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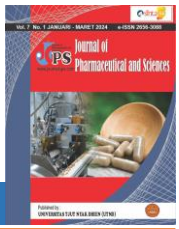

The effect of turmeric parent extract gel (*Curcuma longa* Linn) on incision wound healing in male white rats (*Rattus norvegicus*)

Pengaruh gel ekstrak induk kunyit (*Curcuma longa* linn) terhadap penyembuhan luka sayat pada tikus putih jantan (*Rattus norvegicus*)

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Abstract

One plant that has been shown to aid wound healing is turmeric. Turmeric has been scientifically proven to have choleretic and anti-inflammatory properties. Turmeric contains curcumin, which has antibacterial and antioxidant qualities that can accelerate the migration and re-epithelialization of cells useful in wound healing, including myofibroblasts, fibroblasts, and macrophages. This study aimed to determine the effect of turmeric mother extract gel on wound healing in male white rats (Rattus norvegicus). This study was conducted using experimental tests. Turmeric extract was prepared using 96% ethanol solvent with a maceration process. A 2 cm long incision wound was made on the back of white rats. The test animals were then divided into five groups to receive different treatments. Groups 3, 4, and 5 received turmeric mother extract gel with concentrations of 1%, 5%, and 10%, while Group 1 was negative control and Group 2 was positive control. The results showed that the incision wounds in male white rats could heal faster - on average, about 7.10 days - when treated with 96% ethanol extract of turmeric mother with doses of 1%, 5%, and 10%. This study concludes that a 10% turmeric mother extract gel is the best method to accelerate wound healing.

Keywords: Turmeric Parent, Curcumin, Turmeric Parent 96% Ethanol Extract Gel, Wound Healing

Abstrak

Salah satu tanaman yang telah terbukti membantu penyembuhan luka adalah kunyit. Kunyit telah terbukti secara ilmiah memiliki sifat koleretik dan anti-inflamasi. Kunyit mengandung bahan kimia yang disebut kurkumin, yang memiliki kualitas antibakteri dan antioksidan yang dapat mempercepat migrasi dan re-epitelisasi sel-sel yang berguna dalam penyembuhan luka, termasuk myofibroblas, fibroblas, dan makrofag. Tujuan dari penelitian ini adalah untuk mengetahui pengaruh gel ekstrak induk kunyit terhadap penyembuhan luka pada tikus putih jantan (Rattus norvegicus). Penelitian ini dilakukan dengan menggunakan uji eksperimental. Pembuatan ekstrak kunyit dilakukan dengan menggunakan pelarut etanol 96% dengan proses maserasi. Luka sayatan sepanjang 2 cm dibuat pada punggung tikus putih. Hewan uji kemudian dibagi menjadi lima kelompok untuk mendapatkan perlakuan yang berbeda. Kelompok 3, 4, dan 5 mendapatkan gel ekstrak induk kunyit dengan konsentrasi 1%, 5%, dan 10%, sedangkan kelompok 1 sebagai kontrol negatif dan kelompok 2 sebagai kontrol positif. Hasil penelitian menunjukkan bahwa luka sayat pada tikus putih jantan dapat sembuh lebih cepat - rata-rata sekitar 7,10 hari - ketika diberi perlakuan dengan ekstrak etanol 96% induk kunyit dengan dosis 1%, 5%, dan 10%. Kesimpulan dari penelitian ini adalah bahwa metode terbaik untuk mempercepat penyembuhan luka adalah dengan menggunakan gel yang mengandung ekstrak induk kunyit 10%.

Kata Kunci: *Induk Kuniyt, Kurkumin, Gel Ekstrak Etanol 96% Induk Kunyit, Penyembuhan Luka*

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Introduction

Skin is the widest and largest layer of the human body, covering and protecting the entire body. It plays an important role as the main protector from environmental disturbances and threats. However, skin is often subjected to external disturbances that can cause damage, such as scratches by sharp objects that can open the skin layer. Wounds are one of the most common injuries in humans. [1]. A wound is a damage to normal anatomical structure and function resulting from pathological diseases that impact organs inside or outside the body. Various things, including damage from blunt or sharp objects, high or low temperatures, harmful chemicals, explosions, electric shock, or animal bites, can cause wounds. The type of wound-such as a cut from a sharp object or a stab wound from a pointed object-depends on the cause [2].

