

Effectiveness Of Trembesi Leaf Extract Gel On Angiogenesis After Tooth Extraction

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ABSTRACT

Background: Post-extraction wound healing involves hemostasis, inflammation, proliferation, and maturation, with angiogenesis supporting tissue regeneration by supplying oxygen and nutrients. Trembesi leaves (*Samanea saman* (Jacq.) Merr.) contain bioactive compounds with antioxidant and anti-inflammatory properties that may support wound healing and neovascularization. Therefore, this study aimed to analyze the effect of trembesi leaf extract gel (*Samanea saman* (Jacq.) Merr.) on angiogenesis expression during post-extraction wound healing.

Method: This laboratory experimental study used a post-test-only control group design involving eight male Wistar rats (*Rattus norvegicus*) randomly divided into two groups (n = 4): a treatment group receiving 12% trembesi leaf extract gel and a control group receiving placebo gel. Following mandibular incisor extraction, the gels were applied topically twice daily for 7 days. On day 7, extraction socket tissues were collected and examined histopathologically using Hematoxylin–Eosin staining. Angiogenesis was assessed by counting identifiable newly formed blood vessels in five microscopic fields at 400× magnification. Data were analyzed using the independent *t*-test with a significance level of $p < 0.05$.

Result: The mean number of newly formed blood vessels was higher in the treatment group (1.05) than in the control group (0.40). The independent *t*-test demonstrated a statistically significant difference between the groups ($p = 0.014$).

Conclusion: The 12% trembesi leaf extract gel significantly increased the number of histologically identifiable newly formed blood vessels during post-extraction wound healing. However, the findings should be interpreted cautiously because the relatively low number of vessels observed may not fully represent overall neovascularization.

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INTRODUCTION

Tooth extraction is a commonly performed dental procedure intended to remove teeth that can no longer be preserved. This procedure inevitably causes tissue damage, thereby initiating a series of wound healing responses. The 2023 Indonesian Health Survey (SKI 2023) reported that 56.9% of the Indonesian population aged ≥ 3 years experienced oral and dental problems, while only 11.2% received treatment from dental health professionals.¹ These findings indicate that oral and dental health problems remain a substantial public health concern and highlight the importance of appropriate management of dental conditions requiring extraction and optimal post-extraction wound healing.

The healing process of post-extraction wounds involves four interconnected phases, namely hemostasis, inflammation, proliferation, and remodeling. Hemostasis occurs immediately after tooth extraction and involves vasoconstriction, platelet activation, and blood clot formation, which provides a temporary matrix for subsequent cellular migration and tissue repair. The inflammatory phase is initiated immediately following tissue injury and is characterized by an immune response that functions to eliminate microorganisms and remove damaged tissue from the wound site. Subsequently, the proliferative phase is marked by granulation tissue formation, cell migration, and angiogenesis. During the proliferative phase, which becomes prominent within the first week after injury, angiogenesis and granulation tissue formation contribute substantially to tissue repair. The final phase is remodeling, which involves tissue maturation until it approaches normal physiological conditions. Each phase is interrelated and contributes significantly to the overall outcome of the healing response.^{2,3}

Angiogenesis is essential for tissue regeneration during wound healing and is regulated by various growth factors, including vascular endothelial growth factor (VEGF) and transforming growth factor-beta (TGF- β).^{4,5} Given its importance in tissue repair, modulation of angiogenesis may influence the outcome of post-extraction wound healing. Therefore, natural compounds with potential angiogenic activity, such as those present in trembesi leaf extract, warrant further investigation.

The use of natural products in wound management has gained increasing interest because various plant-derived bioactive compounds possess antioxidant, anti-inflammatory, and tissue-repair properties. These properties may support the wound-healing process and potentially modulate angiogenesis, which is essential for tissue regeneration. Therefore, plant-derived materials with potential effects on angiogenesis may serve as promising candidates for enhancing post-extraction wound healing.⁶

Trembesi leaf (*Samanea saman* (Jacq.) Merr.) was selected as a potential plant-based therapeutic agent because previous studies have demonstrated its wound-healing, antioxidant, and anti-inflammatory activities. Phytochemical studies have identified phenolic compounds and flavonoids as important constituents of trembesi leaves, along with tannins, saponins, alkaloids, and triterpenoids.⁷ These polyphenolic compounds may contribute to tissue repair by reducing oxidative stress and inflammation, thereby supporting fibroblast activity, collagen formation, and angiogenesis.⁸ Therefore, trembesi leaf extract may have potential to support post-extraction wound healing through modulation of the angiogenic process. Although several studies have highlighted the anti-inflammatory potential of trembesi leaf extract, investigations regarding its effect on angiogenesis during post-extraction

wound healing are still limited. Based on these considerations, this study aimed to analyze the effect of trembesi leaf extract gel on angiogenesis during the post-extraction healing process.

RESEARCH METHOD

This study employed a laboratory experimental design using a post-test-only control group approach. Eight male Wistar rats (*Rattus norvegicus*) were randomly divided into two groups ($n = 4$ per group), consisting of a treatment group received topical application 12% trembesi leaf extract gel and a control group treated with placebo gel. The 12% concentration was selected based on previous experimental evidence regarding the wound-healing potential of trembesi leaf extract gel.

