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Effect of Turmeric Ethanol Extract *(Curcuma Longa Linn.)* on Tumor Necrosis Factor alpha (TNFα) and the extent of wound lesions (Experimental Study on Wistar Rats Exposed to UVB Rays)

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Continuous exposure to ultraviolet B (UVB) radiation can induce photoaging and accelerate premature skin aging. Turmeric (*Curcuma longa*) is a medicinal plant that contains curcumin, an active compound known for its anti-inflammatory properties and its role in accelerating wound healing. This study aimed to evaluate the effect of turmeric ethanol extract on TNF-α levels and wound lesion areas in Wistar rats exposed to UVB radiation. A post-test-only control group design was employed, involving 24 Wistar rats divided into four groups: a healthy control group (K1), a negative control group (K2), and two treatment groups receiving oral turmeric ethanol extract at doses of 100 mg/kg BW (K3) and 200 mg/kg BW (K4) for 14 days, with concurrent UVB exposure. TNF-α levels were assessed using one-way ANOVA followed by Tukey's post hoc test, while wound lesion areas were analyzed using the Kruskal–Wallis test followed by the Mann–Whitney U test. The results showed that the highest TNF-α levels were observed in the healthy control group (129.14 ng/L), although no statistically significant differences were found between groups ($p = 0.538$). In contrast, a significant difference was observed in wound lesion areas ($p < 0.001$), with the largest lesions occurring in the negative control group. In conclusion, oral administration of turmeric ethanol extract did not significantly affect TNF-α levels but was effective in reducing the area of wound lesions caused by UVB exposure.

Keywords: Anti-inflammatory, TNF-α, Turmeric, UVB, Wound

INTRODUCTION

Exposure to ultraviolet B (UVB) radiation is a major factor contributing to both acute and chronic skin damage (Cavinato *et al.*, 2017). UVB rays can penetrate the epidermis, leading to the generation of reactive oxygen species (ROS), which induce oxidative stress and activate inflammatory pathways in the skin (Tobin, 2017). A key mediator in this inflammatory response is tumor necrosis factor-alpha (TNF-α), a pro-inflammatory cytokine secreted by keratinocytes and Langerhans cells in response to UVB-induced cellular damage (Chen *et al.*, 2018; Huang & Chien, 2020b).

UVB-induced inflammation can impair wound healing and increase the risk of chronic skin lesions (Monika *et al.*, 2022). Therefore, intervention using agents with anti inflammatory properties and the ability to accelerate tissue regeneration is essential for the healing process of the wound (Huang & Chien, 2020a; Pittayapruek *et al.*, 2016). Turmeric (Curcuma longa) is a well-known medicinal plant that contains curcumin, a bioactive compound demonstrated to possess antioxidant and anti-inflammatory properties (Lubis *et al.*, 2022), as well as to enhance the wound healing process by promoting fibroblast proliferation and collagen synthesis (Silalahi, 2017). Several studies have shown that turmeric extract can reduce TNF-α levels and accelerate tissue repair in various wound models (Salenda, 2021; Sabarees et al., 2024; Dahliana, 2021).

Although numerous studies have highlighted the effects of curcumin on wound healing and the reduction of TNF-α levels independently, research that investigates both parameters simultaneously in a UVB-induced skin damage model remains limited (Sharma *et al.*, 2021; Shedoeva *et al.*, 2019). However, such data are crucial for reinforcing the therapeutic potential of curcumin as a

photoprotective agent and a treatment for radiation-induced skin injuries (Li *et al.*, 2018; Wolnicka-Glubisz & Wisniewska-Becker, 2023).

Therefore, this study was conducted to simultaneously evaluate the effects of turmeric (Curcuma longa) ethanol extract on TNF-α levels and the extent of wound lesions in Wistar rats exposed to UVB radiation. The findings are intended to provide a scientific basis for the development of safe and effective herbal-based therapies for the prevention and treatment of UV-induced skin damage.