A skin wound is the loss of an important part of the skin to the human body, which can result from an ulcer, physical trauma, or physiological disturbance. These wounds, such as scratches or sharp object injuries, prevent the skin from functioning properly. The wound healing process begins with the regeneration of new skin cells, taking place automatically and naturally through three main phases: the inflammatory phase (initial inflammatory reaction), the proliferation phase (formation of new tissue), and the remodeling phase (repair and refinement of skin tissue). These three phases are essential to ensure optimal wound healing. [3].

The complex process of wound healing seeks to repair damage to the skin and restore normal tissue structure and function. Several phases include inflammation, debridement, repair, and maturation. [4]Several variables can affect how long it takes for a wound to heal, including age, anemia, disease, vascularity, diet, obesity, medication use, hygiene, stress, necrosis, and infection. The ultimate goal is to return skin tissue to its normal state, restore skin function, reduce complications, and close the wound for new tissue formation. [5].

In Indonesia, more than 7,000 types of medicinal plants are spread from Sabang to Merauke, including turmeric, which can be used to heal wounds. The use of medicinal plants is increasingly popular due to their fewer side effects compared to chemical drugs, more affordable price, and ease of access. [6]. Apart from traditional medicine, medicinal plants are also frequently used in modern medicine systems, with more than 60% of pharmaceutical products being plant-based. Medicinal plants are usually made into teas, spices, or topical treatments to aid wound healing. One of the most frequently used herbs for therapeutic purposes is turmeric. [7].

Turmeric (Curcuma longa Linn) is an herbal plant that contains curcumin as its main active ingredient [8]. In traditional medicine, turmeric is often used for its anti-inflammatory and antiseptic properties and its ability to treat liver disorders and wounds. Curcumin has various biological activities that effectively treat microbial and parasitic infections. In addition, turmeric is also used in culinary and cosmetics, such as treating skin and accelerating wound healing by increasing collagen and cell proliferation [9]. Previous studies have shown that turmeric extract can accelerate the closure of incision wounds, confirming turmeric's potential as a therapeutic agent in traditional and modern medicine [10]. Conventional wound treatment usually uses topical preparations, and gels are an effective alternative. Gels have advantages such as a cooling effect from high water content and better penetration of active substances. They are non-sticky and easy to clean, thus increasing patient comfort and accelerating wound healing [11]. Because of the above background, the author

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is interested in researching the effectiveness of turmeric extract extracted by maceration method using ethanol solvent on wound healing in rabbits as experimental animals.

Experimental Section

Materials and Apparatus

Apparatus: rat cage, hand scoop, mask, stirring rod, beaker glass, vaporizer cup, measuring cup, filter paper, mortar and stamper, scalpel, water bath, watch glass, blender, analytical balance, Sudip, spatula, alcohol swab, napkin, glass object, weights, container (gel pot), glass bottle, cotton bud, camera.

Materials: mother turmeric (Curcuma longa Linn) and chemicals used are distilled water, 96% alcohol, glycerin, propylene glycol, triethanolamine, sodium carboxymethylcellulose (CMC-Na).

Sample Preparation

The parent turmeric was collected in quantities up to 1 kg, after which the skin was peeled off; the turmeric was sliced thinly, cleaned with clear water, drained, and dried until more brittle. Then, the sample was blended into a fine powder after drying. Samples weighing as much as 200 grams are dissolved in 96% alcohol solvent. By soaking the simplisia in the solvent, the extraction principle is used in the maceration process. After soaking for seven days, the material was filtered and separated between the filtrate and the residue. The filtrate was evaporated with a vaporizer cup in a water bath until a thick extract was obtained and stored in a glass bottle. [12], [13].

Formulation of the Preparation

Table 1 shows the gel formulation of turmeric mother extract at concentrations of 1%, 5%, and 10%.

Table 1. Gel formulation of turmeric parent extract (Curcuma longa Linn.)

Ingredients	Formula (gram)		
	F1	F2	F3
Turmeric Parent Extract	1	5	10
CMC-Na	5	5	5
Gliserin	5	5	5
Propilenglikol	5	5	5
TEA	2.5	2.5	2.5
Aquades	Ad 50	Ad 30	Ad 30

Preparation of Turmeric (*Curcuma longa* Linn) Parent Extract Gel

The gel base used in the gel preparation formulation consisted of distilled water, CMC-Na, glycerin, propylene glycol, and triethanolamine. The turmeric extract gel preparation formula prepared three different extract concentration formulations. Three different extracts: Formula 1 (1%), Formula 2 (5%), and Formula 3 (10%). The mortar was filled with 25 ml of heated distilled water, then sprinkled with CMC-Na evenly, then covered and waited to expand for 15 minutes. After that, it was crushed when it had developed and added to the turmeric mother extract according to the adjusted concentration. Then, glycerin and propylene glycol were used as humectants, and TEA was used as an emulsifier to dissolve in hot water. The mixture is then poured into a room-temperature container (gel pot) [14].

