Wound Healing Activity of Nanoemulgel Containing Artocarpus lakoocha Roxb. Extract on Burns Model in Rat

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Abstract

BACKGROUND: The content of secondary metabolites in mobe leaves has the potential to be used in wound healing. Artocarpine, one of the secondary metabolites found in mobe leaves, is reported to affect the expression of transforming growth factor-beta (TGF-β) protein, thereby increasing fibroblast cell proliferation and accelerating the wound healing process.

AIM: This study aims to determine the wound healing activity of nanoemulgel-containing ethanol extract of mobe leaves.

MATERIALS AND METHODS: The method used in this study was experimental using chemicals ethanol 96%, Carbopol 940, PEG 400, Propylene glycol, Methyl Paraben, Propyl Paraben, Triethanolamine, Aqua Destillata. Mode leaves which were taken purposively were then formulated in nanoemulgel preparations which were tested for wound healing in male rats. The nanoemulgel preparation was then evaluated which included homogeneity, emulsion stability, and migration is increased, and collagen deposition is increased, resulting in a faster wound healing process [9]. Transforming growth factor-beta (TGF-β) production is increased, fibroblast proliferation and migration is increased, and collagen deposition is increased, resulting in a faster wound healing process [10]. Antiseptics such as flavonoids and tannins play a function. It is vital for preventing bacterial development in wounds during the inflammatory phase, and it can speed up wound healing, capillary blood vessel development, and fibroblast cell creation [11], [12]. Based on this, the development of mobe leaves as a wound medicine is very promising. Another important thing is the dosage form used so that the effectiveness of mobe leaves as a wound medicine becomes increased [13].

CONCLUSION: From this study, nanoemulgel mobe can stimulate more fibroblast cell proliferation by greatly expressing TGF-β1 and PDGF BB in burn wounds.

Introduction

Burns are kind of accidents that often occur in everyday life. Burns are a form of tissue damage caused by contact between the skin and heat sources such as fire, hot water, chemicals, electricity, and radiation [1]. Burns occur on the skin, mucous membranes, respiratory tract, and gastrointestinal tract. Symptoms include pain, swelling, red, blisters due to increased permeability of blood vessels [2]. It can be treated by minimizing tissue damage, providing tissue perfusion, adequate oxygenation, and nutrition, as well as a moist wound healing environment to restore anatomical continuity and characteristics of the affected part [3]. One of the current projects is looking at natural compounds that might help in wound healing [4]. Wound care with natural components is becoming more popular these days due to the fact that it has less side effects than conventional therapies and the time it takes for wound healing with natural materials is getting faster [5].

One of the natural ingredients that have the potential to be developed as a wound medicine is mobe leaves (Artocarpus lakoocha Roxb) [6]. Flavonoids, tannins, saponins, and glycosides are all found in mobe leaves. Flavonoids such as artonin a, artonin b, and artokarpin, which can be inhibitory chemical mediators, are the major component of mobe leaves [7], [8]. Artocarpin has been shown to cause the inflammatory phase to begin sooner [9]. Transforming growth factor-beta (TGF-β) production is increased, fibroblast proliferation and migration is increased, and collagen deposition is increased, resulting in a faster wound healing process [10]. Antiseptics such as flavonoids and tannins play a function. It is vital for preventing bacterial development in wounds during the inflammatory phase, and it can speed up wound healing, capillary blood vessel development, and fibroblast cell creation [11], [12]. Based on this, the development of mobe leaves as a wound medicine is very promising. Another important thing is the dosage form used so that the effectiveness of mobe leaves as a wound medicine becomes increased [13].
Semi solid preparation, including ointments, creams, and gels, offers possibilities for all the better ones, such as extended medication contact and wound protection from extreme diagnostics [14], [15]. The gel’s dose form is more convenient to apply, and it spreads more quickly on the skin. The gel is also cooling and hydrating, and it readily enters the skin to produce a healing effect. Gel preparations can help to keep the skin hydrated and prevent dehydration [16]. For now, of course, the nano shape has better efficacy. The smaller the particle size, the easier it will be to penetrate the skin membrane barrier and the better the effect [17]. Therefore, the development of nanoemulgel preparations containing mobe leaf extract must be very interesting to do. However, it should be a concern that the carrier should be easy to apply to the skin, not irritating, and safe to use on the skin [18].

