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**Bioactive Cosmetic Potential of SCOBY-Fermented Mango Leaf Extract: Antioxidant, Photoprotective, and Wound Healing Properties**M. Rifqi Efendi<sup>1\*</sup>, Maimum<sup>1</sup>, Rion Nofrianda<sup>2</sup>, Elisma<sup>1</sup>, Raudatul Jannah<sup>1</sup>, Zahriana Putri<sup>1</sup> and Mesa S. Rusdi<sup>3</sup><sup>1</sup>Department of Pharmacy, Faculty of Medicine and Health Sciences, Universitas Jambi, Jambi, 36122, Indonesia<sup>2</sup>Department of Psychology, Faculty of Medicine and Health Sciences, Universitas Jambi, Jambi, 36122, Indonesia<sup>3</sup>Department of Pharmacy, Politeknik Kesehatan Kementerian Kesehatan Jambi, Jambi, 36128, Indonesia\*Corresponding author: [mrifqi@unja.ac.id](mailto:mrifqi@unja.ac.id)

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**Abstract**

Traditionally produced from tea and sugar using a symbiotic culture of bacteria and yeast (SCOBY), Kombucha is a fermented beverage that has recently been expanded to include variety of plant-based substrates for cosmetic purposes. Mangiferin, tannins, and gallic acid derivatives, which have antioxidant, antidiabetic, anti-inflammatory, and antibacterial properties, are abundant in Mango (*Mangifera indica* L.) leaves, a byproduct of mango farming. This study investigated the antioxidant, UV-protective potentials, and wound-healing of mango leaf kombucha for cosmeceutical use. The study involved four main stages; mango leaf extraction, fermentation, product standardization, and pharmacological evaluation. Total phenolic and flavonoid contents were quantified, and bioactive constituents were identified using UPLC–MS. Total phenolic ( $29.1 \pm 0.09$  mg GAE/g) and flavonoid ( $9.14 \pm 0.07$  mg QE/g) contents were substantially higher in the fermented product than in the infusion ( $19.6 \pm 0.33$  mg GAE/g and  $7.59 \pm 0.03$  mg QE/g, respectively). Nineteen bioactive compounds, including xanthenes, flavonoids, and benzophenones, were detected. Mango leaf kombucha outperformed the infusion in terms of antioxidant activity ( $IC_{50} = 14$   $\mu$ g/mL vs. 24  $\mu$ g/mL), UV protection (SPF  $22.76 \pm 0.68$ ), and wound-healing efficacy ( $98.85\% \pm 1.34$ ). These results demonstrate the potential of mango leaf kombucha as a natural component in cosmeceutical formulations aimed at photoprotection and skin restoration.

**Keywords:** *Mangifera indica* L., Kombucha, Antioxidant, SPF, Wound healing

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**1. Introduction**

The pharmaceutical and cosmetic industries are paying more and more attention to fermentation, a biological process in which microorganisms break down complex chemical molecules into simpler useful substances [1]. Improved antioxidant, anti-inflammatory, and antibacterial properties result from this process, which increases the bioavailability and effectiveness of natural components such polyphenols, vitamins, and organic acids [2]. Fermentation-derived cosmetics are prized for their ability to improve skin moisture, encourage collagen synthesis, and guard against oxidative damage and hyperpigmentation [3].

An example of a flexible fermentation system is kombucha, which is usually made from tea and sugar using a symbiotic culture of bacteria and yeast (SCOBY). Organic acids, amino acids, and phenolic metabolites with significant biological activity are produced by its microbial metabolism [4]. Beyond tea, plant-based materials high in bioactive chemicals have recently been added to kombucha substrates, opening up new possibilities for functional and cosmetic applications [4].

In Indonesia, mangos (*Mangifera indica* L.) are widely grown for their fruit, while their leaves are frequently thrown away as agricultural waste [5]. Nonetheless, mangiferin, isomangiferin, tannins, and gallic acid derivatives, all of which have antioxidant, anti-inflammatory, antibacterial, and anti-tyrosinase qualities, are important phytochemicals found in mango leaves [6,7]. These compounds contribute to maintaining skin health by reducing oxidative stress, promoting cell regeneration, and accelerating wound closure. Previous studies have

demonstrated that mango peel extracts exhibit wound-healing and antioxidant potential [8], yet similar exploration of mango leaf, especially after fermentation, remains limited.

