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# Utilization of Corn Silk as Anti-Inflammatory and Wound Healing Ointment

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# ABSTRACT

Postoperative wound care generally uses synthetic drugs that can cause antibiotic resistance, so a safer and more effective alternative is needed. Corn hair (*Zea mays* L.) is an abundant waste and rich in phenolic compounds that have anti-inflammatory and wound healing activities. This study aims to develop and evaluate ointment from corn hair extract as an anti-inflammatory and wound-healing agent. Corn hair extract ointment concentrations of 5, 7, and 9% were tested *in vivo* using a cut wound model in mice (*Mus musculus*) to determine the wound healing process. In addition, hematology tests and histopathology tests of mice were conducted to see the healing response of corn hair ointment. Data were analyzed using One Way ANOVA with the IBM SPSS® 25 program. The test results showed that corn hair extract ointment with a concentration of 7% has great potential as an effective and safe natural alternative for postoperative wound care, with significant anti-inflammatory and wound healing abilities.

Key words: Anti-inflammatory, Corn Silk, Ointment, Wound Healing.

# **INTRODUCTION**

Based on data from Hasanuddin University Teaching Animal Hospital, 50% of health cases are treated with surgery. Optimal postoperative care is essential to reduce the risk of infection and accelerate wound healing. Postoperative wounds can lead to infections that increase morbidity, mortality and treatment costs, and negatively impact the emotional state of the animal owner (Ruperez et al. 2019). Therefore, controlling postoperative wound infection is very important. This is because infection can inhibit the inflammatory process and hinder tissue repair.

Inflammation is one of the most important processes required in the defense of animal cells against physical trauma, damaging chemicals or microbiological agents. Inflammation is an attempt to inactivate or destroy foreign organisms, eliminate irritants. Signs of inflammation are rubor (redness), calor (heat), dolor (pain), and tumor (swelling) (Octavian 2022). In general, restoration of homeostasis is achieved as a result of these complex biological responses. However, if inflammatory mediators are released and harmful signal transduction pathways are activated, inflammation will persist, and a mild but longterm proinflammatory state may develop. A variety of chronic health conditions and disorders, such as diabetes, obesity, cancer, and cardiovascular disease, are associated with low levels of inflammation (Nunes et al. 2020). The wound healing process consists of four phases, namely hemostasis, inflammation, proliferation, and remodeling phases (Fitrianti et al. 2023). Hemostasis occurs immediately to stop bleeding with blood clots and platelets. This process lasts minutes to hours. Inflammation is the phase of wound cleansing from bacteria and dead cells (0-3 days) characterized by redness, swelling, heat, and pain. Proliferation is the phase of new tissue formation with collagen (3-20 days). New blood vessels and skin cells are formed. Remodeling or tissue refinement phase, strengthening new tissue and scarring begins to fade (21 days - 1 year) (Hadi et al. 2021).

Current wound treatment generally uses chemical synthetic drugs that have anti-inflammatory and antibiotic activity (Rahimah et al. 2023). The skin, which is the largest organ in the body, functions as an important protective layer in various body processes, such as maintaining moisture, regulating temperature, the immune system, responding to external stimuli, and helping to synthesize vitamin D. In addition, the skin also acts as a physical barrier that protects the body from ultraviolet rays, harmful chemicals, and pathogens. Due to frequent exposure to various external factors, the skin is susceptible

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Myrtus communis leaves are also known to have

antimicrobial, anti-inflammatory and wound healing

properties. Studies showed that Myrtus communis, rich in

tannins, flavonoids, and vitamin C, which increase antioxidant defense, eliminates the final product of lipid

peroxidation (MDA) and NO free radicals. Therefore, one of

the reasons for the antioxidant properties of Myrtus

communis in the present study may be associated with these

compounds (Jafari et al. 2024). Ajuga integrifolia leaves are

a great substitute for anti-oxidant, anti-bacterial, and

antidiabetic medications, according to the results of the

observed studies. This study provides pharmacological

evidence in favour of the traditional use of Aiuga integrifolia

in the management and treatment of a number of human

diseases and as an anti-inflammatory agent. Moreover, it has

been declared that methanol extract is the most effective.

