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Anti-Inflammatory Effects of Cayenne Pepper Extract on Wound Healing

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Abstract

Inflammation is the body's natural biological response to tissue injury, playing a crucial role in the wound healing process. However, excessive inflammation can prolong the initial phase of healing, thereby inhibiting tissue repair. One natural alternative known for its anti-inflammatory effects is cayenne pepper extract (*Capsicum frutescens L*). Cayenne pepper contains the main bioactive compounds, namely vitamin C and capsaicin. Vitamin C acts as an antioxidant, supports collagen synthesis, and has anti-inflammatory properties. Meanwhile, capsaicin functions as an antimicrobial, anti-inflammatory, and stimulates fibroblast activity and angiogenesis. This combination of active substances creates an environment conducive to accelerating the transition from the inflammatory to the proliferative phase, thereby promoting faster wound healing. This study aims to determine the transition from the inflammatory to the proliferative phase, thereby promoting faster wound healing. Methods: A pretest–posttest control group design with five treatment groups: negative control group (NaCl 0.9%), positive control group (povidone-iodine 10%), and three treatment groups with 5%, 10%, and 15% concentrations of cayenne pepper extract ointment. Results showed that cayenne pepper extract significantly reduced erythema, suppressed edema, decreased wound fluid production, accelerated granulation tissue formation, and hastened wound length reduction, providing a superior effect in wound healing compared to the control groups. Thus, cayenne pepper extract has the potential to be an effective natural topical agent in accelerating wound healing through anti-inflammatory, antioxidant, and antimicrobial mechanisms. Conclusion: The 15% concentration of cayenne pepper extract was found to be the most effective and optimal dose for accelerating wound healing.

Keywords: Inflammation; *Capsicum frutescens L*; Cayenne pepper; Wound healing; Capsaicin; Vitamin C.

1. Introduction

Cayenne pepper (*Capsicum frutescens L.*) is a horticultural plant known not only as a kitchen spice butalso for its various bioactive compounds with medical potential. The main compounds contained in cayenne pepper include capsaicin and vitamin C, which are known to have anti-inflammatory effects, so they can help speed up wound healing. Capsaicin works by suppressing the production of inflammatory mediators and reducing the infiltration of inflammatory cells in the wound area, while vitamin C plays an important role in collagen synthesis and acts as an antioxidant, protecting cells from oxidative damage. (1, 2)

In addition, cayenne pepper also contains various other components, such as flavonoids, saponins, alkaloids, and terpenoids. Each of these has pharmacological activity, including antibacterial, antioxidant, and immune-system support. The antibacterial activity of these compounds can inhibit the growth of pathogenic microbes in the wound area,

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thereby preventing infection and speeding up the healing process. The antioxidant properties of vitamin C and flavonoids also play a role in neutralizing free radicals that can worsen the condition of wound tissue. Thus, the combination of the anti-inflammatory, antibacterial, and antioxidant effects of cayenne pepper creates an environment conducive to tissue regeneration. (3, 4)

The use of chemical antiseptics, such as povidone-iodine, is indeed widely applied in daily wound care practice. However, its use is inseparable from the risk of skin irritation and potential cellular toxicity. This condition highlights the need for alternative treatments that are safer, more effective, and more readily accessible from natural sources. Herbal plants, such as cayenne pepper, are a promising candidate due to their wide availability, relatively low cost, and bioactive content that supports the wound healing process. (5)

Based on this description, this research is important to be carried out as an effort to find alternative natural treatments that can support the tissue regeneration process while minimizing the side effects of using chemical drugs.

2. Materials and methods

2.1. Material

The main ingredients are cayenne pepper (*Capsicum frutescens L*), 96% ethanol, Adeps lanae, CMC, petroleum jelly, povidone iodine, NaCl 0.9%, and Wistar rats. Equipment includes rotary evaporators, blenders, ovens, sterile surgical instruments, and wound care equipment.

