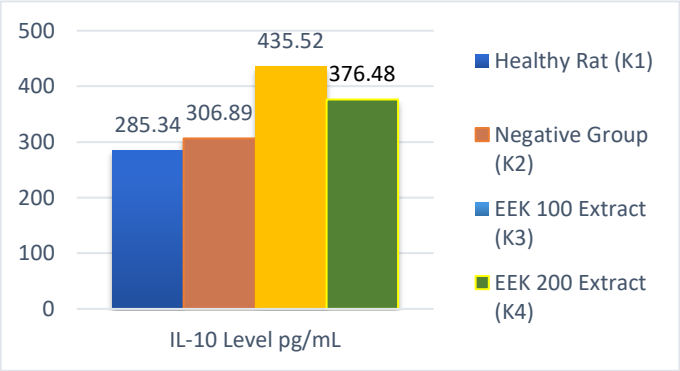

Figure 2. Mean Il-10 Levels Between Treatment Groups

Statistical analysis with the One Way Anova test obtained a significant value of $p=0.001$ ($p<0.05$) so that it can be concluded that there is a significant difference in the average IL-10 level between the treatment groups

Discussion

Dynamic changes by environmental factors, namely UVB exposure, occur in stages, starting from one cell, to tissues, and ending with organs. Changes that occur in the skin include decreased elasticity, skin discoloration and reduced work of the sebaceous glands, which leads to decreased moisture and disruption of the skin's water-lipid layer (Ryser et al., 2014). This study showed that oral administration of turmeric ethanol extract (EEK) to rats that experienced skin damage due to exposure to UVB rays was not effective in improving very dry skin conditions. Although turmeric is known to have anti-inflammatory and antioxidant properties, in this study EEK was not able to increase the number of fibroblasts or collagen production needed to repair skin damage. Exposure to UVB rays causes varying degrees of skin damage, ranging from mild redness to severe burns. This skin damage is caused by an inflammatory process that involves the production of various inflammatory substances and the death of skin cells. The results of this study indicate that the mechanism of skin damage caused by UVB rays is more complex than that EEK can overcome in this study, so further research is needed to find effective solutions in overcoming skin problems caused by sun exposure (Ryser et al., 2014).

The results of the analysis of average IL-6 levels in rat serum showed that, statistically, the K1 and K2 groups were similar; however, clinically, there was an increase in IL-6 levels in the K2 group. The administration of turmeric ethanol extract (TEE) at a dose of 200 mg/kg body weight resulted in the most significant reduction in IL-6 levels compared to the other groups, followed by the group that received TEE at a dose of 100 mg/kg body weight. EEK is beneficial for inflammation/erythema, targeting ROS by lowering the number of free radicals, blocking monocyte activation and cytokine secretion that act as inflammatory mediators, thereby lowering IL-6 levels. When hemostatic occurs, polyphenol compounds in turmeric extract and its derivatives such as *demethoxycurcumin* and *until-demethoxycurcumin* increase the release of PDGF, TGF-β, FGF, and EGF by platelets. To prevent the inflammatory phase from elongating and prevent tissue damage (D'Orazio et al., 2013). In line with the research of Cenar et al. (2023) with the local application of curcumin gel as an addition *scaling* and *root planing* (SRP) against inflammatory biomarkers MMP-8, IL-6, CRP, and ALP, and anti-inflammatory biomarkers IL-10 in mice with periodontitis. Curcumin has a reduction effect of pro-inflammatory biomarkers (MMP-8, IL-6, CRP, and ALP) and an increase in anti-inflammatory biomarkers (IL-10) compared to tetracycline after 6 weeks. IL-10 levels gradually increase after 2 weeks, peak at 4 weeks, and then decrease after 6 weeks (Mohammad et al., 2023).

Curcumin, the active compound in turmeric, has great potential in the treatment of various diseases due to its ability to modulate various biological processes in the body. However, the oral use of curcumin is often limited due to its poor absorption in the body. Thanks to technological advances, various innovative curcumin preparations have now been developed that can increase the bioavailability of curcumin in the body. These preparations allow curcumin to reach its molecular targets more effectively, such as cytokines, antioxidant enzymes, and other important proteins.(Yuan Shan & Iskandar, 2018) Thus, curcumin can provide more optimal health benefits, including reducing inflammation and protecting cells from damage (Kasprzak-Drozd et al., 2024). This study proves that oral administration has an effect on ROS which lowers levels of pro-inflammatory cytokines (IL-6) and increases IL-10 levels in mice exposed to UVB light. The results of the study with EEK administration significantly increased IL-10 levels highest in the 100 mg/kgBB dose group and then at the 200 mg/kgBB dose. The increase in IL-10 gradually increased after 2 weeks, peaking at 4 weeks (Mohammad et al., 2023).

IL-10 plays an important role in regulating homeostasis, including addressing inflammation during acute infection or tissue injury at both the local and systemic levels. At the same time, many pathogens have harnessed the pleiotropic power of IL-10 to facilitate the inflammatory state that triggers chronic infections.(Singampalli et al., 2020) Increased levels of IL-10 can moderate the rate of apoptosis, IL-10 induced in response to infection. The mice also developed severe inflammation, and experienced increased rates of apoptosis. IL-10 can be produced to reduce inflammation and minimize pathology (Kasprzak-Drozd et al., 2024).

UVB radiation is known to cause skin inflammation, (Kim et al., 2017) UVB reveals facilitating skin inflammation by increasing keratinocyte responses to IL-22. IL-22, which is produced by activated CD4+ cells and NK cells, plays a pathogenic role in acute and chronic skin

diseases. At the same time, IL-22 increased the production of IL-1β, IL-6, and IL-18 in UVB-irradiated mouse cells and human primary keratinocytes. (Lubis et al., 2023) reported the effectiveness of white turmeric extract in lowering IL-6 in white rats administered orally. Administration of white turmeric extract at a dose of 750 mg has the best effectiveness in reducing IL-6 levels. The results of this study are in line with the research conducted by (Shafia et al., 2023) proving the effect of bay leaf extract gel on the expression of IL-10 and IL-6 genes in traumatic ulcers. Treatment with bay leaf gel extract (*Syzygium polyanthum*) was shown to significantly increase IL-10 gene expression and decrease IL-6 gene expression in traumatic ulcer model Wistar mice.

CONCLUSIONS

The administration of turmeric ethanol extract (EEK) influenced inflammatory cytokine profiles in UVB-exposed Wistar rats. A significant reduction in IL-6 levels and an increase in IL-10 levels were observed, particularly at the 100 mg/kg BW dose, indicating the anti-inflammatory potential of the extract. However, despite these biochemical changes, all treatment groups still exhibited signs of reduced skin moisture, suggesting that while EEK modulates cytokine responses, its effect on improving skin hydration under prolonged UVB exposure may be limited.

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