

THE EFFECT OF RED DRAGON FRUIT PEEL EXTRACT GEL ON RATTUS NORVEGICUS STRAIN WISTAR OF GRADE IIA BURNS SURFACE AREA

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Article Info

Article history:

Received December 10th, 2022

Revised December 28th, 2022

Accepted January 4th, 2023

Keywords:

Decreased wound area

Hylocereus polyrhizus

Red dragon fruit peel extract

gel

Second degree burns

ABSTRACT

Background: Burns are injuries to body tissues by electric shocks, chemicals, or hot objects. Peel of red dragon fruit contains anti-inflammatory and antibacterial compounds, so it can accelerate the healing of grade IIA burns.

Purpose: To prove the effect of red dragon fruit peel extract gel on the surface area of grade IIA burns of *Rattus norvegicus strain wistar*. **Methods:** Experimental with post test only control group design. The samples were divided into 5 groups, 1 (Base Gel), 2 (Burnazin plus cream), 3 (Red dragon fruit peel extract gel 10%), 4 (Red dragon fruit peel extract gel 15%), 5 (Red dragon fruit peel extract gel 20%). The rats' backs were attached by a metal that has been heated in water at 100 ° C for 3 minutes without pressing for 10 seconds. The treatment was carried out for 14 days, then the wound area was measured on the 4th, 7th, and 14th days. The data were analyzed using MANOVA test, *Post-hoc Bonferroni* and *Pearson Correlation*. **Results:** The results of the MANOVA test showed significant differences in the area of the wound on the 14th day. *Post-hoc* test showed a significant difference occurred in group 5. *Pearson Correlation* test showed that the effect of red dragon fruit peel extract gel on day 14 was 0.820 which was included in the strong category. **Conclusion:** There is an effect of red dragon fruit peel extract gel on the area of second degree burns of *Rattus norvegicus strain wistar*.

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1. INTRODUCTION

Burns are injuries to body tissues by electric shock, chemicals, hot objects, or heat from liquids, steam, fire, or radiation, causing injury. [1] The most incidence of burns occurs in the household environment and the highest prevalence of burns belongs to second degree burns. [2] Second degree burns cause the most painful sensation among burns of other degrees. [3] Bullae in grade IIA burns provide an excellent environment for the growth of microorganisms and increase the risk of infection. [4]

Silver sulfadiazine (SSD) is the gold standard drug for the treatment of burns that has been approved by the United States Food and Drug Administration (FDA). The 1% SSD that will be used as a control group is in cream preparations (burnazine plus). The SSD preparation produces a moist environment, a cool sensation, is soothing for burns, has a wide spectrum of activity against gram-positive and gram-negative bacteria. [5,6]

The content of hyaluronic acid in the cream can stimulate tissue regeneration, cellular migration, and angiogenesis.[7] SSD has disadvantages, including hepatotoxicity, kidney toxicity, increased bacterial resistance due to prolonged use, and inhibits wound contraction. [5,8]

Red dragon fruit peel extract gel once contained vitamin C, flavonoids, tannins, alkaloids, steroids, and saponins. [9] Alkaloids, flavonoids, and vitamin C as anti-inflammatory. Flavonoids, steroids, and saponins as antibacterial. Saponins support the epithelialization process, and tannins can act as astringent agents. Alkaloids, flavonoids, and vitamin C as anti-inflammatory, flavonoids, steroids, and saponins as antibacterials, so that these bioactives produce synergistic effects in supporting the inflammatory phase of burns. Saponins support the epithelialization process, tannins act as astringent agents, so that saponins and tannins produce a synergistic effect in supporting the proliferation phase of burns. A moist environment has also been shown to improve the quality of wound healing by reducing scarring, supporting autolytic debridement (from macrophages), encouraging the angiogenesis process, accelerating the epithelialization process, and reducing pain sensations. [10,11]

2. METHOD

This research is an experimental study with post test only control group design. This research was conducted at the Biomedical Laboratory of the Faculty of Medicine, University of Muhammadiyah Malang. 20 tails of *Rattus norvegicus wistar* strains were divided into 5 groups, namely group 1 (Gel Base), 2 (burnazin plus cream), 3 (Red dragon fruit peel extract gel 10%), 4 (Red dragon fruit peel extract gel 15%) , 5 (Red dragon fruit peel extract gel 20%). The extract of the red dragon fruit peel was carried out in the Herbal Laboratory of Materia Medica Batu using 96% ethanol as a solvent. Dragon fruit peel extract is used as a gel preparation with a concentration of 10%, 15%, and 20% using the following formulations (Maswadeh et al., 2006)

