JTL 15 (2): JULY-DECEMBER 2026
Page: 195-202

Contents list available at Jurnal Teknologi Laboratorium

JURNAL TEKNOLOGI LABORATORIUM

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

OPEN ACCESS

Original Research

# *Influence of Oral Turmeric (Curcuma longa) Extract on MMP-1 Levels and Collagen Density in UV-B-Exposed Wistar Rats*

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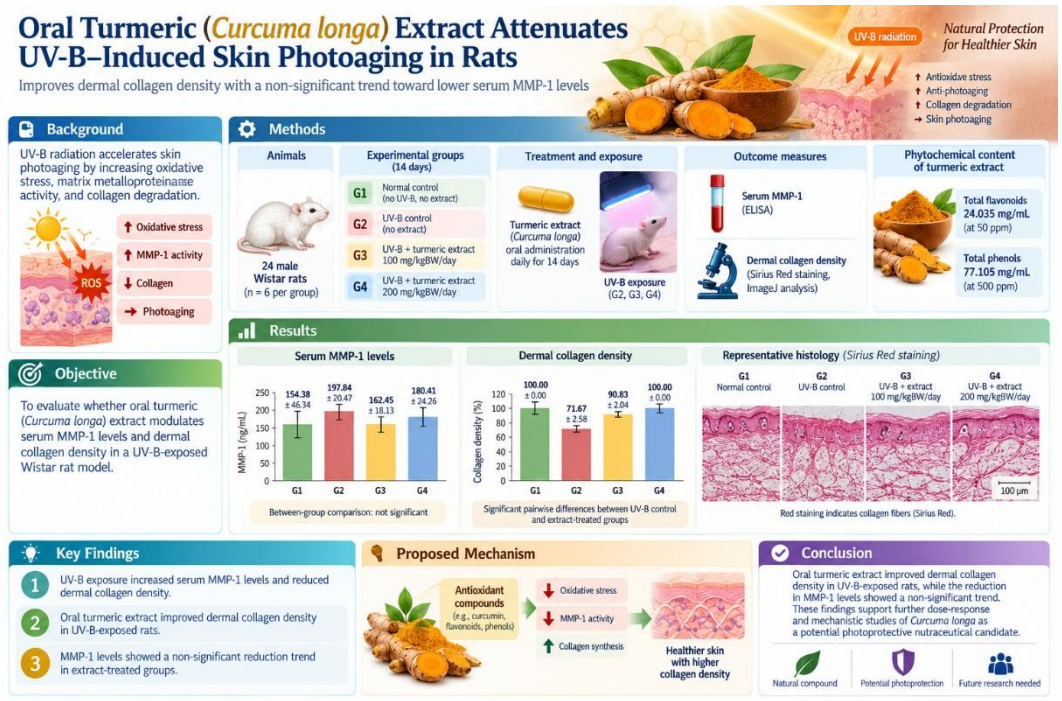
## Graphical Abstract




**Abstract:** Ultraviolet-B (UV-B) radiation accelerates skin photoaging by increasing oxidative stress, matrix metalloproteinase activity, and collagen degradation. Objective: This study evaluated whether oral turmeric (Curcuma longa) extract modulates serum matrix metalloproteinase-1 (MMP-1) levels and dermal collagen density in a UV-B-exposed Wistar rat model. Twenty-four male Wistar rats were allocated into four groups (n = 6 each): normal control without UV-B exposure (G1), UV-B negative control without extract (G2), UV-B plus turmeric extract 100 mg/kgBW/day (G3), and UV-B plus turmeric extract 200 mg/kgBW/day (G4). Treatment was administered orally for 14 days. Serum MMP-1 was measured by enzyme-linked immunosorbent assay, and collagen density was assessed using Sirius Red-stained dorsal skin sections analyzed with ImageJ. The extract contained flavonoids of 24.035 mg/mL at 50 ppm and total phenols of 77.105 mg/mL at 500 ppm. MMP-1 levels were 154.38 +/- 46.34 ng/mL in G1, 197.84 +/- 20.47 ng/mL in G2, 162.45 +/- 18.13 ng/mL in G3, and 180.41 +/- 24.26 ng/mL in G4; the overall between-group