2.1.1. Preparation of Extract and Formulation of Cayenne Pepper Ointment (Capsicum frutescens L)

A total of 500 g of cayenne pepper was extracted by the 96% ethanol maceration method for 3 × 24 hours. The filtrate was evaporated with a rotary evaporator at a temperature of 40–50 °C until a thick extract was obtained. The ointment was formulated in concentrations of 5%, 10%, and 15% using the melting method, then mixed until homogeneous. (6)

2.1.2. Procedure for Manufacturing and Treating Wounds in Wistar Rats (Rattus Norvegicus)

A 2-cm-long incision with a depth of 0.5 cm was made on the back of each rat using a sterile scalpel. The wounds were then treated according to the group: cayenne pepper extract ointment (5%, 10%, 15%), povidone iodine 10%, or NaCl 0.9%. (6)

3. Result

The results of the examination of the healing phase of the incision wound include erythema around the wound, edema around the wound, fluid produced by the wound, granulated tissue, and wound length.

3.1. Erythema Observation Around the Wound

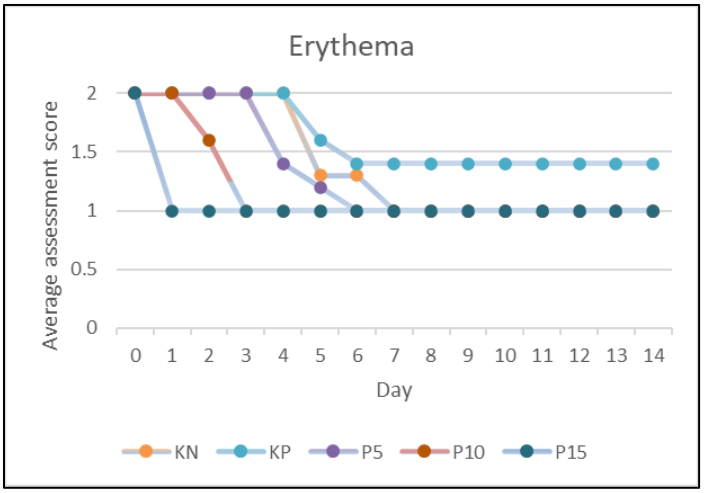

Figure 1 Erythema around the wound

Based on the results of erythema observation from day 1 to day 14, all groups showed erythema after the incision wound was made. In the P15 group, a decrease in erythema was seen from the first day, with the absence of erythema signs. The P10 group began to show a decrease on day 2 and reached a stable condition without erythema on day 3. In the P5 group, the decrease occurred on day 4 and was stable without erythema until day 6. The KN and KP groups began to decrease on day 5, but KP did not show improvement until the end of observation, while KN showed no complete erythema (score 1) on day 7.