According to our study, Ajuga integrifolia is a valuable

natural source of antioxidants and can lessen the impact of

generated ROS in the cell during specific illnesses. The study

reports beneficial effects may be associated with the presence

of significant bioactive metabolites, specifically the favonoids, alkaloids, and phenols (Singh et al. 2024). In

addition, the plant commonly used as wound healing is corn

(Zea mays L). The part of the plant that is often used is corn hair, corn hair is a waste from the food industry. Corn hair

is often used as a traditional medicine because it has many

useful ingredients. Some of the contents possessed by corn

hair are alkaloids, flavonoids, phenolics, steroids, tannins, and saponins (Fajrina et al. 2021). In addition,

flavonoids, alkaloids, saponins, and steroids contained

in corn hair can be antimicrobial agents that help in the

The study by Putri et al. (2021) showed that corn hair

extract was able to accelerate wound healing in

experimental animal models in the form of gel preparations

(Putri et al. 2021). However, gel preparations have several

disadvantages, such as easy loss and risk of irritation

(Astriana and Satria 2019). Ointments, on the other hand,

provide a number of benefits, including the ability to

protect the skin from mechanical, thermal, and chemical

irritation, to be stable during use and storage, to be easy to

wear, and to spread uniformly (Davis et al. 2022).

wound healing process in animals (Rawung et al. 2020).

to injury that can damage its structure and disrupt its function. When an injury occurs, the body activates the wound healing process, which is a series of complex biological steps to restore tissue and maintain local balance. This process takes place in three main phases, namely inflammation, proliferative, and remodeling, which overlap each other. Each requires a highly coordinated communication phase between various types of cells such as keratinocytes, fibroblasts, and endothelial cells, which produce cytokines, growth factors, and collagen. In this process, various stages occur, starting from inflammation. formation of granulation tissue. narrowing of the wound, formation of collagen, closing the wound with epithelium, to the formation of scar tissue. If all these stages go well, the wound can heal perfectly (Cordero et al. 2023). However, irrational use of antibiotics can lead to antibiotic resistance (Rahimah et al. 2023). Resistance is immunity to antibiotics where the ability of bacteria to withstand the effects of drugs, as a result the bacteria do not die after administering antibiotics and the function of the drug does not provide therapeutic effects. Antibiotic resistance to bacteria can cause fatal therapeutic failure to death (Mulatsari et al. 2023). Antimicrobial resistance (AMR) is an inevitable phenomenon because microbes develop genetic mutations to mitigate its lethal effect (Subramaniam & Girish 2020). AMR refers to bacteria and other microorganisms' capacity to withstand the impact of an antibiotic to which they were previously susceptible, allowing germs to survive and thrive. Microorganisms, such as bacteria are living organisms that adapt over time. Their main objective is to replicate, survive, and spread as rapidly as possible. As a result, microbes adjust to their surroundings and evolve in ways that guarantee their continued existence. If something stops their ability to grow, such as an antibiotic, genetic modifications may arise, making the bacteria immune to the medication and allowing them to survive (Uddin et al. 2021). It is the natural process of bacteria to develop drug resistance. However, several elements remain currently at stake in the multifaceted etiology of antibiotic resistance. This involves antibiotic overuse and abuse, inexact diagnosis and improper antibiotic prescribing, patient sensitivity loss and self-medication, bad healthcare environments, poor personal hygiene, and widespread agricultural use (Chokshi et al. 2019). One of the reasons behind antibiotic resistance is selective pressure can be defined as environmental conditions that allow the survival and proliferation of organisms with new mutations or newly developed characteristics. When treated with antimicrobials, the microbes will be killed or if they have resistance genes, they will survive. These survivors will reproduce, and the newly developed resistant microbes will quickly take over the microbial population as the dominant form (Zhao et al. 2019). Therefore, there is a need for safer and more effective alternatives for postoperative wound care.