Furthermore, the high polyphenol content in mango leaves offers potential UV-protective properties [9]. This is particularly relevant in tropical countries like Indonesia, where chronic ultraviolet (UV) exposure is a major factor contributing to skin aging, hyperpigmentation, and carcinogenesis [10]. Therefore, there is growing interest in cosmeceutical research for natural compounds that can both improve wound healing and offer photoprotection. However, no prior studies have investigated the effects of SCOBY-fermented mango leaf (kombucha) on wound healing and UV protection, particularly in gel formulations designed for topical use. Through the biotransformation of phenolic compounds, fermentation and mango leaf phytochemicals may provide a synergistic augmentation of biological activity, increasing their cosmetic efficacy.

## 2. Materials and methods

### 2.1 Plant material and instrument

Mature mango leaves were gathered from Nipah Panjang, Tanjung Jabung Timur District, Jambi, Indonesia, and verified as *M. indica* L. at the Plant Taxonomy Laboratory, Department of Biology, FMIPA Universitas Padjadjaran (Identification No. 53/HB/01/2024). The leaves were oven-dried at 55 °C for 72 h, producing 23.3% (w/w) dried simplicia. The fermentation SCOBY was purchased commercially. Instruments included UV-Vis spectrophotometer (Genesys® 10S UV-Vis, Thermo Scientific, Waltham, MA, USA), ELISA microplate reader (EL-10A, BIOBASE, Jinan, Shandong, China), hot plate stirrer (AREX Digital Pro, VELP Scientifica, Usmate Velate, Italy), laboratory oven (UN30, Memmert GmbH + Co.KG, Schwabach, Germany), ultra-performance liquid chromatography system (ACQUITY UPLC® H-Class System, Waters Corporation, Milford, MA, USA), mass spectrometer (Xevo G2-S QToF, Waters Corporation, Milford, MA, USA), water bath (WNB 7, Memmert GmbH + Co.KG, Schwabach, Germany), UV lamp (Repti Glo 10.0, Exo Terra, Mansfield, MA, USA), and lux meter (AS803, Smart Sensor, Guangdong, China).

### 2.2 Research material and reagent

All reagents were of analytical grade. Major chemicals included methanol p.a. (Emsure®, Merck KGaA, Darmstadt, Germany), sodium carboxymethyl cellulose (NaCMC, Sigma-Aldrich, St. Louis, MO, USA), Folin–Ciocalteu reagent (Supelco®, Bellefonte, PA, USA), sodium hydroxide (NaOH, Supelco®, Bellefonte, PA, USA), aluminum chloride (AlCl<sub>3</sub>, Sigma-Aldrich, St. Louis, MO, USA), sodium acetate (CH<sub>3</sub>COONa, Supelco®, Bellefonte, PA, USA), quercetin (Sigma-Aldrich, St. Louis, MO, USA), gallic acid (Sigma-Aldrich, St. Louis, MO, USA), and 2,2-diphenyl-1-picrylhydrazyl (DPPH, Sigma-Aldrich, St. Louis, MO, USA) were used for antioxidant and phytochemical assays. Additional materials used in this study included propylene glycol (Brataco Chemical, Jakarta, Indonesia), acepromazine (Castran®, Interchemie werken “De Adelaar” B.V., Venray, The Netherlands), povidone-iodine ointment 10% (Betadine®, Mundipharma, Basel, Switzerland), hydroxypropyl methylcellulose (HPMC, Brataco Chemical, Jakarta, Indonesia), ethanol 70% and 96% (Sigma-Aldrich, St. Louis, MO, USA), xylene, paraffin, and formalin (all obtained from local commercial suppliers, Jakarta, Indonesia).

### 2.3 Ethics statement and animal preparation

The Biomedical Research Ethics Committee of Universitas Jambi approved all animal procedures in accordance with ARRIVE criteria (Approval No. 754/UN21.8/PT.01.04/2024). We utilized male Swiss Webster mice weighing 20–30 g and aged two to three months. The animals were kept in controlled environments with free access to food and water (22 ± 2 °C, 12 h light/dark cycle, 50–60% humidity). The study did not include any animals exhibiting symptoms of disease or suffering.