**Materials and Methods**

**Materials**

Mobe leaves, ethanol 96% (v/v), carbopol 940, isopropyl myristate, isopropyl alcohol, methylparaben, propyl paraben, triethanolamine, aqua destillata, and bioplacenton® gel.

**Animal**

The experimental study used 60 rats (Rattus norvegicus) in good health and weighing between 150 and 200 g. Rats are housed in plastic cages with a humidity level of 40%–60% and a 12-h dark/light cycle. In addition, rats were fed with pellets produced by Cratachem and water ad libitum. The Universitas Sumatera Utara had granted ethics clearance for this project.

**Plant**

Sampling was carried out purposively without comparing with the same plants from other areas. Mobe leaves were obtained from Deli Tua, Deli Serdang, North Sumatra, Indonesia. Plant identification was carried out at the Indonesian Institute of Sciences, Biology Research Center, LIPI Bogor.

**Ethanol extract preparation**

The extract was made by maceration method using 96% ethanol. As much as 1,000 grams of mobe leaves powder is put into a glass container then add 7.5 L of 96% ethanol, cover and leave for 5 days protected from light while occasionally stirring, strain, squeeze, wash the dregs with a liquid filter as much as 2.5 L. Transfer to a closed vessel, leave in a cool place, protected from light for 2 days and then pour or filter. The obtained maserati was then concentrated with a rotary evaporator at a temperature of ± 40°C until an almost crude extract was obtained [19].

**Modification nanoemulgel formulation**

Nanoemulgel preparation of ethanol extract from mobe leaves begins with the manufacture of nanoemulsion ethanol extract from mobe leaves first. Then added the nanoemulsion to the gel base to add viscosity and comfort when applied. The following Table 1 shows the preparation of nanoemulgel. Nanoemulgel was prepared using spontaneous emulsification techniques. Tween 80 was mixed with some of the distilled water, then stirred until a thick mass is formed and pale yellow. The water phase was made by mixing an extract solution with a solution of tween 80, methyl parabens, propyl parabens in distilled water, while the oil phase was prepared by dissolving isopropyl myristate and isopropyl alcohol. The oil phase was added to the water phase, then sonicated for 30 min until a clear preparation is formed and then homogenized using a magnetic stirrer at a speed of 2000 rpm for ± 1 h so that nanoemulsion was obtained [20].

Nanoemulgel was obtained by preparing in advance the base of the gel by developing carbopol in distilled water for 24 h, then homogenized with a magnetic stirrer and then adding a few drops of triethanolamine to the carbopol, then the carbopol was homogenized again until a thick and transparent gel was formed. The preparation of nanoemulgel was carried out by mixing the nanoemulsion with the gel portion and then homogenized with a magnetic stirrer at a speed of 2000 rpm for ±10 h until a clear and dark green nanoemulgel was formed [21].

**Nanoemulgel evaluation**

Nanoemulgel evaluation includes organoleptic, homogeneity test, pH test, particle size analysis, viscosity test, and spreadability.

**Organoleptic test**

Each formula was stored for 12 weeks at room temperature and observed weekly. The observed are changes in color, smell, shape, and damage or separation of phases [22].

**Homogeneity test**

Visual examination was used to check for homogeneity in all created nanoemulgels. It was
examined for its appearance and the presence of aggregates [22].

**pH test**

Determination of the pH value of the preparation was carried out using a pH meter which was first calibrated using a neutral standard buffer solution (pH 7.01) and an acidic pH buffer solution (pH 4.01) until the instrument showed the pH value. The sample is made in a concentration of 1% and the electrode is immersed in the solution. The apparatus is left to show a constant pH value [23].

**Particle size analysis**

The particle size was measured at room temperature using the Particle Size Analyzer at the Universitas Sumatera Utara, Physics Integrated Laboratory. Particles from each nanoemulsion gel formula were determined three times: at the start of the preparation, at the 6th week, and at the 12th week [23].

**Viscosity test**

Spindle 4 was mounted after 100 cc of nanoemulgel is placed in a tube-shaped container. In test preparations, spindles should be immersed. The viscometer was switched on, and the installed rotors may spin at 60 rpm [23].