Evaluation Test of Turmeric (Curcuma longa Linn) Parent Extract Gel Preparation

Organoleptic Test

The organoleptic evaluation will use the Turmeric Parent Extract Gel (TPEG) formulation to identify its shape, color, odor, and taste. [15].

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Homogeneity test

The homogeneity of TPEG was tested by placing 0.5 grams of gel onto one glass object and then connecting another to it. The TPEG preparation should have a uniform composition without any discernible large particles. [14].

Spreadability test

The spreadability test involves weighing a 1-gram gel preparation and placing it in the center of a watch glass. Another watch glass, also weighed, is then placed on top, and a load of 100 grams is applied. The measurement is taken using a caliper. [16].

pH test

Gel compositions are tested using a specialized instrument known as a pH meter. The gel preparation is placed in a glass beaker container and assessed using a pH meter. To meet the criteria, the preparation must have a pH of 4.5 to 6.5. [14].

Male Rat Incision Creation

Ensure the rats have been acclimatized in the cage for 7 days to adapt to the new environment. The test animals weigh about 120 grams. Before the incision and shaving, the rats must be anesthetized first. Then, the rats on the back, an alcohol swab at the marked point, and an incision on the back of the rat with a sterile scalpel 2 cm long. Treatment of each test group. [17].

Treatment of incision wounds in male rats

Wound treatment was performed by applying gel base for the negative control group, povidone-iodine for the positive control group, TPEG (turmeric mother extract) with different concentration variations F1 (1%), F2 (5%), F3 (10%), performed every 2×1 day (morning & night) on the wound surface for 7 days.

Data Analysis

Data were analyzed statistically with Way ANOVA (one-way ANOVA) with a confidence level of 95% and a significance level (of 5% error rate (α = 0.05). Data is said to be significant if the p-value is <0.05, and the data is insignificant if the p-value is >0.05. Furthermore, further analysis was carried out with Post-Hoc Tuckey to confirm the gel preparations' effectiveness. The existence of significant differences can explain the effectiveness of the gel preparations made to heal wounds.

Results And Discussion

Organoleptic of Turmeric Parent Extract Gel

This study observed the organoleptic results of turmeric parent extract gel preparations over 7 days. Three formulas were tested: F1 (1% concentration), F2 (5% concentration), and F3 (10% concentration). All formulas exhibited a semi-solid form. F1 displayed a maroon-red color, while F2 and F3 showed reddish-brown. None of the formulas had any detectable taste or odor.

The organoleptic testing of the turmeric parent extract gel formulation revealed that the preparations were homogeneous, had a characteristic odor derived from the turmeric extract, and exhibited colors ranging from deep red to reddish-brown, depending on the concentration of the extract used. Higher concentrations of the extract resulted in a more intense gel color. This physical observation is crucial as it helps ensure the gel formulation's uniformity and consistency. [18], [19].

According to existing literature, turmeric contains curcumin, which has high antioxidant and anti-inflammatory properties, providing additional benefits for topical preparations such as gels. The variation in color due to different concentrations of curcumin is consistent with findings that F1 had a maroon-red color while F2 and F3 had a reddish-brown color. This organoleptic stability is important to ensure consumer acceptance and continued product use. A characteristic odor further confirms the authenticity and presence of turmeric extract in the formulations. [20].

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Homogeneity of Turmeric Parent Extract Gel

This study observed the homogeneity of turmeric parent extract gel preparations over 7 days. Three formulas were tested: F1 (1% concentration), F2 (5% concentration), and F3 (10% concentration). All three formulas were found to be homogeneous.

Homogeneity testing is crucial in evaluating whether a gel is uniform in its composition. A non-homogeneous gel can affect its efficacy and usability, making it difficult to apply evenly and potentially leading to inconsistent therapeutic outcomes. Ensuring homogeneity in gel formulations is essential for effectively delivering active ingredients. This study found that all three tested formulas (F1, F2, and F3) were homogeneous, indicating that the gel's consistency was uniform regardless of the turmeric extract concentration. [21].