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DOI: 10.29238/teknolabjournal.v15i2.581
Received 14 February 2025; Received in revised form 13 September 2025; Accepted 18 September 2026

comparison was not significant. Collagen density was 100.00 +/- 0.00% in G1, 71.67 +/- 2.58% in G2, 90.83 +/- 2.04% in G3, and 100.00 +/- 0.00% in G4, with significant pairwise differences between UV-B control and extract-treated groups. Oral turmeric extract improved dermal collagen density in UV-B-exposed rats, while the reduction in MMP-1 levels showed a non-significant trend. These findings support further dose-response and mechanistic studies of Curcuma longa as a photoprotective nutraceutical candidate.

**Keywords:** collagen; Curcuma longa; matrix metalloproteinase-1; photoaging; turmeric; UV-B.

## INTRODUCTION

Skin photoaging is driven by chronic ultraviolet exposure and is characterized by dermal matrix remodeling, reduced collagen integrity, wrinkling, pigmentary alteration, and impaired barrier homeostasis.[1-6] UV-B radiation promotes reactive oxygen species generation and activates signaling cascades involving mitogen-activated protein kinases, AP-1, and NF-kB, which increase matrix metalloproteinase expression and accelerate extracellular matrix degradation.[3,5,7-10] MMP-1 is especially relevant because it initiates cleavage of fibrillar type I and type III collagen, thereby linking UV-B exposure to measurable collagen loss and dermal structural weakening.[3,8-12]

Botanical antioxidants are increasingly investigated as adjunctive photoprotective agents because oxidative stress is a central upstream event in UV-mediated photoaging.[5,11-14] Turmeric (Curcuma longa) contains curcuminoids and phenolic constituents with antioxidant, anti-inflammatory, and wound-healing activities.[13-20] Curcumin can scavenge free radicals, regulate redox-sensitive transcription factors, and modulate inflammatory mediators, although its biological effect is influenced by formulation, dose, stability, and bioavailability.[16-23]

Experimental and translational studies support the relevance of Curcuma longa and curcumin for skin biology. Curcumin has been reported to reduce UV-B-induced MMP-1/MMP-3 expression in dermal fibroblasts, suppress gelatinase activity, enhance wound collagen deposition, and improve tissue remodeling in skin injury models.[10,24-29] However, many studies use topical preparations or in vitro systems; fewer reports address oral Curcuma longa extract in an in vivo UV-B photoaging model using both MMP-1 and collagen density as paired outcomes. The present study therefore evaluated oral turmeric extract at 100 and 200 mg/kgBW/day in UV-B-exposed Wistar rats while preserving the original post-test-only experimental design.[30,31]

## MATERIALS AND METHODS

### Study design, setting, and ethical approval

This study used a randomized post-test-only control group design. The work was conducted at the Integrated Biomedical Laboratory and the Pathology Laboratory, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Central Java, Indonesia, from August to October 2024. Ethical approval was obtained from the Bioethics Committee of the Faculty of Medicine, Sultan Agung Islamic University (No. 381/IX/2024/Komisi Bioetik, issued 30 September 2024). Reporting and animal handling principles were aligned with commonly used laboratory animal reporting recommendations.[30,31]

### Animals and grouping

Twenty-four male Wistar rats aged 3-4 months and weighing 200-250 g were included. Animals were acclimatized for seven days, maintained under standard laboratory conditions, and then randomized into four groups of six animals each: G1, normal control without UV-B exposure and without extract; G2, UV-B exposure without extract; G3, UV-B exposure plus turmeric extract 100 mg/kgBW/day; and G4, UV-B exposure plus turmeric extract 200 mg/kgBW/day.