### 2.4 Preparation of mango leaf infusion and kombucha and its gel

The infusion was prepared by weighing 125 g of mango leaf and adding them to 500 mL of distilled water, which was boiled at 100°C for 30 minutes. After boiling, the infusion was filtered, and the volume was adjusted to 500 mL by passing it through the mango leaf residue. Following cooling to 25 °C, 50 g sugar and 15 g SCOBY were added, and fermentation process was continued for 14 days at room temperature in the dark. In order to create gel formulations, 2 grams of HPMC and 10 grams of propylene glycol were added to 100 milliliters of infusion or kombucha, and the mixture was then thoroughly mixed.

### 2.5 Determination of total phenol content and total flavonoid content

The Folin-Ciocalteu and  $\text{AlCl}_3$  colorimetric techniques were used to estimate TPC and TFC in accordance with the Indonesian Herbal Pharmacopoeia [11]. Gallic acid and quercetin were served as standards. All measurements were performed in triplicate ( $n = 3$ ). Results were expressed as mg GAE/g and mg QE/g dry sample.

### 2.6 Secondary metabolite profiling with UPLC-MS

A UPLC system connected to a mass spectrometer running in positive electrospray ionization (ESI) mode ( $m/z$  50–1200) was used to perform metabolite profiling. Water with 5 mM ammonium formate (A) and acetonitrile with 0.05% formic acid (B) in a gradient elution (23 min, 0.2 mL/min) made up the mobile phase. MassLynx 4.1 was used to collect the data [12].

### 2.7 Determination of antioxidant activity

The DPPH radical scavenging assay (RSA) was developed in accordance with Tang et al. [13]. After mixing each sample (0–50  $\mu\text{g/mL}$ ) with a 0.1 mM DPPH solution (1:1, v/v), the mixture was incubated at 25 °C for 30 minutes. At 517 nm, absorbance was measured. The formula  $\% \text{RSA} = [(A_{\text{control}} - A_{\text{sample}})/A_{\text{control}}] \times 100$  was used to determine RSA (%). Every sample was examined in triplicate ( $n = 3$ ). Regression analysis was used to determine  $\text{IC}_{50}$  values.

### 2.8 SPF evaluation

Using a UV-Vis spectrophotometer, the absorbance of fermented kombucha and 25% mango leaf infusion was measured at intervals of 5 nm between 290 and 320 nm, with distilled water serving as the blank. This allowed for the determination of in vitro SPF. Every sample was examined three times. According to Mansur et al. [14], SPF values were computed using the Mansur equation, which included absorbance data ( $A_\lambda$ ), erythema efficiency ( $\text{EE}_\lambda$ ), and sun intensity ( $I_\lambda$ ), with a correction factor (CF) of 10. Using a modified methodology from Lee et al., in vivo SPF was assessed in mice ( $n = 6$  per group) based on erythema and edema 24, 48, and 72 hours after UV exposure [15]. Mice were divided into 3 groups ( $n=6$ ), negative control (UV + placebo gel), and two treatment groups (mango leaf infusion gel and mango leaf kombucha gel). Test gels were applied topically to shaved dorsal skin, followed by UV exposure. Skin reactions were scored using the Draize Criteria, and mean scores were calculated. Histological evaluation of skin lesions was performed using H&E staining and light microscopy at 400x magnification.

### 2.9 Wound healing activity

Under anesthesia (acepromazine 1.5%, 0.2 mL/20 g i.p.), circular excision wounds (15 mm) were made. Mice were divided into four groups ( $n = 5$ ), placebo, povidone-iodine (positive control), mango leaf infusion gel, and kombucha gel. Gels were applied daily for 21 days. Wound area reduction was measured using ImageJ software Java 8 (National Institutes of Health), and histological analysis was performed post-treatment [16].

### 2.10 Data analysis

The results are expressed as means  $\pm$  standard deviation. Statistical analyses were conducted using an independent T-test to evaluate TPC and TFC. Antioxidant, wound contraction, and SPF data: One-way ANOVA followed by Duncan's multiple range test for pairwise comparisons. Differences were considered significant at  $p < 0.05$ .

