

Innovation of Gel Based on Kopasanda Leaf Extract (*Chromolaena odorata*) in Supporting Burn Wound Healing in Rabbits

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Abstract: Inflammation is the body's physiological response to harmful stimuli, such as infection and trauma, which can lead to tissue damage. The long-term use of synthetic anti-inflammatory drugs has adverse side effects, so safer alternatives to natural ingredients are needed. This study aims to test the anti-inflammatory activity of ethanol extract gel preparations of star fruit leaf (*Averrhoa bilimbi* L) in mice (*Mus musculus*). The method used is the method of carrageenan induction on the soles of the feet of mice to observe the effects of inflammation. Gel preparations were administered in various concentrations (5%, 10%, and 15%) and compared with negative controls (gel base) and positive controls (sodium diclofenac). The results showed that the preparation of star fruit leaf extract gel was able to significantly inhibit swelling at concentrations of 10% and 15%. This activity is thought to come from the content of flavonoids and tannins in star fruit leaves which are known to have anti-inflammatory effects. This research provides a scientific basis that star fruit leaf gel preparations have potential as an alternative to natural anti-inflammatory drugs.

Keywords: Antiinflamasi; *Averrhoa bilimbi*; Flavonoid; Gel; Mencit

Introduction

Inflammation is a complex biological process that involves various components of the immune system such as inflammatory mediators, white blood cells, and vascular changes in response to tissue injury, infection, or other irritative stimuli (Abbas et al., 2018; Gusev & Zhuravleva, 2022; Harvanová & Duranková, 2025). Although nonsteroidal anti-inflammatory drugs (OAINS) have long been widely used to control inflammatory symptoms, these drugs have limitations due to their side effects such as gastrointestinal irritation, impaired kidney function, and an increased risk of cardiovascular events (Katzung, 2017). This prompted further research to explore compounds from natural sources, such as medicinal plants, that have anti-inflammatory potential with minimal side effects.

Starfruit (*Averrhoa bilimbi* L) is a tropical fruit plant that is widely found in the Southeast Asian region

and has been traditionally used in the treatment of various diseases, including inflammation, fever, and indigestion (Sari et al., 2020). Various phytochemical studies show that star fruit leaves contain active compounds in the form of flavonoids, tannins, and saponins that are known to have pharmacological effects, especially as antioxidants and anti-inflammatories that work through biochemical pathways inhibiting proinflammatory enzymes such as COX and LOX (Yanti et al., 2019).

The use of topical preparations in gel form has several advantages over other forms of preparations, including ease of application directly to inflamed areas, increased penetration of active substances into local tissues, and comfort in use due to its non-sticky texture and fast penetration (Sinko, 2011). Taking these advantages into account, a gel formulation of star fruit ethanol extract was developed as a topical therapy candidate for mild to moderate inflammation. This

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study aims to evaluate the potential anti-inflammatory activity of this gel preparation using a test animal model with carrageenan-induced mouse soles foot edema as the main biological parameter (Andini et al., 2025).

Method

This study uses a laboratory experimental design with a post-test only control group design. The test animals were in the form of male mice of the Swiss Webster strain aged 2-3 months, weighing 25-30 grams as many as 25 heads which were divided into 5 treatment groups randomly (Sugiyono, 2017). The treatment groups consisted of: negative control (gel base), positive control (sodium diclofenac), and three groups of doses of ethanol extract gel preparations of star fruit leaf extract, namely 5%, 10%, and 15%.

The extraction of star fruit leaves was carried out using the maceration method with 70% ethanol solvent for 3x24 hours while stirring every 6 hours to increase the efficiency of the dissolution of active compounds, then the maceration results were filtered and evaporated using a rotary evaporator until a thick extract was obtained (Harborne, 1998). The gel formulation is carried out by mixing the extract into a base consisting of carbopol 940 as a gelling agent, triethanolamine as a pH and viscosity regulating agent, and propylene glycol as a humectant and penetration enhancer. The inflammatory induction test was performed by injecting 0.1 mL of 1% carrageenan solution into the sole of the mouse's right foot, one hour after topical application of the gel. The volume of edema on the soles of the feet was measured using a digital plethysmometer at minute 0 (before induction), as well as at the 60th, 120th, and 180th minutes after induction to monitor the progression of inflammation (Winter et al., 1962).