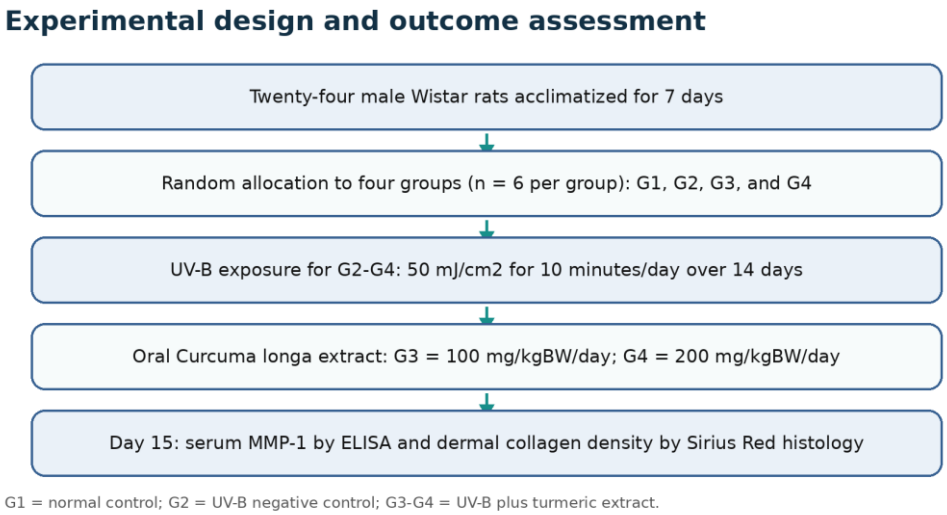


**Figure 1.** Experimental design and outcome assessment.

The schematic summarizes group allocation, UV-B exposure, oral extract dosing, and endpoint measurements. G1 = normal control; G2 = UV-B negative control; G3 = UV-B plus Curcuma longa extract 100 mg/kgBW/day; G4 = UV-B plus Curcuma longa extract 200 mg/kgBW/day.

## Preparation and administration of turmeric extract

Turmeric rhizomes were dried, powdered, and macerated with 70% ethanol using a 1:10 w/v ratio. The filtrate was concentrated by rotary evaporation under reduced pressure at 50 deg C. The final extract was stored in amber glass containers at 4 deg C and freshly dissolved in sterile distilled water before oral gavage. Extract was administered once daily for 14 days at 100 mg/kgBW/day in G3 and 200 mg/kgBW/day in G4.

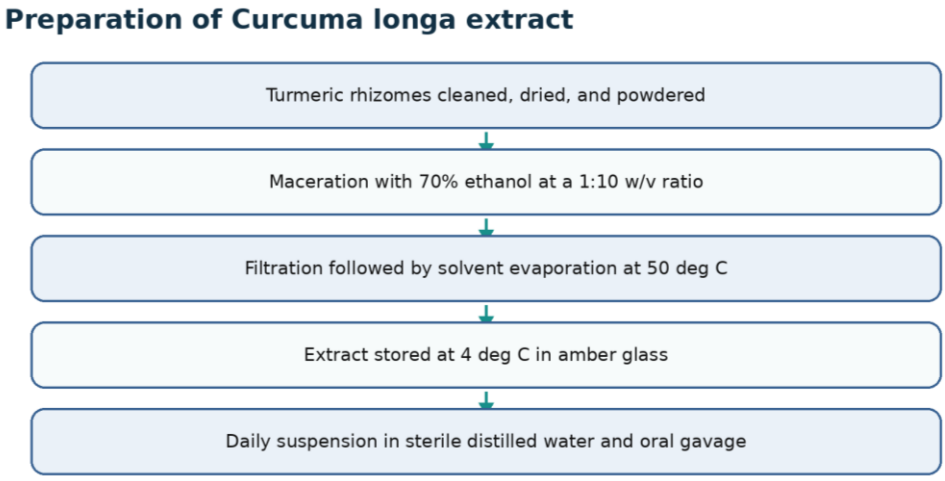


**Figure 2.** Preparation workflow for Curcuma longa extract used in the study.

The figure summarizes drying, powdering, ethanol maceration, filtration, evaporation, refrigerated storage, and oral administration.