METHODS

This study employed an experimental laboratory design using a post-test-only control group approach. The study was conducted at the Chemistry Laboratory, Faculty of Pharmacy, Sultan Agung Islamic University (UNISSULA), Semarang. A total of 24 male Wistar rats, aged 8–10 weeks and weighing 200–250 grams, were used as experimental subjects. Following a seven-day acclimatization period, the rats were randomly assigned to four groups. Group K1 served as the healthy control and received no treatment or UVB exposure. Group K2, the negative control, was exposed to UVB radiation at a dose of 0.5 J/cm² for 10 minutes daily without administration of turmeric extract. Groups K3 and K4 were administered turmeric ethanol extract orally at doses of 100 mg/kg BW and 200 mg/kg BW, respectively, and were also exposed to UVB radiation at the same dose and duration as Group K2 for 14 consecutive days (Rosita & Prakoeswa, 2023a; Treuting *et al.*, 2017).

On the 15th day, blood samples were collected via the orbital vein to assess TNF-α levels. The analysis of TNF-α was conducted using the Enzyme-Linked Immunosorbent Assay (ELISA) method with a commercial mouse-specific kit (Çetin *et al.*, 2018). A total of 40 µL of serum was added to a microtiter well, followed by 10 µL of anti-TNF-α antibody and 50 µL of streptavidin-HRP solution. The samples were incubated at 37°C for 60 minutes, washed, and subsequently treated with 50 µL each of substrate solutions A and B. After a second incubation in the dark for 10 minutes, the reaction was terminated using a stop solution, and absorbance was measured at 450 nm with a microplate reader (Liu *et al.*, 2019; Rosita & Prakoeswa, 2023b).

The assessment of UVB-induced wound lesions was conducted through daily macroscopic observation of erythema on the dorsal skin of the rats for a period of 14 days (Liu *et al.*, 2019; Rosita & Prakoeswa, 2023b). Lesion areas were measured using a ruler or digital caliper and recorded in square centimeters (cm²). Changes in lesion size were usedThe data were analyzed using the Shapiro–Wilk test to assess normality and Levene's test to evaluate the homogeneity of variances. If the data were normally distributed and homogeneous, they were further analyzed using one-way ANOVA followed by a post hoc test. If the assumptions of normality and homogeneity were not met, the Kruskal–Wallis test and Mann–Whitney U test were employed as non-parametric alternatives. All statistical analyses were conducted using SPSS for Windows.

RESULTS AND DISCUSSION

The study involved 24 Wistar rats, each exposed to UVB radiation at a wavelength of 302 nm and a dose of 0.5 J/cm² for 10 minutes daily over a 14-day (Liu *et al.*, 2019). The rats were randomly divided into four groups, each consisting of six rats: a healthy control group (K1), a negative control group (K2), and two treatment groups (K3 and K4). Group K1 received neither UVB exposure nor turmeric extract, while Group K2 was exposed to UVB radiation without administration of turmeric extract. Group K3 received 100 mg/kg body weight of turmeric ethanol extract in combination with UVB exposure, and Group K4 received 200 mg/kg body weight of the extract under the same UVB conditions. At the end of the 14-day treatment period, samples were collected to assess TNF-α levels and the extent of wound lesions. The results demonstrated that the negative control group (K2) exhibited larger erythema areas and delayed wound healing compared to both the treatment groups (K3 and K4) and the healthy control group (K1).

Table 1
Eritem Area Measurement Results

Group	Measurement Day				
	Day 3/cm²	Day 6/cm²	Day 9/cm²	Day 12/cm²	Day 14/cm²
K1	0	0	0	0	0
K2	0.07	0.05	0.11	0.18	0.35
K3	0.06	0.23	0.18	0.11	0.05
K4	0.05	0.14	0.18	0.08	0.05

Table 1 presents the results of changes in erythema lesion area among the negative control group (K2), treatment group 1 (K3), and treatment group 2 (K4). The data indicate that the negative control group (K2), which did not receive any therapeutic intervention, exhibited the slowest reduction in lesion size. In contrast, treatment group 1 (K3), which received a lower dose of turmeric ethanol extract, showed a moderate rate of reduction. The most significant and rapid decrease in erythema lesion area was observed in treatment group 2 (K4), which received the higher dose of the extract.