Trembesi leaf extract (*Samanea saman* (Jacq.) Merr.) was obtained by maceration using 96% ethanol and formulated as a CMC-Na-based gel. The gel formulation was selected because it allows topical application and facilitates direct contact of the extract with the extraction socket. Following an adaptation period, the right mandibular incisors were extracted from anesthetized rats, and the respective gel preparations were topically applied twice daily for 7 days. The 7-day observation period was selected because it corresponds to the proliferative phase of wound healing, during which granulation tissue formation and angiogenesis are actively involved in tissue repair. On day 7, the extraction socket tissues were collected after euthanasia and

processed for histopathological examination using Hematoxylin–Eosin (HE) staining. Histological evaluation was performed in the granulation tissue of the extraction socket, and angiogenesis was assessed by counting identifiable blood capillaries in five different fields of view at 400× magnification. The 400× magnification was selected to facilitate morphological identification of small blood vessels. The data were analyzed using the Shapiro–Wilk normality test, Levene's test for homogeneity, followed by an independent t-test, with statistical significance set at $p < 0.05$. Ethical clearance was obtained under registration number 369/FKG/EP/II/2025.

RESULTS

This study was conducted to evaluate the effect of trembesi leaf extract gel (*Samanea saman* (Jacq.) Merr.) on angiogenesis during the wound healing process following tooth extraction. Histopathological examination using Hematoxylin–Eosin (HE) staining in both groups demonstrated angiogenesis features characterized by rounded structures with well-defined borders. The lumen wall consisted of a single layer of endothelial cells with purple-stained nuclei located at the cell periphery, while the lumen appeared empty (white-colored) and partially contained erythrocytes appearing as red granules.⁹ The histopathological features of angiogenesis in both the treatment and control groups are presented in Figure 1.

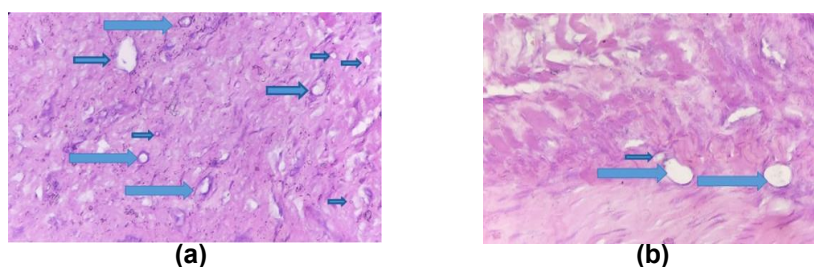


Figure 1. Histopathological appearance of angiogenesis in (a) the 12% trembesi leaf extract gel treatment group and (b) the CMC-Na gel control group.

Table 1. Mean Angiogenesis Results

Sample	Control	Treatment
1	0,2	1
2	0,8	1,4
3	0,4	1
4	0,2	0,8
Mean	0,40	1,05

Based on Table 1, the mean number of newly formed blood vessels was higher in the 12% trembesi leaf extract gel group (1.05) than in the CMC-Na control group (0.40). Individual observations showed some variation among samples in both groups. Although the number of newly formed blood vessels observed at 400× magnification was relatively low, the treatment group demonstrated a higher mean value than the control group.

DISCUSSION

The present study demonstrated that topical application of 12% trembesi leaf extract gel resulted in a higher mean number of newly formed blood vessels than the CMC-Na control group (1.05 vs. 0.40, respectively). The difference between groups was statistically significant ($p = 0.014$), indicating that treatment with 12% trembesi leaf extract gel was associated with increased histologically observed neovascularization during post-extraction wound healing.

The observed effect may be related to the phytochemical constituents of trembesi leaves. Previous phytochemical studies have identified phenolic compounds and flavonoids as important constituents of ethanolic trembesi leaf extract, with reported total phenolic and flavonoid contents of 2,544.62 mg GAE/100 g and 1,233.30 mg QE/100 g, respectively.¹⁰ These findings indicate that phenolic compounds were present at a higher total concentration than flavonoids in the reported extract. However, because the present study did not quantitatively determine individual phytochemical constituents, these values cannot be directly attributed to the 12% gel formulation used in this study, and no specific compound can be considered definitively responsible for the observed effect.

Among the reported phytochemical constituents, flavonoids may contribute to the

observed angiogenic response based on their previously described biological activities. Flavonoids may modulate angiogenesis through pathways involving HIF-1 and VEGF, while their antioxidant and anti-inflammatory activities may create a tissue environment that supports vascular formation.^{11,12} Other constituents may also contribute to the observed response. Tannins have antioxidant and astringent properties that may support tissue repair, while saponins have been reported to influence VEGF production and wound healing.^{13,14} Triterpenoids may additionally contribute through anti-inflammatory effects by modulating pro-inflammatory mediators such as TNF- α , IL-1 β , and IL-6.¹⁵

In the present study, the 12% trembesi leaf extract gel group showed a higher number of newly formed blood vessels than the control group, suggesting that the formulation may support neovascularization during post-extraction wound healing. Angiogenesis was assessed by counting identifiable blood capillaries in five microscopic fields at 400× magnification. However, the relatively low number of vessels observed, particularly in the control group, limits the extent to which these measurements can represent overall neovascularization throughout the extraction socket.

Further studies are warranted to strengthen these findings by quantifying the phytochemical constituents of the 12% trembesi leaf extract gel and evaluating specific angiogenic markers, such as VEGF and CD31. These approaches would help clarify which active compounds and molecular pathways contribute to the observed increase in blood vessel formation.

CONCLUSION

This study found that 12% trembesi leaf extract gel significantly increased angiogenesis during post-extraction wound healing, as indicated by a higher number of newly formed blood vessels compared with the placebo group ($p = 0.014$). These findings demonstrate that 12% trembesi leaf extract gel has an effect on angiogenesis in post-extraction wound healing.

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