Homogeneous gels ensure that the active ingredients are evenly distributed throughout the preparation, providing consistent therapeutic benefits with each application. This is particularly important for gels containing turmeric extract, which relies on the even dispersion of curcumin for its anti-inflammatory and antioxidant properties. Research supports that well-formulated turmeric gels can effectively deliver curcumin's benefits, provided the preparation remains homogeneous. Studies on similar formulations indicate that maintaining homogeneity is vital for achieving the desired therapeutic effects and ensuring patient satisfaction. [22].

Spreadability of Turmeric Parent Extract Gel

Table 2 shows the results of the spreadability test of the turmeric mother extract gel preparation, and the graph of the spreadability measurement is shown in Figure 1 below.

Table 2. Results of Spreadability of Turmeric Parent Extract Gel

Duration of Observation (Day)	Gel Dosage Formula Measurement of spreadability (cm)		
	F1	F2	F3
1	6.5	6.4	6.2
2	6.5	6.2	6.1
3	6.2	6.1	5.8
4	5.8	5.8	5.6
5	5.7	5.6	5.6
6	5.5	5.4	5.4
7	5.4	5.3	5.2
Average	5.94 ± 0.45	5.82 ± 0.41	5.70 ± 0.36

Spreadability testing aims to determine how well a gel spreads on the skin's surface, which can significantly affect the drug's absorption and the release of active ingredients at the application site. A gel that spreads well ensures better contact with the skin, leading to more effective and even absorption of the active compounds. [23].

The results indicate that all three formulations show a gradual decrease in spreadability over the observation period. This decrease could be due to gel viscosity changes or consistency over time. A 5–7 cm spreadability range is generally considered good, ensuring the gel can be applied easily and comfortably on the skin. [24], [25]

The relationship between viscosity and spreadability is inversely proportional; higher viscosity typically results in lower spreadability. In this study, as the gels aged, their spreadability decreased, which might be attributed to increased viscosity over time. Appropriate gelling agents, such as Carbopol 940, are crucial in maintaining the balance between viscosity and spreadability [26]. Ensuring good spreadability is essential for the practical application of topical gels. It ensures that the active ingredients, like curcumin in turmeric, are delivered effectively across the application area, enhancing their therapeutic benefits.

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Formulating a gel with optimal spreadability enhances user compliance and maximizes the gel's efficacy in delivering the intended therapeutic effects [27], [28], [29].

The One-way ANOVA data analysis reveals that the spreadability data in the test group is normally distributed and homogenous, as indicated by a significance value of 0.738 (p>0.05) in the Test of Normality. The statistical test used is One-way ANOVA, with Tuckey analysis employed to identify the variations among the test groups. Further statistical analysis using Tuckey Post-Hoc reveals a significant difference between the Formula 1 and F3 gel groups, with a significance value of 0.00 (p <0.05). However, there is no significant difference between the Formula 1 and F2 gel groups, with a significance value of 0.123 (p>0.05). The test findings indicate that using turmeric extract impacts gel formulations' capacity to spread.