The results showed that the negative control group (K2) had the highest mean TNF-α levels, followed by treatment group 1 (K3), treatment group 2 (K4), and the healthy control group (K1), which exhibited the lowest mean level. The distribution and variance of TNF-α data met the assumptions of normality and homogeneity; therefore, one-way ANOVA was used, revealing no statistically significant differences in mean TNF-α levels among the groups ($p = 0.538$).

Table 2
Results of Research ON TNF-α Levels and Wound Lesion Area

Variable	Group				
	K1	**K2**	**K3**	**K4**	***p value***
	Mean±SD n = 6	**Mean±SD** n = 6	**Mean±SD** n = 6	**Mean±SD** n = 6	
TNF-α level ng/mL	103.34±20.9	129.14±24.10.115	118.45±24.10.367	111.61±29.05	
Saphiro Wilk	0.852			0.864	
Levene's Test					0.715
One Way Anova					0.538
Area of Wound Lesions	0	0.29±0.052	0.17±0.073	0.085±0.040	
Saphiro Wilk	0	0.519	0.253	0.504	
Levene's Test					0.008
Kruskal Wallis					0.000

Regarding wound lesion area, group K2 had the highest mean lesion size, followed by K3, K4, and K1. Although the data were normally distributed, the assumption of homogeneity of variance was not met. As a result, the Kruskal–Wallis test was applied and revealed a statistically significant difference among the groups (p = 0.000). The fastest wound healing was observed in group K4, while group K2 showed the slowest healing progression.

Table 3
Mann Whitney Test of Wound Lesions

	Group	**Comparison Group**	**Significance**
Area of Wound Lesions	K1	K2	0.002*
		K3	0.002*
		K4	0.002*
	K2	K3	0.009*
		K4	0.002*
	K3	K4	0.041*

Description: * Means p<0.05

The results of the Mann Whitney test showed that there were significant differences in the area of wound lesions measured based on the area of erythema between different groups. Specifically, the comparison between the Healthy Group (K1) and Negative Control (K2), Treatment 1 (K3), and Treatment 2 (K4) showed a p value <0.05, indicating a significant difference. In addition, there were significant differences between Negative Control (K2) and Treatment 1 (K3) and Treatment 2 (K4), as well as between Treatment 1 (K3) and Treatment 2 (K4). These results indicate that the treatment given significantly affected the area of wound lesions compared to the negative control, and the differences were consistent among all groups tested. As illustrated in Figure 1, the Mann Whitney test graph below:

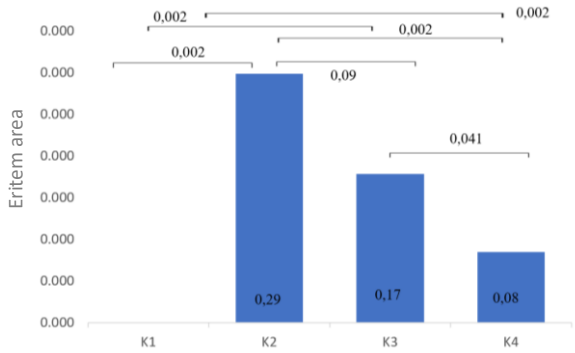

Figure 1. Mann Whitney Test of Wound Lesions

Although both doses of turmeric ethanol extract accelerated wound healing, the higher dose administered in the K4 group demonstrated a significantly greater effect compared to the lower dose used in the K3 group, as indicated by the smaller average lesion area.

TNF-α Levels

Exposure to ultraviolet B (UVB) radiation induces oxidative stress and DNA damage in keratinocytes, leading to the activation of the nuclear factor-kappa B (NF-κB) signaling pathway (Guan et al., 2021). This activation promotes the release of several pro-inflammatory cytokines, particularly tumor necrosis factor-alpha (TNF-α), which plays a key role in mediating cutaneous inflammatory responses (Zhao et al., 2021). In the present study, administration of turmeric ethanol extract (*Curcuma longa* L.) at doses of 100 mg/kg and 200 mg/kg resulted in a reduction in TNF-α levels compared to the negative control group (K2), which was exposed to UVB radiation without treatment. However, the observed reduction was not statistically significant.