3.2. Observation of edema around the wound

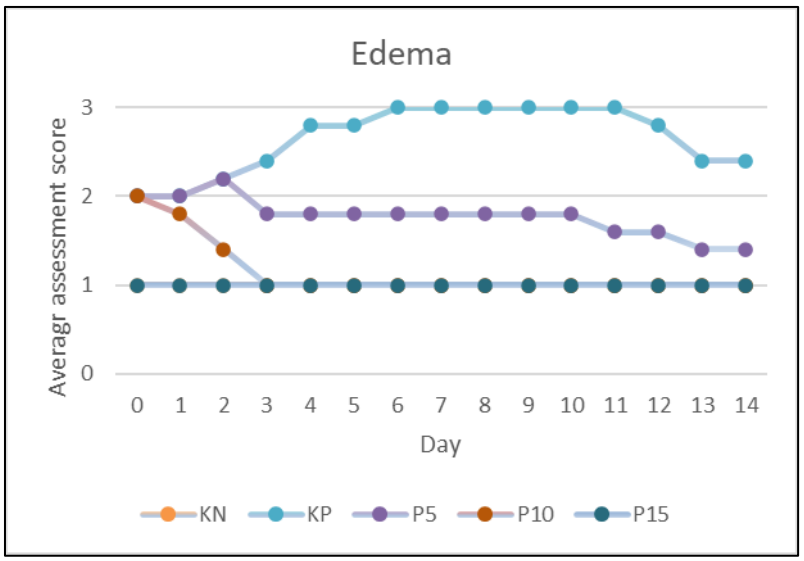

Figure 2 Observation of Edema in the Inflammatory Phase

Based on the results of edema observation from day 1 to day 14, the P15 group showed no signs of edema from the first day to the end of observation. In the P10 group, edema was still visible on the first day, but began to decline on day 2 and disappeared completely on day 3. The P5 group showed a decrease on day 3 and reached a milder state on day 11, although it was not entirely edema-free until the end of observation. In the KN group, no edema was found from the beginning to the end of observation. In contrast, the KP group experienced increased edema on day 2 to day 4 with the highest mean of around (score 3), and showed no significant improvement until the end of observation.

3.3. Observation of Fluid Produced by Wounds

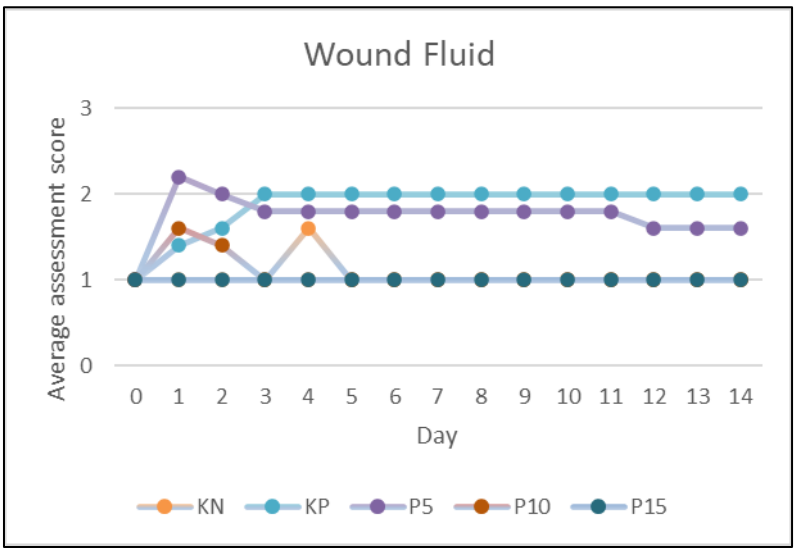

Figure 3 Results of Observation of Wound Fluid in the Inflammatory Phase

Based on the results of the observation of wound fluid from day 1 to day 14, the P15 group showed no fluid from the first day to the end of observation. In the P10 group, the wound fluid was still visible on the first day, but began to decline on day 2 and disappeared completely on day 3. The P5 group showed a decrease from day 3 and reached a milder condition on day 12, although it was not completely dry by the end of observation. In the KN group, the wound remained dry from the beginning, although on day 4 of observation, there was a slight fluctuation. In contrast, the KP group showed an increase in wound fluid from day 1 and did not experience significant improvement until the end of observation.