Table 1. Red Dragon Fruit Peel Extract Gel Formulation

Substance	Concentration		
	10%	15%	20%
Red dragon fruit peel extract gel	5 g	7,5 g	10 g
Natrium Carboxy Methyl Cellulose (Na CMC)			
Glycerin	2,5 g	2,5 g	2,5 g
Propylene Glycol	5 ml	5 ml	5 ml
Aquadest	2,5 ml	2,5 ml	2,5 ml
	50 ml	50 ml	50 ml

The rats' backs were attached to a metal with a diameter of 2 cm which had been heated in water with a temperature of 100 ° C for 3 minutes without pressing for 10 seconds. In order not to be licked by fellow rats, the wound that has been smeared according to the treatment, after 30 minutes is covered with hypafix (IONI Compilation Team, 2014) The treatment was carried out for 14 days, then the area of the wound was measured on the 4th, 7th and 4th day 14. Data on the area of second degree burns on these days were measured using the ImageJ application. Data were analyzed using SPSS 25 with MANOVA Test, Post-hoc Bonferroni and Pearson Correlation.

3. RESULTS AND DISCUSSION

The wound area pattern that has been drawn on mica paper is scanned first, then calibrated, and measured virtually with the ImageJ application. The results of these measurements indicate that each treatment has a different effect on the area of second degree burns, as shown in Figure 1, 2, and 3

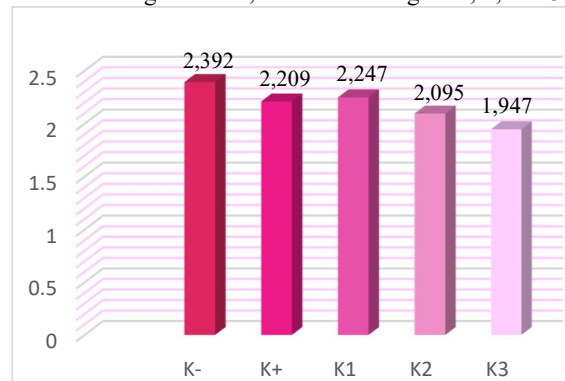


Figure 1. Average Area of Grade IIA Burns Day 4 (cm²)

Giving red dragon fruit peel extract gel starting from a concentration of 10%, 15%, and 20% reduced the average area of second degree burns. The measurement of day 4 showed that the average area of second degree burns treated with red dragon fruit peel extract gel with a concentration of 10% was smaller than the average area of second degree burns treated with gel base, but was still larger than the average area of second degree burns treated with silver sulfadiazine (burnazine plus cream). The average area of second degree burns treated with red dragon fruit peel extract gel with a concentration of 15% and 20% was smaller than the average area of second degree burns treated with gel and silver sulfadiazine (burnazin plus cream). Based on the average area of second degree burns on day 4, it can be concluded that red dragon fruit peel extract gel has an effect on the area of second degree burns in the inflammatory phase of burn healing.

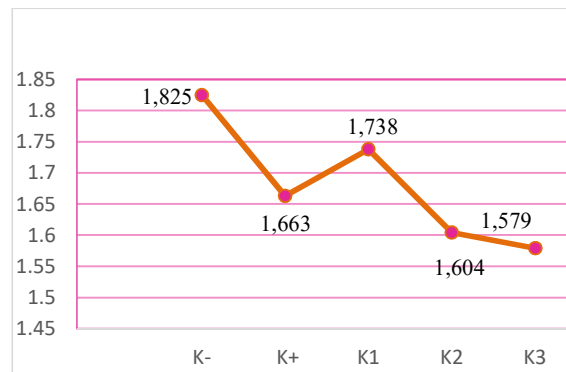


Figure 2. Average Area of Grade IIA Burns Day 7 (cm²)

The 7th day measurement showed that the average area of second degree burns treated with red dragon fruit peel extract gel with a concentration of 10% was smaller than the average area of second degree burns treated with gel base, but was still larger than the average area of second degree burns treated with (burnazin plus cream). The average area of second degree burns treated with red dragon fruit peel extract gel with a concentration of 15% and 20% was smaller than the average area of second degree burns treated with gel base and silver sulfadiazine (burnazin plus cream). Based on the average area of second degree burns on day 7, it can be concluded that red dragon fruit skin extract gel affects the area of second degree burns in the early proliferation phase of burn healing.