## 3. Result and discussion

### 3.1 Biological substance profile and antioxidant activity

TPC and TFC of mango leaf infusion and its kombucha values were calculated from the calibration curve of gallic acid ( $y = 0.0135x + 0.0279$ ;  $R^2 = 0.9916$ ), while TFC was determined from the quercetin calibration curve ( $y = 0.0095x + 0.2247$ ;  $R^2 = 0.99$ ). The kombucha sample exhibited a significantly higher TPC ( $29.1 \pm 0.09$  mg GAE/g) and TFC ( $9.14 \pm 0.07$  mg QE/g) than the infusion ( $19.6 \pm 0.33$  mg GAE/g and  $7.59 \pm 0.03$  mg QE/g;  $p = 0.001$ ,  $p < 0.05$ ) (Table 1). The increased TPC and TFC following fermentation can be explained by microbial enzymatic biotransformation. Enzymes such as  $\beta$ -glucosidase, tannase, and esterase produced by *Acetobacter* and *Saccharomyces* species hydrolyze glycosidic and ester bonds in complex polyphenols, releasing simpler

aglycones with higher antioxidant reactivity. Furthermore, fermentation often enhances extractability of bound phenolics through mild acidification and oxidative polymer breakdown [17]. This finding aligns with earlier studies showing that kombucha made from mulberry leaves significantly boosts both total phenolic compounds and total flavonoids, with increases of 7.38 and 12.24 times, respectively [18].

The antioxidant activity of mango leaf kombucha was notably stronger, with an  $IC_{50}$  value of 14  $\mu\text{g/mL}$ , compared to the mango leaf infusion alone, which showed an  $IC_{50}$  of 24  $\mu\text{g/mL}$ , though remained below that of ascorbic acid ( $IC_{50} = 5.39 \mu\text{g/mL}$ ) (Table 1). The superior activity of the kombucha aligns with observations in fermented green-tea or guava-leaf kombuchas, where  $IC_{50}$  values improved two- to threefold relative to non-fermented extracts [19,20]. The observed increase in total phenolic and flavonoid contents, and antioxidant activity during fermentation can be attributed to the enzymatic activity of lactic acid bacteria, which degrade plant cell walls and other structural components in the substrate. Furthermore, the osmotic pressure produced by acidic metabolites and the high initial sugar content may promote the release of phenolic compounds or change bound macromolecular phenols into free, low-molecular-weight forms, increasing their total concentration [21].

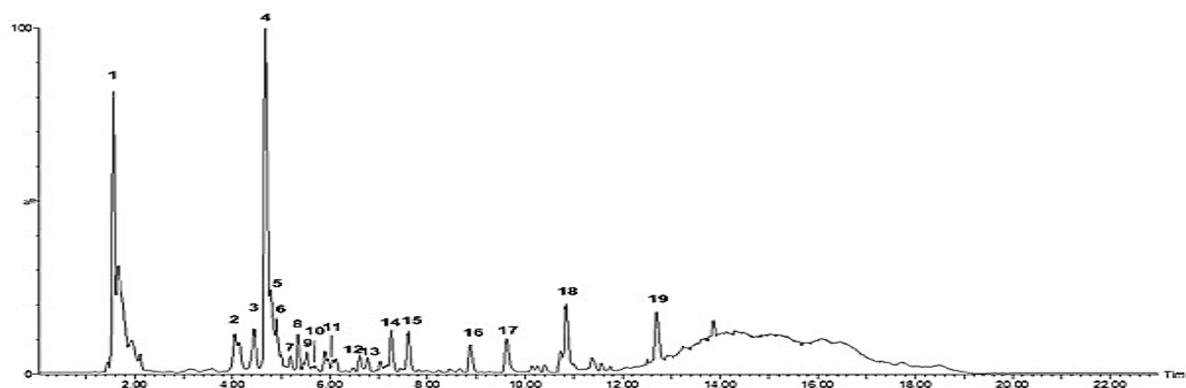
**Table 1** TPC, TFC,  $IC_{50}$  of DPPH scavenging activity and SPF value of mango leaf infusion and kombucha.

Samples	TPC (mg GAE/g)	TFC (mg QE/g)	$IC_{50}$ of DPPH Radical scavenging activity ( $\mu\text{g/mL}$ )	SPF
Mango leaf kombucha	29.1 $\pm$ 0.09 <sup>a</sup>	9.14 $\pm$ 0.07 <sup>a</sup>	14	22.76 $\pm$ 0.679
Mango leaf infusion	19.6 $\pm$ 0.33 <sup>b</sup>	7.59 $\pm$ 0.03 <sup>b</sup>	24	20.33 $\pm$ 0.783
Ascorbic acid	-	-	5.39	-

The values are presented as mean  $\pm$  SD (n=3). Different superscript letters indicate significant differences ( $p < 0.05$ ).