3.4. Observation of Granulation Tissue

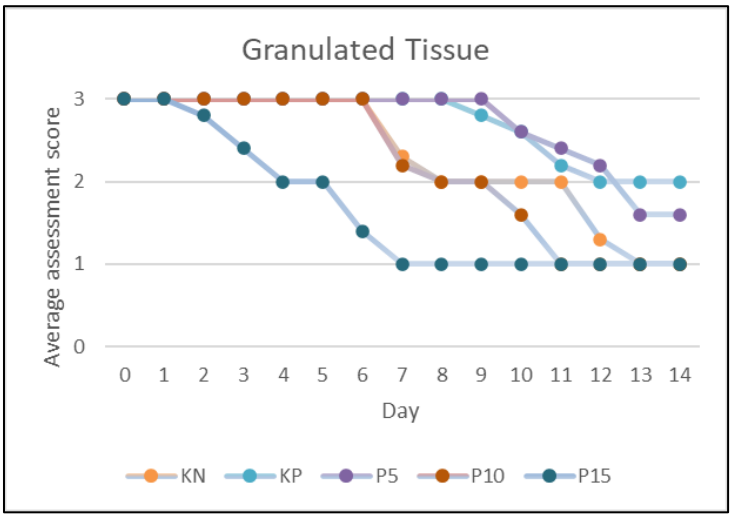

Figure 4 Observation of Granulated Tissue in the Proliferation Phase

Based on the results of the observation of granulated tissue from day 1 to day 14, the P15 group showed the fastest granulation formation, characterized by a decrease in score from day 2 and achieving full granulation on day 7 to the end of observation. In the P10 group, granulation began to appear on day 7 and reached full condition on day 11. The P5 group showed a decrease in granulation score on day 10 and only approached full granulation on day 13, although it was not entirely complete by the end of observation. In the KN group, the formation of partial granulation was seen from day 7 and reached the condition of thorough granulation formation on day 13 until the end of observation. In contrast, the KP group did not show meaningful granulation formation, with scores remaining high from baseline until only partially decreasing on days 12–14 and not reaching full granulation until the end of observation.

3.5. Long Wound Observation

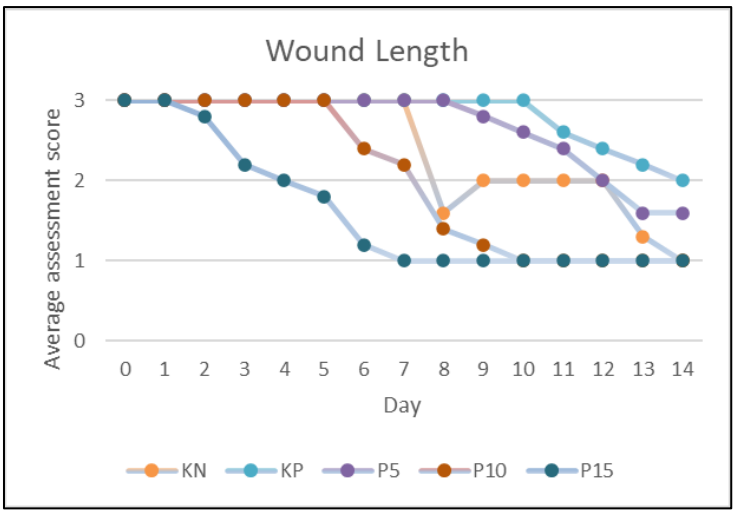

Figure 5 Results of Observation of Wound Length in the Proliferation Phase

Based on the results of the observation of wound length from day 1 to day 14, the P15 group showed the fastest healing, with a decrease in score from day 2 until the wound closed completely (score 1) on day 7 and remained stable until the end of observation. In the P10 group, a decrease began to be seen on day 6, and the lesion closed completely on day 10 to the end of observation (score 1). The P5 group healed more slowly, with (score 3) until day 8, then gradually decreased from day 9, but by the end of observation, the wound had not completely closed. In the KN group, the length of the wound began to decrease on day 8, and only completely closed on day 14 (score 1). In contrast, the KP group did not show any meaningful improvement, with (score 3) until day 10 and only decreased slowly to (score 2) on day 14, so the wound did not close completely until the end of observation.