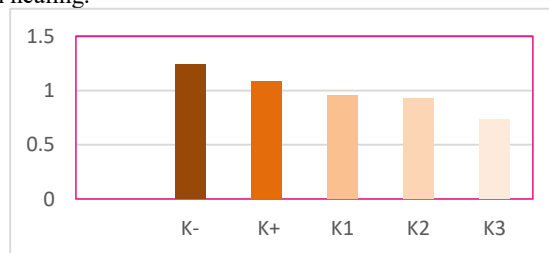


Figure 2. Average Area of Grade IIA Burns Day 14 (cm²)

Measurement of day 14 showed that the average area of second degree burns treated with red dragon fruit peel extract gel concentrations of 10%, 15%, and 20% were smaller than the average area of second degree burns treated with gel and silver base. sulfadiazine (burnazine plus cream). Based on the average area of second

degree burns on day 14, it can be concluded that red dragon fruit peel extract gel affects the area of second degree burns and the end of the proliferation phase of burn healing.

Table 2 MANOVA Test Results

Variable	Sig.
Wound area on day 4	0,134
Wound area on day 7	0,322
Wound area on day 14	0,001

Based on Table 2, the area of IIA degree burns in each treatment, both day 4 and day 7, did not have a significant difference in effect, because the sig. value is > 0.05 . The extent of second-degree burns on day 14 had a significant difference in effect, because the sig. value is < 0.05 for each treatment.

Table 3 Bonferroni Post-hoc Test Results

Variable	Intergroup Comparisons		Mean Difference (cm ²)
Wound area on day 14	K (-)	K (+)	0,15 ^b
		Extract Gel 10%	0,28 ^b
		Extract Gel 15%	0,31 ^a
		Extract Gel 20%	0,50 ^a
	K (+)	K (-)	0,15 ^b
		Extract Gel 10%	0,12 ^b
		Extract Gel 15%	0,15 ^b
		Extract Gel 20%	0,34 ^a
	Extract Gel 10%	Extract Gel 15%	0,037 ^b
		Extract Gel 20%	0,22 ^b
Extract Gel 15%	Extract Gel 20%	0,18 ^b	

a : Significant

b : Not significant

Based on table 3, there is a significant difference between the mean area of wounds treated with a 15% concentration of red dragon fruit peel extract gel and the average wound area treated with gel-based wounds. Significant differences also occurred between the average burn area treated with a 20% concentration of red dragon fruit peel extract gel and the average wound area treated with gel-based. The mean area of burns treated with red dragon fruit peel extract gel with a concentration of 20% was also significantly different from the average burn area given silver sulfadiazine (cream burnazin plus).

The silver sulfadiazine (burnazin plus cream) group and the gel-based group had differences in the mean burn area, but not significantly. Silver sulfadiazine (SSD) is still quite good as a standard therapy, because the mean area of 0.15 cm² is smaller than the average wound area in the gel-based group. The mean of wound area between the group given gel base and the group given 10% red dragon fruit peel extract gel also had no significant difference. Red dragon fruit peel extract gel with a concentration of 10% was still better in reducing the area of second degree burns, because the mean area was still 0.28 cm² smaller than the broad average in the gel-based group.

The group given red dragon fruit peel extract gel with concentrations of 10%, 15%, and 20% had insignificant differences in wound area. The mean difference between the groups given red dragon fruit peel extract gel was 10% and 15%, which was only 0.037 cm². The mean difference between the groups given red dragon fruit peel extract gel 15% and 20% was only 0.18 cm². The mean difference between the groups given red dragon fruit peel extract gel 10% and 20% was only 0.22 cm². This is because the red dragon fruit peel extract in each gel differs from only 2.5 grams in each concentration.