Innovation in the use of natural ingredients for wound healing is growing. One of the traditional medicinal plants that has been widely utilized is ambarella fruit leaves (Spondias dulcis Frost). This plant has been scientifically proven to have anti-inflammatory properties because it contains secondary metabolite compounds, flavonoids, which have anti-inflammatory properties (Hasibuan 2021).

Innovation of corn hair extract ointment can improve the safety profile and higher efficacy in accelerating the wound healing process and anti-inflammatory agents. Therefore, the renewal of the previous method can be done by making ointment from corn hair extract formulated in ointment MATERIALS AND METHODS Ethical approval The test protocol has been declared ethically feasible by the Research Ethics Committee of Hasanuddin University with Protocol Number UH24040258. **Tools and materials** The tools used were microtome, hair clippers, ruler, knife, gloves, syringe, EDTA tube, animal scales, and tissue cassette. The materials used were distilled water, absolute alcohol, 70% alcohol, 80% alcohol, 90% alcohol, aluminum foil, ether, 10% formalin, mice, methanol, sodium chloride (NaCl) 0.9%, hematoxylin staining and

form.

eosin staining (HE), Bioplacenton® ointment, corn hair ointment concentrations of 5, 7, 9% and xylol.

# Research implementation procedure *In vivo* test (Wound healing activity)

Male and female White Mice (*Mus musculus*) (20-35g) were obtained from the Biofarmasetics Laboratory, Faculty of Pharmacy, Hasanuddin University. The test animals were acclimatized for 7 days in proper cage conditions (Ifana et al. 2024). Mice were given standard pellets and water during the experiment (Tamuntuan et al. 2021). The number of animals used in each group was 8.

# **Preparation for testing**

In this *in vivo* test, corn hair extract ointment preparations were prepared at concentrations of 5, 7 and 9%. The prepared test preparations were applied topically to the wound immediately after each wound was made with a scalpel. In the negative control group/- the test animals were not treated, while the comparison drug group (positive control/+) was treated with Bioplacenton® ointment.

#### Incision wound model

The back area of all test animals was shaved and cleaned with 70% alcohol. Animals were locally anesthetized using ether. A 1cm long incision was made with a sterile scalpel and the wound depth was 0.25cm on the dorsal side. The test animals were divided into five groups: a negative control group, a positive control group (administered Bioplacenton® ointment) and groups administered the test ointment preparations at concentrations of 5, 7 and 9% in each group. The wound of each test animal was applied topically twice a day for 14 days. Evaluation of wound healing was done by measuring wound length, histopathology test and hematology test on days 7 and 14. Wound incisions were measured using a caliper, and the longitudinal incision wound model was used to assess wound healing activity in vivo to determine wound healing (Tamuntuan et al. 2021).

#### Hematology test

Hematology tests were performed by taking 1mL of mice blood on days 7 and 14 and then stored in EDTA tubes. Blood samples were tested using the Hematology Analyzer method at the Maros Veterinary Center (BBVet) (Fatimah et al. 2022).

### Histopathology test

Histopathology analysis was performed starting from fixation, dehydration, impregnation, cutting, staining, and microscopic examination (Tandi et al. 2019). Wound healing assessment was assessed using histopathological scoring on several key parameters, namely reepithelialization, neovascularization, granulation tissue, granulation maturation, presence of inflammatory cells, and ulceration according to Table 1 (Yudhantoro et al. 2019). Histopathological scoring was based on criteria listed in Table 1.

# **RESULTS AND DISCUSSION**

### Statistical analysis

The test profile data of corn hair extract and so on were collected from each test then tabulated and analyzed statistically. Data were analyzed using One Way ANOVA with IBM SPSS® 25 program using T-test at  $\alpha$ =0.05.

#### In vivo test (Wound healing activity)

Wound healing was carried out through three main phases. The first phase was the inflammatory phase which begins with the hemostasis response to stop bleeding. This was followed by the removal of dead tissue and inhibition of colonization and infection from pathogenic microbes by neutrophils, lymphocytes and macrophages. The second phase was proliferation where in this phase blood vessel formation occurs, extracellular matrix formation by fibroblasts stimulated by various growth factors and basement membrane formation by kertinocytes and collagen. The last phase was remodeling which is the process of collagen synthesis and degradation that results in scarring of the wound area (Qamarani and Aryani 2023).