Table 1 Kruskal-Wallis Test Results

Variabel		P value
1	Erythema around the wound	0.000
2	Edema around the wound	0.000
3	Fluid produced by the wound	0.000
4	Granulation tissue	0.000
5	Length of the wound	0.000

Table 2 Dunn's Post Hoc Test Results

Variabel		**Group**	**P value**
1	Erythema around the wound	15% treatment - positive control	0.000
		10% treatment - positive control	0.000
		5% treatment - negative control	0.000
		Negative control - positive control	0.000
2	Edema around the wound	15% treatment - negative control	0.000
		15% treatment - positive control	0.000
		10% treatment - negative control	0.001
		10% treatment - positive control	0.000
3	Fluid produced by the wound	15% treatment - positive control	0.000
		10% treatment - positive control	0.003
		5% treatment - negative control	0.006
		Negative control - positive control	0.003
4	Granulation tissue	15% treatment - negative control	0.000
		15% treatment - positive control	0.000
		10% treatment - positive control	0.000
		5% treatment - negative control	0.004
		Negative control - positive control	0.006
5	Length of the wound	15% treatment - negative control	0.000
		15% treatment - positive control	0.000
		10% treatment - negative control	0.001
		10% treatment - positive control	0.000
		Negative control - positive control	0.025

4. Discussion

4.1. Erythema around the wound

When tissue is injured, damaged blood vessels in the wound area cause bleeding. As an initial response, the body immediately attempts to stop bleeding by activating intrinsic and extrinsic coagulation pathways. This process triggers platelet clots and the formation of blood clots through vasoconstriction, which refers to the narrowing of injured blood vessels. During this platelet aggregation process, vasoconstriction of blood vessels occurs for approximately 5 to 10 minutes. This condition is then responded to by the body by vasodilation or dilation of blood vessels so that the wound area will appear erythema or red and warm. (7, 8)

Overall, the 15% (P15) treatment group was shown to be the most effective in inhibiting or preventing the onset of erythema from day one, followed by the 10% treatment group (P10), which showed improvement from day two. The 5% (P5) treatment showed slower effectiveness, whereas the erythema negative control group (KN) began to decrease on day five, and the positive control (KP) showed no meaningful improvement until the end of observation. From the results of the comparison of erythema in the five sample groups in this study, it was shown that wound treatment with cayenne pepper extract (*Capsicum frutescens L*) had a better effect on wound healing than the control group. The use of 10% povidone-iodine is less effective in lowering the inflammatory response. The concentration of 15% cayenne pepper extract provides the optimal anti-inflammatory effect in suppressing erythema compared to other groups.

The reduction in erythema occurred more rapidly in the treatment group because cayenne peppers contain vitamin C, which acts as an antioxidant with immune-boosting properties. (9). In addition, vitamin C has anti-inflammatory properties, which play a role in reducing inflammation in the body and is very beneficial in speeding up the wound healing process. (10). Chili peppers also contain capsaicin which is known to have antimicrobial properties, so that bacterial cells are unable to survive and will die over time. (11, 12). In addition, capsaicin also has anti-inflammatory properties that can stimulate macrophage cells to produce pro-inflammatory cytokines, such as TNF-α and IL-1. These cytokines play a role in activating neutrophils, which are responsible for cleaning dirt and bacteria around the wound. (13)

4.2. Edema around the wound

When the body's tissues are injured, there will be the release of various chemicals from within the cell, such as histamine and bradykinin. Histamine plays a role in increasing vascular capillary permeability so that plasma fluids and proteins can move from intravascular to intracellular, which then triggers the formation of edema. (14)

Overall, it was found that treatment with cayenne pepper extract (*Capsicum frutescens L*) concentration of 15% was most effective in preventing and overcoming edema during the inflammatory phase, even from the first day. It was followed by a 10% treatment group that showed good effectiveness. The 5% group showed moderate effects and a slower recovery. In contrast, the positive control group showed a severe and persistent inflammatory response.

From the results of the edema comparison in this study, it was found that the negative control group, namely a 0.9% NaCl solution, did not show any edema during observation due to short-lived edema. According to (15) NaCl 0.9% solution is an isotonic liquid that is safe for the body, does not irritate, helps maintain moisture around the wound, protects granulated tissues from dryness, and supports the optimal wound healing process.