LC-MS profiling confirmed a rich polyphenolic composition in mango leaf kombucha (Figure 1; Table 2). Nineteen compounds were identified, including xanthenes (mangiferin, isomangiferin, mangiferin gallate), flavonoids (vitexin, tricetin, di-O-methylquercetin), gallic acid derivatives, benzophenones, and coumarins. These compounds indicate a rich phytochemical profile, which may enhance the health benefits of mango leaf kombucha made from mango leaves.

The antioxidant activity of plant extracts generally arises from a synergy among various phenolic compounds, as demonstrated *in vitro* with compounds like xanthenes, flavonoids, coumarins, and phenolic acids, acting together to enhance antioxidant efficacy [22]. Due to its C-glycosylxanthone structure, mangiferin, the main bioactive component of mango leaves, has been extensively studied for its antioxidant qualities. Mangiferin's polyhydroxy and C-glucosyl linkage increase its capacity to scavenge free radicals [23,24].



**Figure 1** LC-MS representative chromatograms for mango leaf kombucha

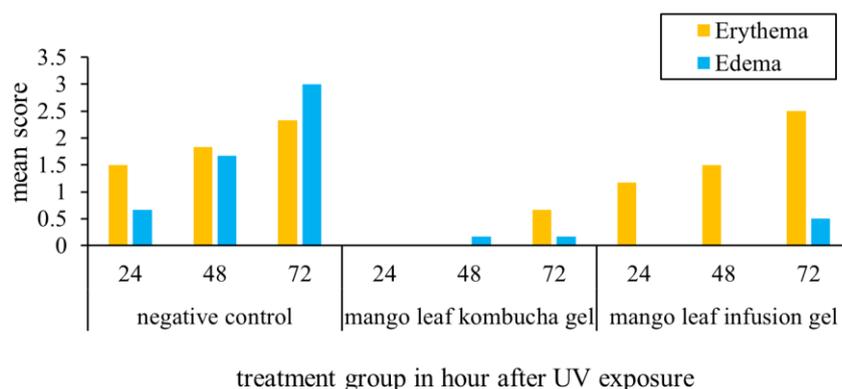
**Table 2** Bioactive compounds detected using LC-MS in mango leaf kombucha.

Comp. No.	Retention time (min)	[M+H] <sup>+</sup> , m/z	Reference mass	Formula	Tentative identification	Class	Ref.
1	1.56	381.081	380.3	C <sub>17</sub> H <sub>16</sub> O <sub>10</sub>	Trimethylenglykol digalloat (Gallic Acid derivatives)	phenol	[25]
2	4.04	843.162	842.668	C <sub>38</sub> H <sub>34</sub> O <sub>22</sub>	Mangiferoxanthone A	xanthone	[26]
3	4.45	409.113	408.4	C <sub>19</sub> H <sub>20</sub> O <sub>10</sub>	Iriflophenone 3-C-glucoside	benzophenones	[27]
4	4.68	423.092	422.342	C <sub>19</sub> H <sub>18</sub> O <sub>11</sub>	Mangiferin	xanthone	[26]
5	4.78	423.093	422.3	C <sub>19</sub> H <sub>18</sub> O <sub>11</sub>	Isomangiferin	xanthone	[28]
6	4.90	437.108	436.4	C <sub>20</sub> H <sub>20</sub> O <sub>11</sub>	Homomangiferin	xanthone	[26]
7	5.17	575.108	574.4	C <sub>26</sub> H <sub>22</sub> O <sub>15</sub>	Mangiferin gallate	xanthone	[27]
8	5.345	433.113	432.4	C <sub>21</sub> H <sub>20</sub> O <sub>10</sub>	Vitexin	flavonoid	[29]
9	5.542	545.121	544.5	C <sub>26</sub> H <sub>24</sub> O <sub>13</sub>	Maclurin 3-C-(6"-p-hydroxybenzoyl-glucoside)	benzophenones	[27]
10	5.655	543.116	542.4	C <sub>26</sub> H <sub>22</sub> O <sub>13</sub>	4'-O-benzoylmangiferin	xanthone	[29]
11	6.048	131.155	330.292	C <sub>17</sub> H <sub>14</sub> O <sub>7</sub>	Di-O-methylquercetin	flavonoid	[30]
12	6.617	239.0919	238.239	C <sub>12</sub> H <sub>14</sub> O <sub>5</sub>	(E)-3,4,5-Trimethoxycinnamic acid	phenol	[30]
13	6.772	758.407	757.7	C <sub>33</sub> H <sub>41</sub> O <sub>20</sub> <sup>+</sup>	Cyanidin 3-(2G-glucosylrutinoside)	flavonoid	[30]
14	7.258	331.156	330.29	C <sub>17</sub> H <sub>14</sub> O <sub>7</sub>	Tricin	flavonoid	[30]
15	7.609	221.082	220.224	C <sub>12</sub> H <sub>12</sub> O <sub>4</sub>	5,7-Dimethoxy-4-methyl coumarin	coumarin	[30]
16	8.881	235.0970	234.251	C <sub>13</sub> H <sub>14</sub> O <sub>4</sub>	trans-p-Coumaryl diacetate	hydroxycinnamoyl derivatives	[30]
17	9.626	207.067	206.19	C <sub>11</sub> H <sub>10</sub> O <sub>4</sub>	6,7-Dimethoxycoumarin	coumarin	[30]
18	10.836	221.0814	220.224	C <sub>12</sub> H <sub>12</sub> O <sub>4</sub>	Eugenetin	coumarin	[30]
19	12.69	305.3056	304.058	C <sub>18</sub> H <sub>40</sub> O <sub>3</sub>	Dihydroquercetin (taxifolin)	flavonoid	[30]