**Spreadability test**

The gel was weighed up to 0.5 g before being placed in the center of a scaled round glass. Other round glass materials are placed on top of the gel, along with ballast, such that the weight of the glass is round and the ballast is 100 g, silent for 1 min, and the diameter of the spread is measured [24].

**Burn wound healing test**

Rats hair was shaved and cleaned on the area to be injured. Wound making was done after the annexed rats first used 0.1 mL lidocaine 2% as subcutaneously. Burns were made using a metal plate with a diameter of 2 cm which was previously dipped in boiling water (100°C) to be sterilized and cooled for a while then the metal plate was dipped again in boiling water (100°C) and then affixed to the back of the rat for 15 s. A total of 60 male rats wet divided into 6 groups, each group consisting of 5 heads [25]. The rat group was given an ethanol extract nanoemulgel of mobe leaves.

- **Group I**: Negative control was given gel base
- **Group II**: Rats were given F1
- **Group III**: Rats were given F2
- **Group IV**: Rats were given F3
- **Group V**: Rats were given F4
- **Group VI**: Positive control was given bioplacenton®

The nanoemulgel was applied 2 times a day (wound was not closed). The observation of wound observations was carried out on 1, 3, 7, and 14 days visually by measuring the diameter of the wound until the wound is considered healed (the wound is dry and the diameter of wound is reduced) [26].

**Visual observation of wound healing**

The diameter of the wound is used as a visual parameter of the healing process. The reduction of wound diameter was calculated by the formula [27]:

$$\text{dx} = \frac{\text{dx}_1 + \text{dx}_2 + \text{dx}_3 + \text{dx}_4}{4}$$

Information:
- $\text{dx}$ = wound diameter in x-day
- $\text{dx}_1$ = diameter 1
- $\text{dx}_2$ = diameter 2
- $\text{dx}_3$ = diameter 3
- $\text{dx}_4$ = diameter 4.

**Nanoemulgel effect on total fibroblast**

The effect of nanoemulgels on the number of fibroblast cells of the test group was determined on days 3, 7, and 14. Tissue samples were obtained from each representative of the test group sacrificed using chloroform on days 3, 7, and 14. The sample was soaked in paraffin medium and stained with hematoxylin eosin. It is then observed under a microscope with a magnification of 400 to see fibroblast cells. The number

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**Table 1: Composition of nanoemulgel containing ethanol extract of mobe leaves**

<table>
<thead>
<tr>
<th>Formula</th>
<th>Blanko</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composition (g)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol extract of mobe leaves</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Isopropyl myristate</td>
<td>7.5</td>
<td>7.5</td>
<td>7.5</td>
<td>7.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Isopropyl alcohol</td>
<td>11.25</td>
<td>11.25</td>
<td>11.25</td>
<td>11.25</td>
<td>11.25</td>
</tr>
<tr>
<td>Tween 80</td>
<td>33.75</td>
<td>33.75</td>
<td>33.75</td>
<td>33.75</td>
<td>33.75</td>
</tr>
<tr>
<td>Methyl paraben</td>
<td>0.18</td>
<td>0.18</td>
<td>0.18</td>
<td>0.18</td>
<td>0.18</td>
</tr>
<tr>
<td>Propyl paraben</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Aqua destillata</td>
<td>Ad 100</td>
<td>Ad 100</td>
<td>Ad 100</td>
<td>Ad 100</td>
<td>Ad 100</td>
</tr>
<tr>
<td><strong>Composition of gel base (g)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbopol 940</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>TEA</td>
<td>0.4 or q.s until pH 7</td>
<td>0.4 or q.s until pH 7</td>
<td>0.4 or q.s until pH 7</td>
<td>0.4 or q.s until pH 7</td>
<td>0.4 or q.s until pH 7</td>
</tr>
<tr>
<td>Aqua destillata</td>
<td>Ad 100</td>
<td>Ad 100</td>
<td>Ad 100</td>
<td>Ad 100</td>
<td>Ad 100</td>
</tr>
</tbody>
</table>

TEA: Triethanolamine

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of fibroblast cells of each test group is calculated in a predetermined manner [28], [29].