The decrease in edema occurred faster in the treatment group because the capsaicin content in cayenne pepper (*Capsicum frutescens L*) can suppress the production of pro-inflammatory cytokines such as IL-6 and TNF-α, which play an important role in triggering acute inflammation. In addition, capsaicin can also reduce the number of neutrophils that migrate to the wound area. Neutrophils are the first immune cells to respond to injury and play a role in the formation of edema. By inhibiting neutrophil activity, capsaicin helps reduce the occurrence of edema in the inflammatory phase, thereby minimizing secondary tissue damage and accelerating the repair process towards the proliferation phase. (16, 17)

4.3. Fluid produced by the wound

The inflammatory phase generally lasts for the first few days after the occurrence of the injury. The appearance of light to moderate amounts of exudate in the first 2 to 3 days is a physiological response where at this stage, vasodilation and increased capillary permeability occur which triggers the release of plasma fluid (exudate), which plays a role in cleaning the wound area and maintaining a moist environmental microcondition that supports the healing process. (18).

Overall, the 15% treatment group (P15) showed the most consistent and effective results in preventing the discharge of wound fluid during the inflammatory phase. The protective effect is visible from day one. The 10% treatment group (P10) also gave good results with gradual improvement and total recovery from day three. Meanwhile, the 5% treatment group (P5) showed a decrease in exudate from day three, but it never completely dried up until the end of observation. The negative control group (NaCl 0.9%) remained relatively stable with only a slight increase in mild exudate at several days, while the positive control group (povidone-iodine 10%) produced a larger amount of wound fluid and lasted until the end of observation with no meaningful improvement. These findings show that 15% cayenne pepper extract is the most effective treatment in suppressing inflammation of wound fluid.

The 5% treatment group (P5) and the positive control group (KP) showed an unstable inflammatory response and tended to be severe until the last day of observation of the inflammatory phase. According to (18) If exudation settles after the initial phase, especially with excessive volume, purulent color, unpleasant odor, or persistence for more than 72 hours, this can be an indicator of inflammation or prolonged infection. This reflects wounds trapped in the inflammatory phase, which is characterized by increased cellular activity and sustained vascular permeability. Continued exudation not only hinders the healing process, but also has the potential to worsen the condition of the tissues and become a sign of chronic wound formation, which requires further medical evaluation and treatment. (19)

4.4. Granulation tissue

The formation of granulated tissue is an important part of the proliferation phase in the wound healing process on day 5 after the wound occurs. This tissue is characterized by the proliferation of fibroblasts, the formation of new blood vessels (angiogenesis), as well as the formation of early collagen, which together form the basis of new tissues to close the wound. Healthy granulation will usually reach maximum development in the first to second week, and will gradually decrease as the wound enters the remodeling phase. Under normal healing conditions, thorough (perfect) granulation usually forms within a span of 10 to 14 days. (20, 21)

Overall, the 15% treatment group (P15) showed the fastest and most consistent results in the formation of full granulated tissue on day 7 and lasted until the end of observation. The 10% treatment group (P10) also showed excellent results, with full granulation achieved from day 11. In the treatment group, 5% (P5) was close to full granulation on day 13, although it was not completely complete by the end of observation because there were 2 infected animal samples. Meanwhile, the positive control group (KP) showed slow improvement and did not achieve full granulation until the end of observation. And the negative control group (KN) was the slowest in the world, with complete granulation only achieved on day 13. These findings reinforce that 15% cayenne pepper extract is the most effective treatment in accelerating the formation of granulated tissue in wound healing.

Based on the results of the study (16), Capsaicin plays a role by suppressing inflammatory processes through decreasing the number of neutrophils, monocytes, and the expression of pro-inflammatory cytokines such as IL-6. In addition, capsaicin also promotes fibroblast migration and angiogenesis, which is a key component in the formation of granulated tissues. And supported by research results (22) vitamin C serves as a cofactor in collagen synthesis and as an antioxidant that supports fibroblast activity and extracellular matrix formation. Studies show that vitamin C supplementation significantly increases the thickness and density of granulated tissues. Thus, the combination of the anti-inflammatory effects of capsaicin and the antioxidant effects of vitamin C contributes to the rapid and complete formation of dense granulated tissue.