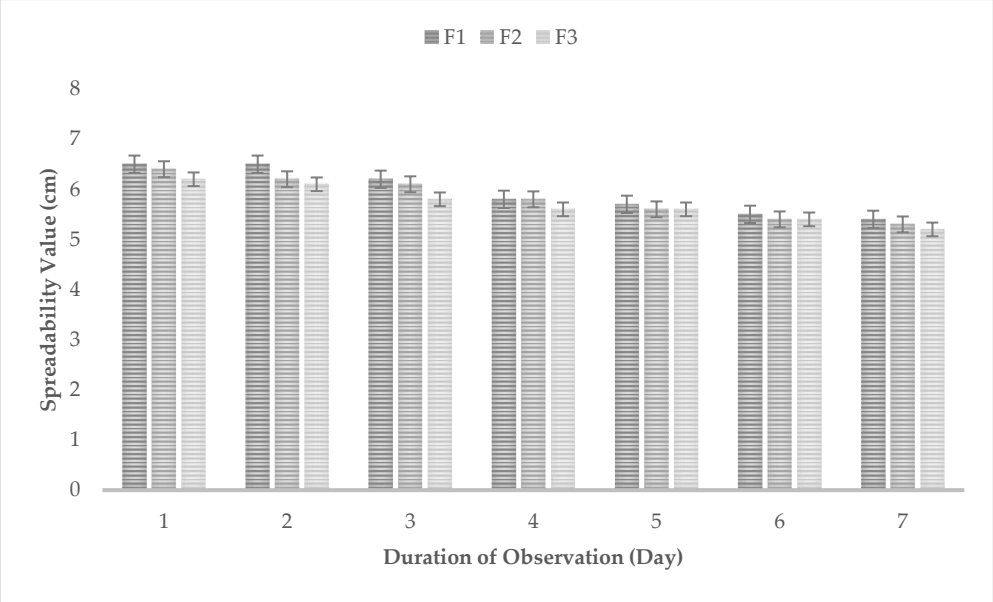

Figure 1. Measurement graph of the spreadability of turmeric mother extract gel

The pH of Turmeric Parent Extract Gel

The results of the pH test of the turmeric mother extract gel preparation are shown in Table 3, and the measurement graph in Figure 2 below.

Table 3. Results of pH of Turmeric Parent Extract Gel

Duration of Observation (Day)	Gel Preparation Formula		
	F1	F2	F3
1	6.4	6.7	6.8
2	6.2	6.4	6.5
3	6.1	6.2	6.3
4	6.0	6.1	6.2
5	5.8	5.9	6.0
6	5.5	5.7	5.8
7	5.3	5.4	5.5
Average	5.90 ± 0.39	6,05 ± 0.43	6.15 ± 0.43

The pH testing of the turmeric parent extract gel shows that all three formulations fall within the acceptable pH range of 4.5-6.5. Maintaining the pH within this range is crucial as it prevents skin irritation and ensures the gel is comfortable. A lower pH can cause skin irritation, while a higher pH can lead to skin dryness and itching. [15].

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Research indicates that the skin's acidic pH is vital in maintaining barrier function and homeostasis. Products should align with the skin's pH to preserve its protective barrier and health. This alignment helps properly absorb active ingredients and maintains the skin's microbiome, which is essential for preventing various skin disorders. [30]. Ensuring the pH stability of gel formulations over time is crucial for their effectiveness and user compliance. Studies have shown that gels with pH values within the skin's natural range are better tolerated and more effective in delivering active ingredients without causing adverse effects. [31].

The One-way ANOVA data analysis reveals that the pH data in the test group follows a normal distribution and is homogenous, as indicated by a significance value of 0.865 ($p>0.05$) obtained from the Test of Normality. The statistical test used is One-way ANOVA, with Tuckey analysis employed to identify the variations between each test group. Further statistical analysis using Tuckey Post-Hoc reveals a significant difference between the Formula 1 and F3 gel groups, with a significance value of 0.00 ($p <0.05$). However, there is no significant difference between the Formula 1 and F2 gel groups, with a significance value of 0.213 ($p>0.05$). The test findings indicate that the concentration of turmeric extract impacts the gel formulation's pH. [32].