### 3.2 SPF evaluation and in vivo testing

Both mango leaf infusion ( $20.33 \pm 0.783$ ) and kombucha ( $22.76 \pm 0.679$ ) were classified as offering extreme protection ( $SPF > 15$ ) [31], with kombucha exhibiting somewhat more protection (Table 1). As a result, they showed great promise as sunscreens that might shield the skin against UV-induced pigmentation and erythema.

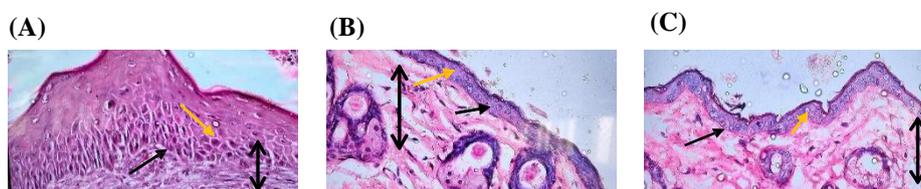
Mango leaf's bioactive components, especially mangiferin, which dramatically lowers UVB-induced inflammatory reactions and aids in preventing skin aging and collagen degradation, are responsible for its preventive properties. In order to maintain skin structure and function under UV exposure, matrix metalloproteinase-9 (MMP-9) activity is downregulated and mitogen-activated protein kinase 1 (MEK) and extracellular signal-regulated kinase (ERK) activation is inhibited [32].



**Figure 2** Erythema and edema score of treatments after UV exposure.

Results demonstrated that both the mango leaf infusion and kombucha gel reduced UV-induced skin reactions (Figure 2). During UV exposure, erythema and edema progressively increased, particularly evident in the negative control group, which received only a placebo gel. The study demonstrated that mango leaf kombucha gel provided superior protection against UV-induced skin damage in mice compared to the infusion gel. Kombucha gel completely prevented erythema and edema at 24 h and maintained strong protection up to 72 h, showing only mild skin reactions. Although the infusion gel was slightly less effective, it still significantly reduced edema compared to the control. These findings were also supported by histological observations, which showed that mice treated with both mango leaf gels exhibited reduced epidermal thickness compared to the negative control group after 72 h of UV exposure (Figure 3).

The fermentation process appears to enhance UV-filter synergy. Studies such as Zofia et al. [33] showed that green coffee kombucha ferments significantly increased SPF values as fermentation time progressed, due to increased phenolic compound release and improved radical scavenging activity. Additionally, Herman & Herman [34] examined fermented plant extracts for dermal applications, highlighting the tremendous potential of kombucha ferments in “nutricosmetic” SPF compositions due to their skin-soothing and photo-protective properties. According to Ziemlewska et al. [35], kombucha ferments also improve skin barrier integrity and decrease trans-epidermal water loss (TEWL), which can benefit overall sunscreen efficacy and sensory performance.



**Figure 3** Histological examination of the skin after 72 h of UV exposure. A = normal control, B = negative control, C = mango leaf kombucha gel, D = mango leaf infusion gel.