## UV-B exposure protocol and sample collection

Dorsal skin was shaved before irradiation. Groups G2, G3, and G4 were exposed to UV-B light at 280-320 nm and 50 mJ/cm2 for 10 minutes/day over 14 days, with the lamp positioned approximately 20 cm above the dorsal skin. Animals were placed in ventilated compartments during irradiation. On day 15, animals were anesthetized with ketamine 60 mg/kg and xylazine 20 mg/kg. Blood was collected from the orbital sinus and centrifuged at 15,000 rpm for 15 minutes at 4 deg C. Full-thickness dorsal skin biopsy samples measuring approximately 2 x 1 cm were collected for histological evaluation.

### Outcome measurements and statistical analysis

Serum MMP-1 concentration was measured using a rat MMP-1 ELISA kit (Abcam, UK), with absorbance read at 450 nm using a Bio-Rad Model 680 reader. Collagen density was assessed on Sirius Red-stained paraffin sections. Tissue samples were fixed in 10% formalin for 24 hours, embedded in paraffin, sectioned at 4-5 microm using a Leica RM2235 microtome, examined using an Olympus BX53 microscope, and quantified with ImageJ version 1.53t. The percentage of red-stained collagen area was calculated from five randomly selected microscopic fields per sample.

Data distribution was assessed with the Shapiro-Wilk test, and variance homogeneity was assessed with Levene's test. Normally distributed MMP-1 data were analyzed using one-way ANOVA. Collagen density data were not normally distributed and were therefore analyzed with non-parametric procedures, followed by Mann-Whitney U tests for pairwise comparisons. Statistical significance was set at $p < 0.05$.

## RESULTS AND DISCUSSION

### Phytochemical characteristics of the extract

The turmeric extract contained flavonoids at an average level of 24.035 mg/mL at 50 ppm and total phenols at 77.105 mg/mL at 500 ppm. These constituents are biologically relevant because phenolic compounds and curcuminoids can modulate oxidative stress and redox-sensitive inflammatory signaling, which are central mechanisms in UV-B-mediated photoaging.[13-23]

### MMP-1 and collagen outcomes

Table 1 presents the post-test outcome data for serum MMP-1 and dermal collagen density. UV-B exposure without extract (G2) was associated with the highest mean MMP-1 level and the lowest mean collagen density. Turmeric extract at 100 mg/kgBW/day (G3) reduced the mean MMP-1 level toward the normal-control range and increased collagen density compared with the UV-B negative control. The 200 mg/kgBW/day dose (G4) produced complete restoration of collagen density in the measured fields, although mean MMP-1 remained higher than in G3.

**Table 1.** Serum MMP-1 level and dermal collagen density by experimental group

| Group | Experimental condition | MMP-1 (ng/mL) | Shapiro-Wilk p | Collagen density (%) | Shapiro-Wilk p |
|---|---|---|---|---|---|
| G1 | Normal control; no UV-B; no extract | 154.38 +/- 46.34 | 0.545 | 100.00 +/- 0.00 | NA |
| G2 | UV-B exposure; no extract | 197.84 +/- 20.47 | 0.569 | 71.67 +/- 2.58 | 0.001 |
| G3 | UV-B + Curcuma longa 100 mg/kgBW/day | 162.45 +/- 18.13 | 0.643 | 90.83 +/- 2.04 | 0.000 |
| G4 | UV-B + Curcuma longa 200 mg/kgBW/day | 180.41 +/- 24.26 | 0.982 | 100.00 +/- 0.00 | NA |

*Values are presented as mean +/- SD. NA indicates that normality testing was not applicable because values were identical within the group. Overall MMP-1 comparison by one-way ANOVA was interpreted as not significant ($p > 0.05$).*