Although statistical analysis did not reveal a significant difference between groups, a clinically observable trend was evident. TNF-α levels were elevated in the negative control group compared to the healthy group, while both treatment groups (K3 and K4) exhibited lower TNF-α levels than the negative control. This

discrepancy between statistical significance and clinical relevance may be attributed to several factors, including individual variability in immune response, the limited sample size, and the pharmacokinetic limitations of curcumin when administered orally without absorption enhancers such as albumin (Kasprzak-Drozd et al., 2024a).

Curcumin is well-documented for its anti-inflammatory properties, particularly through the inhibition of nuclear factor-kappa B (NF-κB) activation via suppression of IκB kinase (Kasprzak-Drozd *et al.*, 2024b; Li *et al.*, 2018). This pathway modulates the release of pro-inflammatory cytokines such as TNF-α, IL-1, IL-6, and IL-8 by keratinocytes. However, the bioavailability of orally administered curcumin remains a critical limitation, especially in short-term studies such as the present one. The absence of statistically significant findings suggests that, although curcumin exhibits anti-inflammatory activity, the dosage or duration of administration may have been insufficient to produce a measurable systemic reduction in TNF-α levels within the 14-day period. It is also possible that the anti-inflammatory effects were predominantly localized and not fully captured through serum TNF-α measurements (van Loo & Bertrand, 2023).

Wound Lesion Area

contrast to the TNF-α findings, measurement of the wound lesion area produced more consistent and favorable outcomes. The groups treated with turmeric ethanol extract exhibited a noticeable reduction in erythema size and accelerated wound healing compared to the negative control group. These findings suggest that turmeric extract, primarily through the activity of its active compound curcumin, exerts a significant effect on local tissue repair processes, even in the absence of statistically significant changes in systemic TNF-α levels.

Curcumin promotes wound healing by stimulating the secretion of several key growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), fibroblast growth factor (FGF), epidermal growth factor (EGF), and vascular endothelial growth factor (VEGF). These growth factors play critical roles in regulating fibroblast proliferation, collagen synthesis, angiogenesis, and re-epithelialization—processes that are essential for tissue regeneration and wound contraction (Kasprzak-Drozd *et al.*, 2024a). The observed reduction in lesion area suggests that curcumin's primary therapeutic effect may be localized at the wound site, enhancing tissue repair even in the presence of elevated systemic inflammatory cytokine levels (Li et al., 2018).

divergence underscores a critical point: the anti-inflammatory and wound-healing effects of curcumin are not solely dependent on the suppression of systemic TNF-α levels (Tampa *et al.*, 2022). Rather, its therapeutic efficacy may be attributed to direct actions on local skin cells, including keratinocytes, fibroblasts, and macrophages. Additionally, curcumin's antioxidant properties contribute to the neutralization of reactive oxygen species (ROS) at the wound site, thereby preventing prolonged inflammation and mitigating tissue damage (Rosyid, 2016; Shams et al., 2022).

These findings support the potential application of curcumin in the treatment of superficial skin injuries, such as radiation-induced burns, with therapeutic effects predominantly observed at the tissue level rather than through systemic biomarker modulation (Aisyah, 2017 ; (Sabarees et al., 2024). However, to enhance its systemic efficacy, future research should explore strategies to improve curcumin's bioavailability, such as the use of absorption enhancers like piperine or albumin, or alternative delivery systems including topical formulations and nanoparticle encapsulation.

CONCLUSIONS

Administration of turmeric ethanol extract (*Curcuma longa* Linn.) demonstrated beneficial effects on wound healing in Wistar rats exposed to UVB radiation. Although no statistically significant difference in serum TNF-α levels was observed between groups , a clear clinical trend indicated reduced TNF-α expression in the treatment groups compared to the negative control. More importantly, the extract significantly reduced the area of erythema-associated wound lesions , suggesting a strong local therapeutic effect.

These findings highlight that curcumin's wound-healing properties may operate primarily at the tissue level, likely through modulation of local inflammatory processes and enhancement of tissue regeneration, rather than systemic cytokine suppression. This supports its potential application as a topical or localized treatment for UVB-induced skin damage and other superficial dermal injuries. Future studies should investigate improved delivery strategies to enhance curcumin's systemic bioavailability and assess long-term outcomes in larger sample sizes.

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