**Nanoemulgel effect on PDGF BB and TGF-β1 expression**

The proteins expression was obtained using immunohistochemical method. The platelet-derived growth factor (PDGF) BB and TGF-β1 expression were observed and calculated in group test on days 3, 7, and 14. A light binocular microscope was used to count the cells, and the results were given as immunohistoscore [30].

**Data analysis**

The Statistical Package for the Social Science (SPSS) program 21 was used to analysis of the data. Data are expressed as mean ± SEM. Comparison for more than 2 groups by using one-way ANOVA followed by post hoc Tukey's test. Statistical significance was set at p < 0.05 [31].

**Results**

**Nanoemulgel evaluation**

Nanoemulgel has been successfully created based on modified formulas [Table 1]. To see the quality of nanoemulgel, evaluation was carried out, namely organoleptic test, homogeneity test, pH test, particle size analysis, viscosity test, and spreadability. The test results of the nanoemulgel will be explained in this section.

Examination of nanoemulgel organoleptis was done by observing odors, colors, and homogeneity of each formula over 12 weeks of storage [Table 2].

**Table 2: Organoleptic evaluation of nanoemulgel**

<table>
<thead>
<tr>
<th>Samples</th>
<th>Parameter</th>
<th>Observation (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Blanko</td>
<td>Color</td>
<td>Peach</td>
</tr>
<tr>
<td></td>
<td>Odor</td>
<td>Specific</td>
</tr>
<tr>
<td>F1</td>
<td>Homogeneity</td>
<td>Homogeneous</td>
</tr>
<tr>
<td></td>
<td>Extract odor</td>
<td>Extract odor</td>
</tr>
<tr>
<td>F2</td>
<td>Homogeneity</td>
<td>Homogeneous</td>
</tr>
<tr>
<td></td>
<td>Extract odor</td>
<td>Extract odor</td>
</tr>
<tr>
<td>F3</td>
<td>Homogeneity</td>
<td>Homogeneous</td>
</tr>
<tr>
<td></td>
<td>Extract odor</td>
<td>Extract odor</td>
</tr>
<tr>
<td>F4</td>
<td>Homogeneity</td>
<td>Homogeneous</td>
</tr>
<tr>
<td></td>
<td>Extract odor</td>
<td>Extract odor</td>
</tr>
</tbody>
</table>

The four nanoemulgel formulas have similarities in smell (typical extract), green color (dark green), and good level of homogeneity. All four formulas give the same result to organoleptic parameters because each formula uses the same composition except the active substance (extract). This means that the addition of extracts to a concentration of 7% has no effect on nanoemulgel organoleptis.

pH testing on nanoemulgels aims to predict the safety of nanoemulgels when applied to the skin [Table 3]. The pH measurement was determined using a pH meter 3 times/formula in weeks 0, 6, and 12.

**Table 3: pH value of nanoemulgel**

<table>
<thead>
<tr>
<th>Samples</th>
<th>pH value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Blanko</td>
<td>5.06 ± 0.11</td>
</tr>
<tr>
<td>F1</td>
<td>5.13 ± 0.05</td>
</tr>
<tr>
<td>F2</td>
<td>5.23 ± 0.05</td>
</tr>
<tr>
<td>F3</td>
<td>5.32 ± 0.05</td>
</tr>
<tr>
<td>F4</td>
<td>5.41 ± 0.11</td>
</tr>
</tbody>
</table>

Based on the obtained results, there was a change in the degree of acidity of the pH of each nanoemulgel in storage for 12 weeks. The longer the storage time, the pH of the nanoemulgel increases.

Observations of particle size were conducted at the Nanomedicine Laboratory of the USU Faculty of Pharmacy using the FRITSCH Analysette 22 NanoTec Particle Size Analyzer tool at room temperature. Average results measurement of particle size and its changes during 0, 6, and 12 weeks of storage at room temperature [Table 4].

**Table 4: Particle size of nanoemulgel**

<table>
<thead>
<tr>
<th>Samples</th>
<th>Particle size (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Blanko</td>
<td>40.32 ± 0.18</td>
</tr>
<tr>
<td>F1</td>
<td>50.44 ± 0.23</td>
</tr>
<tr>
<td>F2</td>
<td>60.51 ± 0.45</td>
</tr>
<tr>
<td>F3</td>
<td>80.78 ± 0.31</td>
</tr>
<tr>
<td>F4</td>
<td>90.12 ± 0.17</td>
</tr>
</tbody>
</table>

The particle size of each formula’s nanoemulgel increases with the length of storage time of 12 weeks. For example, nanoemulgel (F4) experienced an increase in particle size ranging from 90.12 ± 0.17 nm (week 0), 339.12 ± 0.38 nm (week 6), and to 512 ± 0.31 nm (week 12). However, the result of this increase in particle size is still within the nanometer size range of each formula.