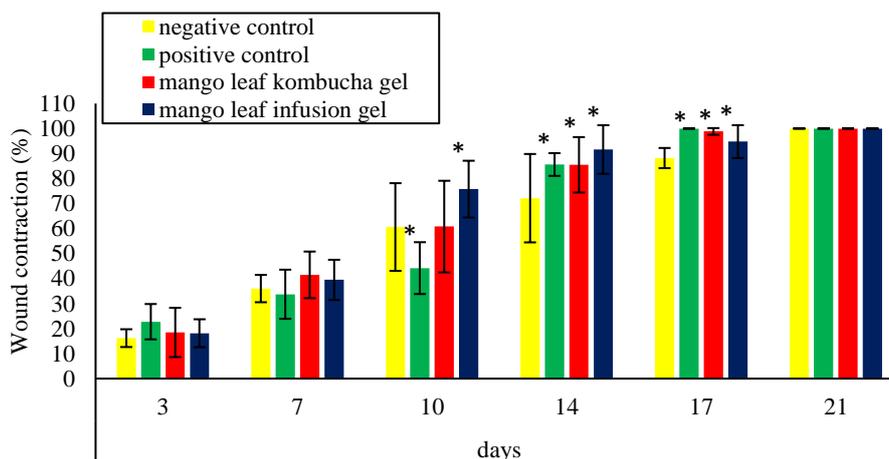
Note: → epidermis → Melanosit ↔ Dermal connective tissue

As a natural defense mechanism to prevent DNA damage, UV radiation increases the skin's production of melanin [36]. The group receiving mango leaf kombucha and infusion gel showed the least rise in melanocytes. Mangiferin, the main bioactive substance found in mango leaves and well-known for its strong antioxidant and

photoprotective qualities, is primarily responsible for this impact. Mangiferin's capacity to reduce melanin formation by inhibiting tyrosinase activity is further demonstrated by studies by Efendi et al. [6], highlighting its potential in cosmeceutical uses. Furthermore, mangiferin has been demonstrated *in vivo* to mitigate UVB-induced skin alterations, including reduced wrinkle depth and length, decreased epidermal thickening, and minimized damage to collagen fibers, all of which are indicators of photoaging [32].

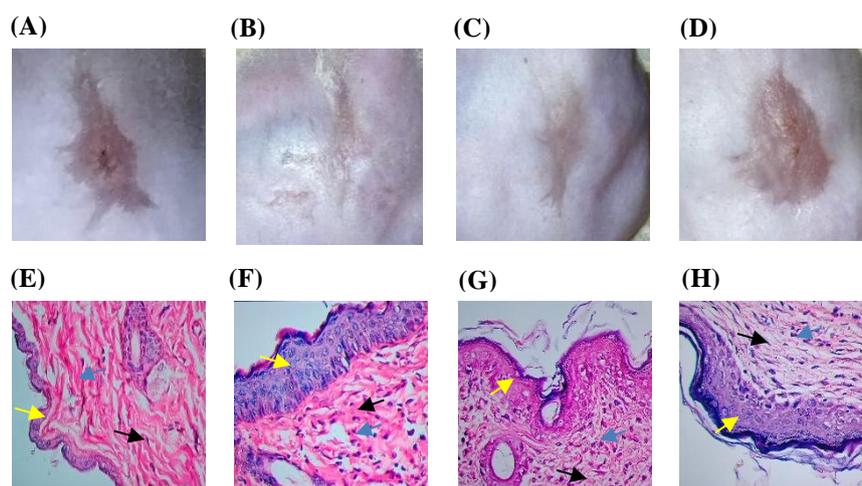
### 3.3 Wound healing activity

All treatment groups showed continuous wound contraction during the course of the trial. When compared to the negative control, animals treated with mango leaf kombucha and infusion gels had noticeably better wound healing. Hemostasis, inflammation, proliferation, and remodeling are phases that overlap in the dynamic and strictly controlled biological process of wound repair. By day 14, the healing process had moved from the proliferative to the early remodeling phase, which is marked by almost total epithelialization, a decrease in fibroblast density, and the replacement of type III collagen with more ordered type I fibers [37]. In comparison to the negative control, all treatment groups showed noticeably better wound closure at this point. Bioactive plant chemicals that speed up fibroblast activation, improve collagen production and alignment, and reduce excessive inflammation are responsible for the better healing shown in the treatment groups. Together, these effects result in faster and better tissue regeneration. By day 17, the treated wounds showed clear signs of tissue regeneration and dry, well-defined margins, similar to the povidone-iodine group. By day 21, all groups, including the negative control, showed full wound closure (Figures 4 and 5).