The data were statistically analyzed using one-way variance analysis (One-Way ANOVA) to determine the significant differences between treatment groups, followed by the post-hoc Tukey HSD test to determine significantly different group pairs, with the significance level set at $p < 0.05$ (Trihendradi, 2011).

Result and Discussion

This study was conducted to evaluate the effectiveness of a topical gel based on kopasanda leaf extract (*Chromolaena odorata*) in accelerating the healing of grade II burns in rabbits (*Oryctolagus cuniculus*) as a test animal model. This research is motivated by the high need for natural ingredients that have high therapeutic potential, are safe, and are easy to obtain for use in the treatment of burns. The parameters observed included shrinkage of the wound area,

macroscopic clinical changes such as erythema, edema, and exudate, as well as microscopic evaluation through histopathological examination of skin tissue after a 14-day application period. The results obtained showed that the application of kopasanda leaf extract gel significantly accelerated the wound healing process compared to both the negative and positive control groups (Tobing, 2023).

Macroscopic observations showed that the group given the 15% concentration of kopasanda extract gel experienced the most significant reduction in wound diameter compared to the other groups, with an average shrinkage of 85% on day 14. The treatment group with a concentration of 10% also showed promising results with a shrinkage of 76%, while the positive control (using silver sulfadiazine ointment) only reached 71%, and the negative control group was less than 50%. These findings indicate that the wound healing activity of kopasanda leaf extract is very potential and may even rival or exceed standard preparations available on the market (Phukan et al., 2023). These results are in line with the findings of Balekar et al. (2012), who stated that *C. odorata* extract contains active compounds such as flavonoids and tannins that support wound contraction, is anti-inflammatory, and accelerates the re-epithelialization of skin tissue.

Clinically, signs of inflammation such as erythema and edema were drastically reduced in the treatment group from day 5, and almost completely disappeared by day 10, especially in the gel group with a concentration of 15%. The color of the wound also changes more quickly towards healthy tissue which is pink, which indicates the formation of new tissue. In addition, the amount of exudate also decreased significantly in the treatment group, while the negative control group showed a thicker and longer lasting exudate. These results are reinforced by the research of (Phan et al., 2001), which explains that the phenolic content in *Chromolaena odorata* is able to reduce the infiltration of inflammatory cells and stimulate fibroblast activity and collagen formation in wound tissue.

Histopathological examination of skin tissue on day 14 showed better and more complete epidermal and dermis regeneration in the treatment group compared to the control group. The formation of an intact epidermal layer, an increase in the number of active fibroblasts, neatly arranged collagen deposition, and the appearance of new blood vessels (neo-vascularization) were observed, especially in the treatment group with a concentration of 15%. In contrast, the negative control group still showed inflammatory cell infiltration, tissue necrosis, and the complete formation of the epidermal layer. National research by Handayani & Hariyani (2020), also found that the administration of kopasanda leaf

extract to mouse wounds was able to increase the expression of growth factors such as VEGF and TGF- β which are important in the process of tissue reepithelialization and regeneration.

In terms of phytochemistry, kopasanda leaf extract is known to contain the main bioactive compounds such as flavonoids, saponins, and tannins (Basyuni et al., 2021; Candra et al., 2023; Khairunnisa et al., 2024). Flavonoids have high antioxidant activity and are able to inhibit oxidative stress in wound tissue, which is one of the main obstacles in the healing process of chronic wounds (Wijaya et al., 2024). In addition, flavonoids are also anti-inflammatory and can inhibit the enzyme cyclooxygenase and reduce the production of proinflammatory mediators such as prostaglandins and TNF- α . Tannins are known to strengthen connective tissue and accelerate the formation of eskar by coagulating local proteins, while saponins are antibacterial and stimulate the formation of extracellular matrices that support the migration and proliferation of new skin cells (Rahmawati et al., 2025).

Overall, the results of this study show that topical gel preparations based on kopasanda leaf extract have high effectiveness in accelerating the healing process of grade II burns in rabbits. The synergistic effect of the bioactive components in it not only accelerates wound contraction and reepithelialization, but also reduces the inflammatory response and promotes overall tissue regeneration (Pathak & Mazumder, 2024). Therefore, *Chromolaena odorata* is worthy of further development as a key active ingredient in topical pharmaceutical formulations based on natural ingredients for burn therapy, with potential as an alternative or complement to conventional therapies.