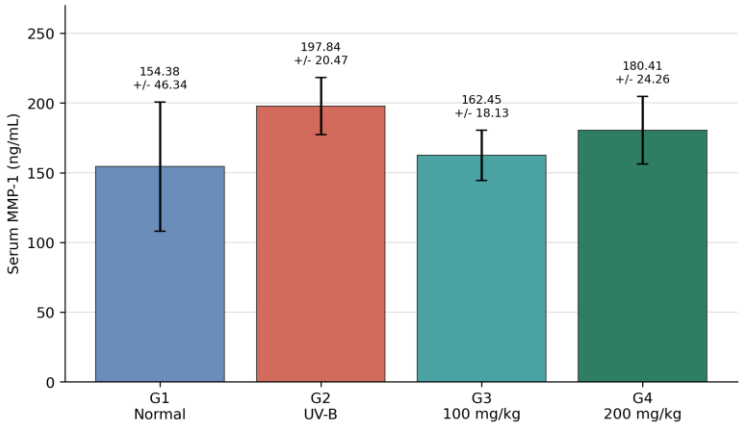


**Figure 3.** Serum MMP-1 levels across experimental groups.

Bars show mean values and error bars indicate standard deviations. The highest mean MMP-1 level was observed in UV-B-exposed rats without extract (G2), while extract-treated groups showed lower mean values; the overall ANOVA comparison was not significant.

The collagen density findings showed clearer separation between groups than MMP-1. Pairwise non-parametric testing demonstrated significant differences between G1 and G2, G1 and G3, G2 and G3, G2 and G4, and G3 and G4, while G1 and G4 were not different because both groups showed 100.00% collagen density in the measured fields (Table 2).

**Table 2.** Pairwise Mann-Whitney U test results for collagen density

| Comparison | G1 | G2 | G3 | G4 |
|---|---|---|---|---|
| G1 | - | 0.002* | 0.001* | - |
| G2 | 0.002* | - | 0.002* | 0.002* |
| G3 | 0.001* | 0.002* | - | 0.001* |
| G4 | - | 0.002* | 0.001* | - |