**Figure 4** Wound healing activity of mango leaf kombucha and infusion gel.

Histological assessments examined collagen fibers, fibroblasts, and the epidermal layer on days 7, 14, and 21 (Figure 5). All groups showed notable wound-healing progress, according to histological evidence, with mango leaf kombucha gel outperforming infusion gel and the negative control over time, as shown by increased fibroblast density, denser collagen, and thicker epidermis. Mango leaf infusion and kombucha gel both performed better than the negative control, although their efficacy was comparable. Kombucha-fermented berry leaf extracts improved skin hydration and promoted cellular regeneration, two essential elements for the best possible wound healing and dermal remodeling, according to a different study [35]. In a similar vein, Rajaei et al. [38] studied an ointment made from the floating cellulose biofilm of tea kombucha and found that it greatly increased the activity of matrix metalloproteinase-1 (MMP-1), an enzyme that breaks down old fibrillar collagen in the wound bed, promotes fibroblast migration and the formation of new tissue, and increases collagen deposition. These results show that a biocompatible wound dressing made from kombucha can speed up tissue repair, re-epithelialization, and overall healing dynamics.



**Figure 5** Wound contraction after 21 days of treatment. A = normal control, B = negative control, C = mango leaf kombucha gel, D = mango leaf infusion gel. Histological examination of wound healing following treatment application. E = normal control, F = negative control, G = mango leaf kombucha gel, H = mango leaf infusion gel.

Note: → Collagen → Epithel → Fibroblast

Bioactive components like mangiferin and its derivatives are responsible for the improved wound healing efficacy seen in mango leaf kombucha and infusion gels. Mangiferin preserves collagen integrity and speeds up wound closure by inhibiting collagenase, the enzyme that breaks down collagen, in a dose-dependent manner. Furthermore, by destabilizing COX-2 mRNA, inhibiting LPS-induced prostaglandin E2 (PGE-2) synthesis, and decreasing the synthesis of 8-iso-prostaglandin F<sub>2</sub>α (8-iso-PGF<sub>2</sub>α), it demonstrates significant anti-inflammatory capabilities that contribute to the control of inflammatory mechanisms [23,24]. Additionally, by promoting fibroblast proliferation and collagen synthesis while reducing inflammation, methoxylated coumarins, which are present in mango leaves, improved wound recovery [39]. In a similar vein, gallic acid exhibits potent antioxidant properties that promote keratinocyte and fibroblast migration and upregulate antioxidant gene expression. Critical growth factor-mediated signaling pathways, focal adhesion kinase (FAK), extracellular signal-regulated kinase (ERK), and c-Jun N-terminal kinase (JNK), are activated by this activity and are necessary for efficient wound healing [40].

#### 4. Conclusion

In comparison to the non-fermented infusion, mango leaf kombucha made via SCOBY fermentation shown better antioxidant, wound-healing, and UV-protective properties, underscoring its promise as a natural cosmeceutical raw material. Microbial biotransformation during fermentation, which raises the availability and potency of phenolic acids and flavonoids, is responsible for these improved biological effects. According to the research, fermented mango leaf extract might be used to skincare formulas to encourage tissue regeneration and guard against UV-induced damage, helping to create safe, environmentally friendly, and multipurpose cosmetics. Nevertheless, the use of animal models, the lack of human clinical trials, and the absence of long-term safety and stability evidence are the study's limitations. To confirm the fermented extract's potential as an environmentally friendly cosmeceutical ingredient, further research should concentrate on integrating it into finished cosmetic formulations, testing formulation stability, and carrying out thorough assessments of human safety and efficacy.

#### 5. Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

The authors utilized ChatGPT to help with language editing and polishing this manuscript. They accepted full responsibility for the work's correctness, integrity, and originality after utilizing this tool to review and amend the content as necessary.

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## 7. Author contributions

M. Rifqi Efendi: Conceptualization, Methodology, Writing – original draft, Supervision; Maimun: Investigation, Data curation, Resources; Rion Nofrianda: Writing – original draft, Visualization, Project administration; Elisma: Resources, Formal analysis, Project administration; Raudatul Jannah: Data curation, Resources, Visualization, Writing – original draft; Zahriana Putri: Data curation, Resources, Writing – original draft; Visualization; Mesa S. Rusdi: Methodology, Formal analysis, Writing – review & editing

## 8. Conflict of interest

The authors declared no conflict of interest.

## 9. References

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