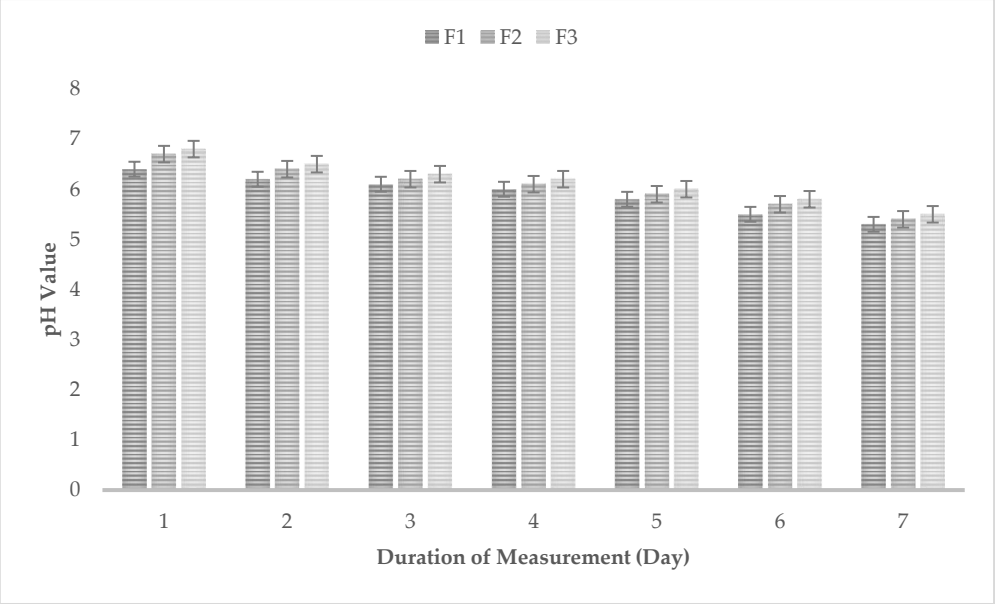

Figure 2. Graph of pH measurement of Turmeric Parent Extract Gel

Observation Result of Turmeric Parent Extract Gel on Wound Healing

The results of observations on Turmeric (Curcuma longa Linn) Parent Extract Gel on Wound Healing for 7 days of observation are shown in Table 4. Testing the gel's effectiveness using povidone-iodine as a positive control and gel base as a negative control.

The study measured the changes in the length of the incision wounds over 7 days for three test groups (F1, F2, F3) and two control groups (negative control K- and positive control K+). The results indicated that all test groups exhibited a reduction in wound length over time, with F3 showing the most significant reduction, followed by F2 and F1. The positive control group (K+) also demonstrated a considerable reduction, comparable to F3. This data suggests that higher concentrations of turmeric extract (F3) are more effective in promoting wound healing than lower concentrations (F1 and F2). The turmeric extract's anti-inflammatory and antimicrobial properties likely accelerate wound healing. Research supports that curcumin, a major component in turmeric, aids in wound healing by reducing inflammation and promoting tissue regeneration. [33].

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Table 4. Results of measurement of changes in the length of the incision wound (cm)

Duration of Observation (Day)	Treatment Group				
	F1	F2	F3	K-	K+
1	2.0	2.0	2.0	2.0	2.0
2	2.0	1.5	1.8	2.0	1.7
3	1.8	1.4	1.5	1.8	1.4
4	1.5	1.2	1.0	1.6	1.0
5	1.0	1.0	0.8	1.5	0.6
6	0.6	0.8	0.4	1.3	0.1
7	0	0.4	0	1.2	0
Average	1.27 ± 0.76	1.18 ± 0.51	1.07 ± 0.73	1.60 ± 0.31	0.97 ± 0.77

The significance test with One Way ANOVA data analysis shows that the incision wound healing data based on the Test of Normality in the test group is normally distributed and homogeneous with a significance value of 0.241 ($p>0.05$). One Way ANOVA statistical test results using Tuckey analysis to see the differences in each test group. Based on further statistical analysis of Tuckey Post - Hoc, it can be seen that a more specific difference between the Formula 1 gel group has a significant difference with the F3 gel group with a significance value of 0.00 ($p <0.05$) but does not have a substantial difference with the F2 gel with a significance value of 0.213 ($p>0.05$). The results of testing the effectiveness of positive control wound healing have a significant difference from the negative control test formula but do not have a substantial difference with the F3 gel formula. The test results showed an effect of turmeric extract concentration on the pH of the gel preparation. The gel containing the extract was carefully applied to the wounded area. Using a scalpel, a 2 cm long incision wound was made on the rat's back. The results of this study showed a comparison of the effectiveness of the three formulas in healing skin wounds, whereas the third formula showed the fastest results in covering the wound. The effectiveness of the third formula is due to the very high concentration of the extract, which is 10%. The presence of extracts in high concentrations increases biological activity that accelerates skin regeneration.

Meanwhile, the gel base without added active substance (K-) was very slow in healing the incision wound. This may be due to the limitation of the gel in providing therapeutic benefits in the absence of active compounds that support the healing process. Meanwhile, the positive control group (K+) using povidone-iodine also showed effectiveness in wound healing but not as effective as the formula with the addition of turmeric mother extract. Povidone iodine is a good antiseptic. Still, it does not have the same regenerative properties as turmeric mother extract, which contains bioactive compounds such as curcumin compounds that have anti-inflammatory and antioxidant properties and support the tissue healing process more effectively. The treated group experienced faster recovery due to the synergistic effect of active compounds in turmeric. The curcumin content in turmeric can suppress the activity of various inflammatory cytokines such as IL-2, IL-6, IL-8, IL-12, tumor necrosis factor-alpha (TNF-α), and migration inhibitory proteins, which accelerate the inflammatory response. The concentration of extract used has also been shown to greatly influence the gel's effectiveness in treating cuts. [34].