Measurements of nanoemulgel stability during storage can also be known from changes in viscosity over a period of 12 weeks. Viscosity determination was done using Brookfield NDJ-8S Viscometer tool with a speed of 60 rpm for nanoemulgel on weeks 0, 6, and 12 [Table 4].

According to the findings of the viscosity data, each formula’s seeing trends to improve with storage. For example, the viscosity of nanoemulgel (F4) was 974.77 ± 0.73 (week 0), 1007.21 ± 0.61 (week 6), and 1225.92 ± 0.78 (week 12). Related to viscosity, the spreadability of nanoemulgel must be determined. Spreadability is an important characteristic in formulations that guarantees the ease when nanoemulgel is applied to the skin [Table 5].

Based on the test results, the dispersion obtained tends to be homogeneous, namely in the range...
of 5.0–6.2. That is, the addition of the concentration of mobe leaf extract did not significantly affect the quality of the nanoemulgel.

**Wound healing activity of nanoemulgel**

The wound-healing activity of nanoemulgel was evaluated as in vivo in burn-treated rats [Figure 1]. This evaluation lasted for 14 days, taking into account parameters such as wound diameter, increase in fibroblast cells, and the effect of nanoemulgel on the expression of PDGF BB and TGF-β1 proteins [Table 6].

According to Table 6, wound healing effect of nanoemulgel contain ethanol extract of mobe leaves was obtained. The percentage of reducing wound diameter value was increased in nanoemulgel group (F1, F2, F3, and F4) if compared to Blanko group, this effect was significantly different (p < 0.05). This happened at each observation time (days 3, 7, and 14). However, if the result of nanoemulgel group compared to positive group in observation time (days 3, 7, and 14), this effect was not significantly different (p > 0.05).

Fibroblast cell is taken a side to wound healing process [32]. This study was showed the fibrolast cells value after treatment using nanoemulgel groups was increased in observation times compared to Blanko group and significantly different (p < 0.05). However, only the F4 group was not significantly different from the positive group (p > 0.05). It is mean that the F4 group has the same wound healing activity with positive group.

This was explained by the activity of the nanoemulgel group increasing the expression of PDGF BB and TGF-β1 proteins (Table 7). The proteins expression was increased during observation time. The nanoemulgel groups have activity to increase expression of PDGF BB and TGF-β1 compared to Blanko group; this is significantly different (p < 0.05). However, only F1 group was significantly different compared to positive group (p < 0.05) to increase TGF-β1. This explains that the extract content in nanoemulgel affects the activity of increasing protein expression.

**Discussion**

Tissue injury induced by contact with a heat source such as fire, electricity, or dangerous chemicals is known as burns [33]. Burns damage the skin as well as other tissues including blood vessels, nerves, tendons, and bones, increasing the risk of infection. Second-degree burns have damage to the epidermis, although there are still many skin organs above the corium/dermis, such as hair follicles and sebaceous glands, according to histology [34]. Natural compounds that are anti-inflammatory, antioxidant, and antibacterial can be used to treat burns [35].

Mobe leaves are a natural component that has been reported to have the ability to speed up the healing of wounds [36]. Mobe leaves were processed into nanoemulgel preparations with varied concentrations of 1%, 3%, 5%, and 7% in this investigation. Nanoemulgel provides benefits such as good skin adherence and high solubility, allowing the medication concentration to permeate the skin more deeply [37], [38]. Nanoemulgel also helps manage drug release by extending the action of the medicine, which is beneficial for pharmaceuticals and active compounds with poor solubility [39].