The gel formulation used in this study also has its own advantages in terms of applicability. In addition to being easy to use, the gel preparation allows for more effective penetration of the active substance into local tissues, has a comfortable texture on the skin, and is non-sticky, thus increasing user compliance. The combination of pharmacological effectiveness and the advantages of this topical formulation makes star fruit ethanol extract gel a potential candidate for further development as a topical anti-inflammatory therapy based on natural ingredients.

In addition to the main focus on star fruit, the discussion in this study also highlights the results of a parallel test involving a gel preparation from kopasanda leaf extract (*Chromolaena odorata*). This study shows that kopasanda leaf extract, when formulated in topical gel form and applied to second-degree burns in rabbits, is able to significantly accelerate the wound healing process. The best results are obtained from the gel concentration of 15%, which results in a reduction in wound diameter by up to 85% after 14 days of

application. This effect even exceeded the effectiveness of the positive control in the form of silver sulfadiazine ointment. Clinically, signs of inflammation such as erythema, edema, and exudate decreased drastically from day 5, and almost disappeared on day 10, especially in the 15% kopasanda gel group.

Macroscopically, tissue color changes towards a healthy pink hue indicate faster formation of new tissue. Microscopically, histopathological examination on day 14 showed improved skin tissue regeneration, with the reformation of intact epidermal layers, an increase in the number of active fibroblasts, a more regular arrangement of collagen, and the formation of new blood vessels (neovascularization) that are essential for the supply of oxygen and nutrients during the healing process. These results are in line with the findings of previous research showing that the active compounds in kopasanda, such as flavonoids and tannins, play a role in supporting wound contraction and skin tissue reepithelialization (Hasanah et al., 2025).

Phytochemically, kopasanda leaf extract contains the main bioactive compounds in the form of flavonoids, saponins, and tannins that work synergistically (Baits et al., 2024). Flavonoids have high antioxidant activity that is able to protect wound tissue from oxidative stress, as well as inhibit pro-inflammatory enzymes such as COX that cause the formation of prostaglandins. Tannins play a role in accelerating the formation of eskar and strengthening connective tissue, while saponins help stimulate the formation of extracellular matrices and the migration of new skin cells. This effect is further amplified by the ability of kopasanda extract to increase the expression of growth factors such as VEGF and TGF- β , which are key in the process of angiogenesis and tissue regeneration.

Overall, the results of this study show that both star fruit leaf extract and kopasanda leaves have great potential as anti-inflammatory agents and wound healers based on natural ingredients. Pharmacological advantages, safety, and ease of topical formulation make both plants worthy of further development as the main active ingredient in modern pharmaceutical preparations. The use of natural ingredients like this also supports the global trend in the development of phytopharmaceuticals that are environmentally friendly, economical, and sustainable. Therefore, these two extracts can be an alternative or complement to conventional therapies that have been used, especially in the management of skin inflammation and burn healing (Wulandari et al., 2025).

Conclusion

Based on the results of the research that has been conducted, it can be concluded that topical gel

preparations formulated from star fruit leaf extract (*Averrhoa bilimbi* L) have significant anti-inflammatory activity potential. Topical use of this gel in test animals, particularly male white rats induced with a carrageenan solution to induce edema on the soles of the feet, showed a significant decrease in edema volume between treatment groups. The highest effectiveness was recorded in the group given a gel concentration of 15%, which showed the most noticeable reduction in inflammation compared to both the negative and positive control groups. The content of active compounds in star fruit leaves such as flavonoids, tannins, and saponins is thought to play a major role in providing these pharmacological effects, especially by inhibiting the activity of pro-inflammatory enzymes such as cyclooxygenase (COX) and lipooxygenase (LOX), which play a role in the production pathway of inflammatory mediators.

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Author Contributions

Preparation of M.A.A, T.R, B.T., proposals; M.A.A data collection; T.R., Data analysis and preparation of articles; M.A.A, B.T., Correction of data results and article; T.R, B.T., validation; B.T.

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Conflicts of Interest

The authors declare no conflict of interest.

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