The use of turmeric extract, which includes secondary metabolites, particularly flavonoids, might expedite the process of wound healing. These chemicals possess both wound-healing acceleration and antibacterial characteristics, which aid in preventing infection. [35]. Flavonoids function by creating intricate molecules on proteins outside of cells, disturbing the structure of bacterial cell membranes. Flavonoids contribute to the prevention of blood vessel blockage by enhancing blood circulation in the body. [3]. Furthermore, flavonoids possess advantageous anti-inflammatory and antioxidant characteristics, effectively alleviating pain in inflamed places or experiencing bleeding. [36].

Curcuminoids are another component of turmeric that accelerates wound healing. Curcuminoids have effective anti-inflammatory activity, equivalent to hydrocortisone acetate and indomethacin. Curcumin

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has also been shown to improve wound healing ability significantly. In addition to flavonoids and curcuminoids, other compounds such as saponins, polyphenols, and volatile oils in turmeric can activate macrophages, which play an important role in wound healing. Therefore, the various components in turmeric, especially flavonoids and curcuminoids, make turmeric effective in wound healing. [5].

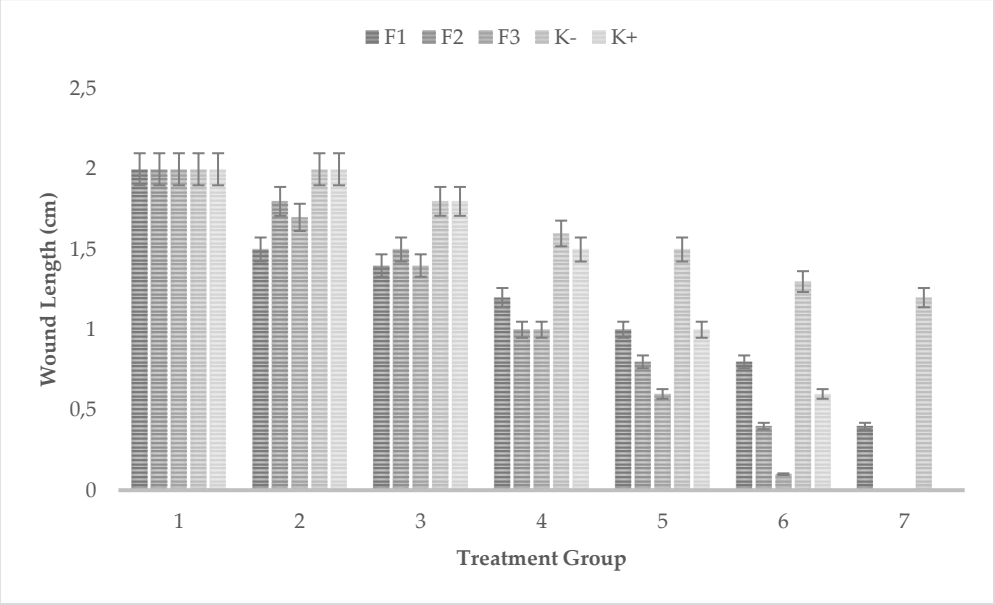

Figure 3: Graph of wound length measurements for each treatment group

Conclusions

Based on the results of this study, it can be concluded that the turmeric (Curcuma longa Linn) parent extract gel at a 10% concentration exhibited the most effective healing properties for incision wounds in male white rats. Although all three formulas (1%, 5%, and 10%) could promote wound closure and healing, the 10% concentration provided the most significant improvement, highlighting the potential of higher concentrations of turmeric extract in enhancing the wound healing process.

Tabel 5. Appearance of The Incision Wound

Duration of Observation	Wound Healing Observation Result	
D1		
D2		

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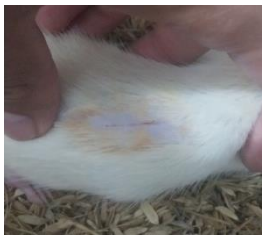
D3

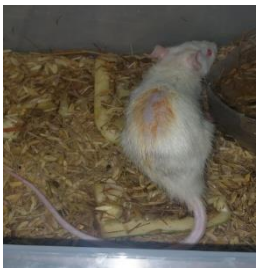
D4

D5



D6

D7



Conflict of Interest

The authors shall declare that there is no conflict of interest.

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