On day 7, the wounds began to shrink with the control condition still showing significant redness, indicating that inflammation was still active. Wounds in animals treated with Bioplacenton® also decreased in size with slightly more redness than controls, indicating ongoing inflammation. The use of 5, 7 and 9% concentrations of ointment showed smaller wounds and signs of the beginning of the proliferation phase, especially in the 5 and 7% concentrations which showed a drier central area of the wound and less redness, indicating that the inflammatory phase was ending and the proliferation of new tissue had begun.

On day 14, it was seen that the wounds in the control animals had shrunk and were pink in color, indicating that new tissue had begun to form but was still healing. Wounds in animals treated with Bioplacenton® were smaller and the skin color was closer to normal, indicating a good proliferation process. The use of 5 and 7% concentrations of ingredients showed the best results with almost completely closed wounds and almost normal skin color, indicating efficient healing. Meanwhile, wounds with 9%

**Table 1:** Wound healing assessment histopathology score (Yudhantoro et al. 2019)

Scoring Criteria	Score				
	0	1	2	3	
Reepithelialization	None	Partial	Complete but immature and thin	Complete and mature	
Neovascularization	Absent	Up to 5/HMF	6-10/HMF	>10/HMF	
Amount of granulation tissue	None	Little	Moderate	Abundant	
Maturation of granulation tissue	Immature	Mild maturation	Moderate maturation	Fully mature	
Inflammatory cells	None	Few	Moderate	Abundant	
Ulceration	Wide and deep, abscess	Wide wounds	None/very small	None	

concentration were also almost completely closed but still showed slight redness, indicating a good healing process but slightly slower than the 5 and 7% concentrations. As shown in Fig. 1, the wound healing progression was recorded. The average wound lengths on days 7 and 14 are presented in Fig. 2.



Fig. 1: Wound healing process on days 0, 7, and 14.

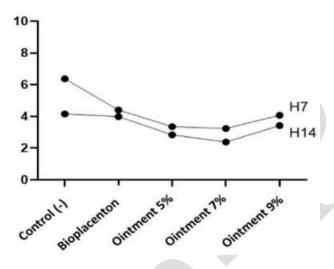


Fig. 2: Average wound length of mice on days 7 and 14.

Based on wound length, ointment with 7% concentration is the best preparation with the smallest average wound length compared to other treatment groups. There was no significant difference between wound length on day 7 and 14 (Sig. (2-tailed) >0.05). So, from this observation, it can be seen that ointment with 7% showed the best results on day 14.

# Hematology test

The leukocyte levels are illustrated in Fig. 3. The inflammatory response allows blood elements, leukocytes and chemical mediators to reach the inflammatory area. Leukocytes are the first cells to arrive at the injury site to fight infection and clear dead tissue. White blood cells circulate in the blood and trigger inflammatory and cellular responses to injury or pathogens (Fatimah et al. 2022). The total leukocyte count in mice is normally between 6-15  $x10^3$ /mm<sup>3</sup> (Dwitiyanti et al. 2022). The test results show that ointment with a concentration of 7% can reduce leukocyte levels in the blood of experimental animals so

that it can be a good anti-inflammatory ointment. Based on the results of statistical analysis, there was no significant difference between the number of leukocytes on days 7 and 14 (Sig. (2-tailed) >0.05).

According to the study of Quijada et al. (2022), concentrations higher than 7% begin to show toxic or adverse effects on mammalian cells or tissues, which can reduce wound healing ability or damage immune cells. Hematology tests may show that a 9% concentration affects blood parameters in leukocyte counts indicating a higher inflammatory response or oxidative stress, suggesting that optimal concentrations of plant extracts may avoid these toxicity effects and provide maximum benefit to the treatment (Quijada et al. 2022).