**p < 0.05. G1 = normal control; G2 = UV-B negative control; G3 = UV-B + 100 mg/kgBW/day; G4 = UV-B + 200 mg/kgBW/day.*

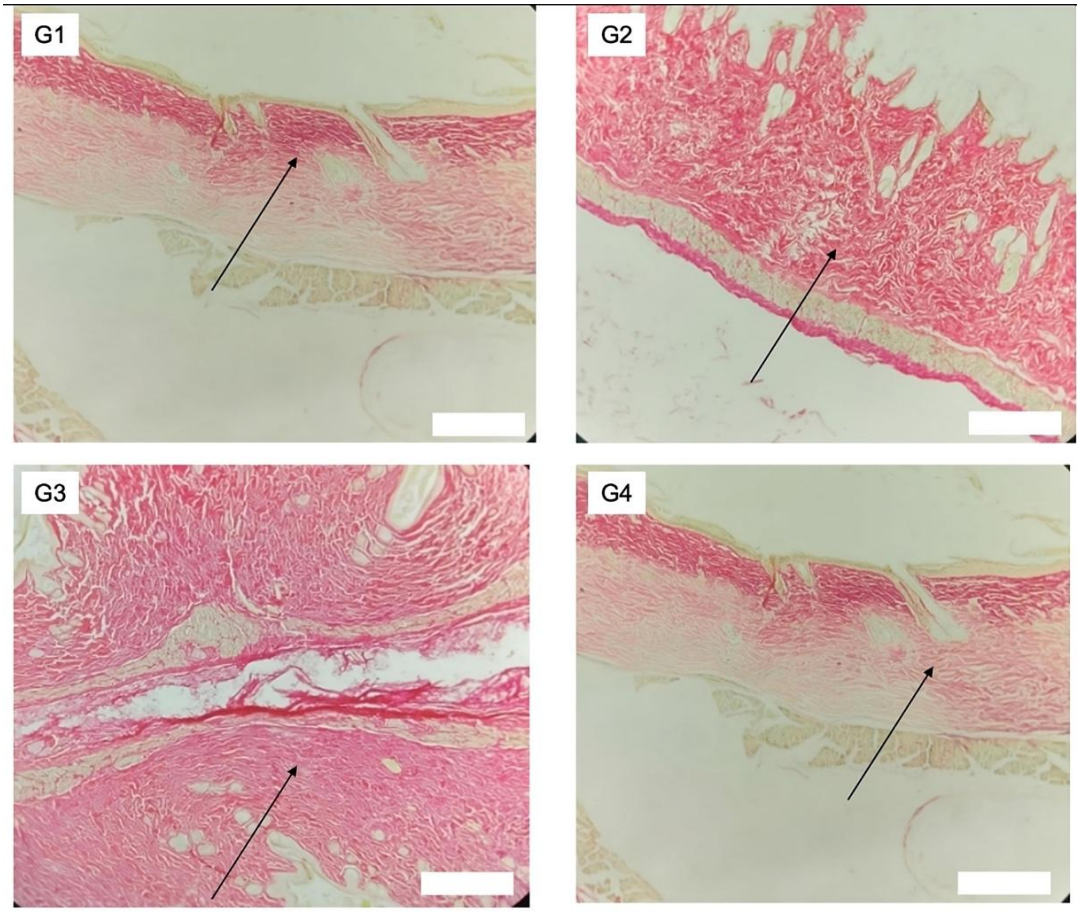


**Figure 4.** Representative Sirius Red-stained dorsal skin sections by group.

G2 showed visibly reduced collagen staining compared with G1, while G3 and G4 showed increased collagen staining after oral Curcuma longa extract administration. Arrows indicate collagen-rich dermal regions.

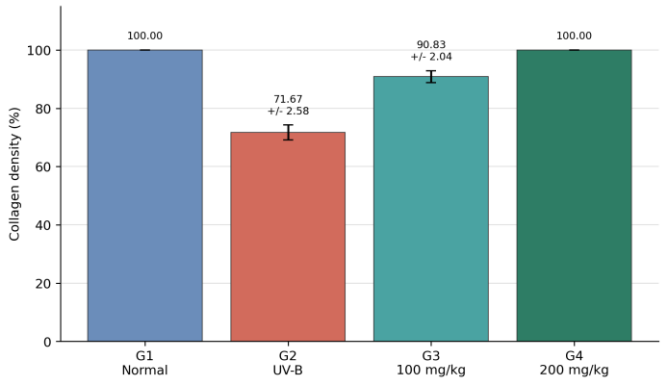


**Figure 5.** Dermal collagen density across experimental groups.

Bars show mean values and error bars indicate standard deviations. Collagen density was lowest in the UV-B negative control group and increased in both turmeric-extract groups.

### Interpretation of MMP-1 response

The observed increase in mean MMP-1 in the UV-B negative control is consistent with the established pathway by which UV-B-induced ROS activate MAPK, AP-1, and NF-kB signaling and promote matrix metalloproteinase expression.[3,5,7-10] The lower mean MMP-1 level in G3 suggests a potentially protective response at 100 mg/kgBW/day, in line with experimental evidence that curcumin can suppress UV-B-induced MMP-1 and MMP-3 expression in dermal fibroblasts.[10,13-20,24-29] However, because the overall comparison was not statistically significant, the MMP-1 finding should be interpreted as a biological trend rather than definitive enzyme suppression.

The non-significant MMP-1 result may reflect the small sample size, post-test-only design, biological variability in serum MMP-1, and the possibility that serum MMP-1 does not fully represent local dermal enzyme activity. UV-B photoaging is a tissue-level process involving keratinocytes, fibroblasts, extracellular matrix turnover, inflammatory mediators, and redox balance; therefore, a systemic MMP-1 measurement may be less sensitive than local skin protein or gene expression assays.[1-12]

### Collagen restoration and dose-response considerations

Collagen density increased substantially in both extract-treated groups compared with the UV-B negative control. This finding is biologically plausible because curcumin and turmeric-derived constituents can reduce oxidative stress, attenuate inflammatory signaling, support wound remodeling, and influence collagen deposition.[11-29] The normalization of collagen density in G4 indicates that the higher dose had a strong histological association with collagen preservation or restoration in this model.