4.5. Wound Length

Reduction in wound length is an important indicator in assessing the success of the proliferation phase in the wound healing process. It is characterized by fibroblast activation, granulation tissue formation, angiogenesis, and re-epithelialization. This process collectively plays a role in gradually closing the wound, either through wound contraction by myofibroblasts or epithelial tissue regrowth. A significant decrease in wound length is usually observed between day 7 to day 14, and this is a sign of the transition from the inflammatory phase to the healthy proliferation phase. In contrast, wounds that do not show any change in size for more than two weeks are often categorized as chronic wounds, due to the presence of resistance in the initial inflammatory phase. (23)

Overall, the 15% treatment group (P15) showed the highest effectiveness in accelerating wound length reduction, with total healing achieved from day 7 and consistent until the end of observation. The 10% treatment group (P10) followed the same pattern, with all wounds completely healed by day 10. The 5% (P5) treatment group showed slower and uneven repair, with most wounds healing by day 13, while some wounds were still not fully healed due to suspected infection. The negative control group (KN) progressed gradually, with the wound closing perfectly on the final day of observation. Meanwhile, the positive control group (KP) showed the worst results, with no lesions achieving complete

repair even up to day 14. These findings suggest that cayenne pepper extract with a concentration of 15% has great potential in accelerating wound healing, in terms of reducing wound length.

These findings suggest that although povidone-iodine is known to be an effective antiseptic with broad antimicrobial properties, its use in high concentrations can actually harm wound healing. According to (14) Povidone-iodine ointment 10% can indeed suppress the growth of microorganisms, reduce erythema, and help create a moist environment that supports angiogenesis. However, at the same time, these high concentrations can inhibit the proliferation of fibroblasts that are essential in the process of forming new tissues. In addition, repeated use without residue cleaning can cause irritation, allergic reactions, and irritant contact dermatitis, thereby worsening the microecology of the wound and prolonging the inflammatory phase.

The results of the study by (24) also support this, where low concentration of povidone-iodine ointment (≤1%) is more effective than standard concentrations (7.5–10%) in accelerating wound healing, reducing inflammation, and increasing re-epithelialization. This suggests that high doses of povidone-iodine, such as those used in the positive control group of this study, have the potential to slow the transition from the inflammatory phase to the proliferation phase. As a result, the formation of granulated tissue is inhibited, wound contraction is not optimal, and wound healing becomes slower.

In contrast, cayenne pepper extract provides a more consistent effect through a combination of its active compounds. Capsaicin has been shown to suppress the inflammatory response by reducing the infiltration of neutrophils, monocytes, and pro-inflammatory cytokines such as IL-6, while increasing fibroblast migration and angiogenesis. The vitamin C it contains also serves as a cofactor of collagen synthesis and antioxidants, which play an important role in the formation of extracellular matrices and dense granulation tissues. The combination of these two mechanisms promotes the acceleration of the transition from the inflammatory phase to the proliferation phase, resulting in faster, more effective, and more stable wound healing than 10% povidone-iodine and other control groups. (25)

5. Conclusion

Cayenne pepper extract (*Capsicum frutescens L*) showed effectiveness in the wound healing process in Wistar rats (*Rattus Norvegicus*), compared to the control group. Therefore, it can be concluded that a 15% concentration of cayenne pepper extract is the most effective and optimal dose for accelerating wound healing.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that they have no competing interests related to this research.

Statement of ethical approval

This research is approved ethically by ethical commision health research Universitas Wijaya Kusuma Surabaya with the number 31/SLE/FK/UWKS/2025 at January 31th 2025

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