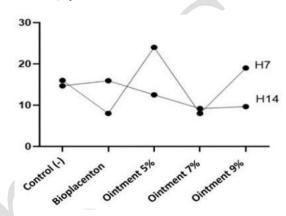
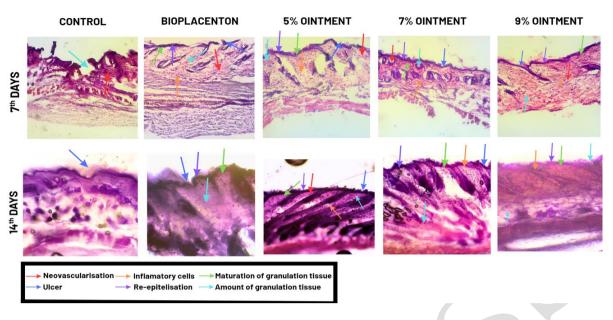


Fig. 3: Average white blood cells of mice on days 7 and 14.

### Histopathology test

Histological healing components are visualized in Fig. The wound healing process was assessed using 4 histopathological scoring on several key parameters re-epithelialization, neovascularization, namely granulation tissue, granulation maturation, presence of inflammatory cells, and ulceration. The first stage is reepithelialization, where new epithelial cells cover the wound surface. Then neovascularization with the formation of new blood vessels that are important for the supply of oxygen and nutrients to the damaged tissue. In addition, the formation and maturation of granulation tissue, which provides the structural basis for healing, is expected to develop from nothing. The presence of inflammatory cells, which indicate the immune response to infection and injury, is expected to decrease from a high number. Lastly, ulcerations or open wounds should be significantly reduced in extent and depth (Yudhantoro et al. 2019).

The histopathology test results for the 7% ointment treatment showed the best wound healing process compared to the other treatments. Re-epithelialization appeared to be complete, with mature new epithelium covering the entire wound. Neovascularization peaked at more than 10 new blood vessels per HMF (High Magnification Field), ensuring optimal blood supply to the wound area. The formation of abundant granulation tissue indicates high activity in new tissue formation. Granulation tissue maturation has also reached an advanced stage, and the number of inflammatory cells is significantly reduced. Ulcerations are small, indicating that the wound is almost completely closed and the healing process is on its way to full recovery.



**Fig. 4:** Histopathology results of mice skin on days 7 and 14 post-wounding. The colored arrows indicate different components of the healing process, with purple indicating re-epithelialization, red indicating neovascularization, light blue indicating granulation tissue formation, green indicating granulation tissue maturation, orange indicating inflammatory cells, and dark blue indicating ulceration.

#### Conclusion

This research shows that the use of corn hair extract ointment with 7% concentration has the best antiinflammatory and wound healing effect compared to other concentrations and the positive control Bioplacenton®. The wound length test on day 14 showed optimal results with 7% ointment, where the wound was almost completely closed with skin color close to normal, indicating an efficient healing process. Histopathology results also confirmed that 7% ointment gave the best results in terms of re-epithelialization, neovascularization and granulation tissue maturation. Decreased inflammatory cell counts and reduced ulceration further supported these findings, suggesting that 7% corn hair extract ointment has significant potential as an effective anti-inflammatory and wound-healing agent.

Thus, the objective of this research to evaluate the effectiveness of various concentrations of corn hair extract ointment in wound healing was achieved, and the 7% concentration was shown to provide the best healing results. These findings can serve as a basis for the development of more effective wound-healing ointment products in the future.

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**Conflict of Interest:** The authors declare that there is no conflict of interest regarding this research.

Author's Contribution: Rini Amriani acted as the main supervisor, was responsible as the principal investigator, provided comprehensive research direction, guided the preparation of the manuscript, ensured scientific accuracy, and gave constructive feedback throughout the research process. Aisyah Susiana was responsible for the implementation of the entire research, playing an important role in the preparation of the manuscript. Iin Anisa Azzahra Irfan conducted research activities and assisted in collecting related literature and preparing the background section of the research. Hanif Semar Gemilang carried out research activities that focused on histopathology tests and assisted in collecting related literature and preparing the background section of the research. Zulva Putri Anggita Miolo designed the experiments, ensured that all research steps were in accordance with scientific standards, and played a role in the interpretation of results and drafting of conclusions. Miftah Riska Awaliyah contributed to the drafting and finalization of the manuscript.

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