The apparent difference between the MMP-1 and collagen outcomes deserves careful discussion. Collagen density is a cumulative histological endpoint reflecting the balance between collagen degradation and synthesis, whereas MMP-1 is only one mediator within a broader matrix-remodeling network. Curcumin may support collagen preservation through mechanisms beyond MMP-1 suppression, including antioxidant effects, inflammatory modulation, fibroblast activity, TGF-beta-related matrix regulation, and effects on other MMPs or tissue inhibitors of metalloproteinases.[3,10,13-29]

The higher mean MMP-1 in G4 compared with G3, despite complete collagen-density restoration, may indicate a non-linear dose-response. Curcumin has concentration-dependent and context-dependent effects, and its systemic activity is shaped by absorption, metabolism, tissue distribution, and formulation stability.[16-23,29] Thus, a higher oral dose may not necessarily produce proportionally lower MMP-1. Future studies should include additional dose levels, measurement of local skin MMP-1 expression, oxidative stress markers, curcuminoid pharmacokinetics, and collagen subtyping to clarify the optimal dose range.

### Strengths, limitations, and implications

A key strength of this study is the use of paired biochemical and histological endpoints in a controlled UV-B-exposed animal model. The inclusion of two extract doses provides preliminary dose-response information, and placement of tables and figures in the body text improves interpretability. Nevertheless, the study remains exploratory. The sample size was small, outcomes were measured only after treatment, and the study did not include baseline measures, local skin MMP-1 immunostaining, collagen subtype analysis, oxidative stress assays, inflammatory cytokines, or curcuminoid blood/tissue concentrations.

The results should therefore be framed as evidence that oral Curcuma longa extract is associated with improved collagen density in UV-B-exposed rats, with a non-significant trend toward lower serum MMP-1 at 100 mg/kgBW/day. The findings support further mechanistic work rather than direct clinical claims. Future research should use larger sample sizes, blinded histomorphometry, local dermal molecular assays, pharmacokinetic assessment, and comparison with topical or formulated curcumin preparations to determine translational potential.[24-31]

## CONCLUSION

Oral Curcuma longa extract improved dermal collagen density in UV-B-exposed Wistar rats, particularly at 200 mg/kgBW/day, while the observed reduction in serum MMP-1 did not reach statistical significance. These results suggest that turmeric extract may support collagen preservation in UV-B-induced photoaging, but its effect on MMP-1 requires confirmation using larger, mechanistically detailed studies.

## AUTHORS' CONTRIBUTIONS

Rifqoh Annisa contributed to study conception, data collection, analysis, and manuscript drafting. Pasid Harlisa contributed to study supervision, dermatology interpretation, and manuscript revision. Eko Setiawan contributed to surgical and laboratory interpretation, data evaluation, and manuscript revision. All authors reviewed and approved the final manuscript.

## ACKNOWLEDGEMENT

The authors thank the Integrated Biomedical Laboratory and Pathology Laboratory, Faculty of Medicine, Sultan Agung Islamic University, Semarang, Indonesia, for supporting the experimental and histological work.

## FUNDING INFORMATION

No specific external funding was reported for this study.

## DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

## ETHICAL CONSIDERATION

This animal study was approved by the Bioethics Committee of the Faculty of Medicine, Sultan Agung Islamic University (No. 381/IX/2024/Komisi Bioetik, issued 30 September 2024).

## AI STATEMENT

Generative artificial intelligence was used to support English language polishing. No AI tool was used to generate original experimental data, change reported numerical results, or fabricate references.

## DISCLOSURE STATEMENT

The authors declare no conflict of interest.

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