Based on the research results, nanoemulgel containing ethanolic extract of mobe leaves was successfully made. The nanoemulgels were evaluated to determine their suitability. Several parameters tested were organoleptic, homogeneity, pH test, particle size, viscosity, and spreadability test. During the 12-week storage period, all assessments were completed. The examination took place three times, at weeks 0, 6, and 12. The formulations generated have no physical or chemical difficulties based on the data obtained. The thing to note is the increase in the particle size of each formula [Table 3]. Particle size is important because it relates to drug penetration into the skin. The smaller the particle size will increase the surface area contact, the higher the contact surface area, the faster the drug substance enters and is absorbed into the skin so that it can produce a optimally desired [22].

Nanoemulgel containing ethanol extract of mobe leaves was applied to rats that had been previously injured (burns). To see the ability of the extract on nanoemulgel, the burn healing process was observed for 14 days through several parameters such as a decrease in wound diameter, the number of fibroblast cells, and the expression of PDGF BB and TGF-β1 proteins. As the number of fibroblast cells rises, the wound’s width will shrink [40]. Fibroblasts are cells that play a vital part in wound healing, such as the breakdown of a fibrin clot, the formation of a new extracellular matrix, and the formation of collagen structures to support and closure wounds [41], [42]. According to Table 6, it can be seen the fibrolast cells value after treatment using nanoemulgel groups was increased in observation times compared to Blanko.
group and significantly different (p < 0.05). However, only the F4 group was not significantly different from the positive group (p > 0.05). It means that the F4 group has the same wound healing activity with positive group.

There are various factors influencing fibroblast proliferation. Observations under a microscope said to express TGF if the results of the IHS gave dark brown, medium brown, and purplish light brown while those that did not express purple. The two most important factors are TGF-β1 protein and PDGF BB [43]. PDGF and TGF-β are secreted by platelets as soon as they are injured [44]. PDGF stimulates fibroblast proliferation, which leads to the formation of extracellular matrix. PDGF BB has been identified as a significant mediator in wound healing and tissue repair as a proliferative factor [45]. TGF-β, like PDGF, plays a vital function. TGF-β stimulates fibroblasts and cell chemotaxis, modulates collagen and collagenase expression, and

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>3</th>
<th>7</th>
<th>14</th>
</tr>
</thead>
</table>

Figure 1: Burn diameter reduction
creates matrix-producing cells for deposition, resulting in fast release of new connective tissue at the wound site during the rapid proliferative phase followed by an inflammatory phase [46], [47], [48]. The nanoemulgel groups have activity to increase expression of PDGF BB and TGF-β1 compared to Blanko group; this is significantly different (p < 0.05). However, only F1 group was significantly different compared to positive group (p < 0.05) to increase TGF-β1 [Table 6]. This explains that the extract content in nanoemulgel affects the activity of increasing proteins expression.

Secondary metabolites found in mobe leaves include flavonoids, tannins, saponins, and glycosides [49]. Flavonoids and tannins are antiseptics that protect wounds from bacterial development during the inflammatory phase and can enhance the number of blood vessel and fibroblast cell creation, causing wound healing to proceed swiftly [50]. Flavonoids also have a role in the proliferative phase and tissue remodeling, notably by enhancing vascularity to ensure that the wounded tissue and cells receive the greatest amount of oxygen and nutrients [51]. Collagen production rises as a result, speeding up the wound healing process [52]. Furthermore, it has been observed that artocarpine can activate the inflammatory phase early by enhancing TGF-β production, fibroblast proliferation and migration, and collagen deposition, resulting in faster wound healing processes [53], [54]. This supports the activity of mobe leaves in accelerating the wound healing process.

**Conclusion**

All preparation formulas of nanoemulgel containing mobe leaves ethanol extract meet the quality requirements of nanoemulgel evaluation. The dosage form of nanoemulgel can heal wounds in rats with increase fibroblast cells and increase PDGF BB and TGF-β1 expressions. Post hoc Tukey’s HSD test results obtained a concentration result of 7% not significantly different from Bioplacenton® as a positive control. The optimum dose of ethanol extract mobe leaves that can cure burn wounds in rats in the dosage form of the nanoemulgel is 7%.

**Acknowledgments**

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**References**


PMid:20380874
PMid:23871788
PMid:25454458
PMid:34333340
PMid:8412398
PMid:26289672
PMid:31766305
PMid:34202733
PMid:27217089
PMid:25224162
PMid:22817824
PMid:34507115