Table 4 Pearson Correlation Test Results

Intergroup Comparisons		r	Sig.
Variable 1	Variable 2		
Red dragon fruit peel extract	Wound area on 4 th day	-0,567	0,009
	Wound area on 7 th day	-0,425	0,062
	Wound area on 14 th day	-0,820	0,000

Based on table 4, it can be concluded that the red dragon fruit peel extract gel has a significant effect on the area of second degree burns on 4th day and 14th day. The effect of red dragon fruit peel extract gel for 4th day and 14th day, respectively, was 0.567 and 0.820 which were in the strong category with a negative relationship direction. The direction of the negative relationship shows that the higher concentration of red dragon fruit peel extract gel, the smaller the mean area of second degree burns affected.

Giving gel base in this study, was able to reduce the area of second-degree burns, both on the 4th day (the area became 2.39 cm²), the 7th day (the area became 1.82 cm²), and the 14th day (the size was to 1.24 cm²), but the area was still the largest average among the groups given silver sulfadiazine (cream burnazin plus) and red dragon fruit peel extract gel. This is because the gel base has no active ingredients and only relies on its properties as a gel, which is moisturizing. Wounds with a moist environment will accelerate healing by supporting autolytic debridement (from macrophages), encouraging the angiogenesis process, accelerating the epithelialization process.[11,12]

Burnazin Plus cream can support wound healing because it contains silver sulfadiazine which acts as an antibacterial, but does not have several active compounds such as red dragon fruit peel extract gel, so the average area of the wound is still smaller than the group given red dragon fruit peel extract gel. concentrations of 15% and 20%. [5,13] Burnazin plus cream also contains hyaluronic acid which can stimulate tissue regeneration, cellular migration, and angiogenesis, so that the average area of second degree burns treated with burnazine plus cream in this study was smaller than the gel-based group. [7]

The mean area of second degree burns treated with 10% concentration of red dragon fruit (*Hylocereus polyrhizus*) peel extract gel, on the 4th and 7th days was greater than the group given burnazin plus cream and was smaller on the 14th day. This is because those who play a role in the proliferation phase of red dragon fruit peel extract gel are more than in burnazin plus cream. Saponins and tannins in red dragon fruit peel extract gel support the epithelialization process by stimulating the formation of structural proteins (collagen), precipitating blood proteins, such as albumin, this process increases platelet aggregation, accelerates the hemostasis process, increases the flow of blood vessels and fibroblasts, deposition of collagen, until produces a synergistic effect in the proliferation phase, while the hyaluronic acid in burnazin plus cream only stimulates tissue regeneration, cellular migration, and angiogenesis. The results of this study are in line with previous studies that examined binahong leaf extract ointment which contains similar content to red dragon fruit peel extract gel, namely flavonoids, saponins, tannins, polyphenols, and steroids with concentrations of 10%, 20%, and 40%. [14] The results of Ahliadi's research, 2014 stated that the 10% concentration did not make a significant difference compared to silver sulfadiazine in reducing the size of second degree burns.

The mean area of second degree burns treated with 15% red dragon fruit peel extract gel did not give a significant difference when compared to the group given silver sulfadiazine. The results of this study are in line with previous research that examined the ethanol extract of jasmine leaves which has a content similar to that of red dragon fruit extract, namely flavonoids, saponins, tannins, alkaloids with concentrations of 15%, 30%, and 45%. [15] The results of the study by Wibawani et al, 2015 stated that the 15% concentration of jasmine leaf extract did not make a significant difference compared to silver sulfadiazine.

The mean area of second degree burns treated with red dragon fruit peel extract gel with a concentration of 20% was the smallest compared to the group treated with gel base and silver sulfadiazine, both on day 4, day 7, and day 14. Red dragon fruit peel extract gel with a concentration of 20% also gave a significant difference compared to the group given silver sulfadiazine. The results of this study are in line with previous studies that examined binahong leaf extract ointment which contains similar content to red dragon fruit peel extract gel, namely flavonoids, saponins, tannins, polyphenols, and steroids with concentrations of 10%, 20%, and 40%. The results of the Ahliadi study, 2014 stated that the concentration of 20% began to make a significant difference compared to silver sulfadiazine in reducing wound size.

Gel content of red dragon fruit peel extract which acts as antibacterial, such as flavonoids, steroids, and saponins will prevent excessive infection in burns. [16-18] Alkaloids, flavonoids, and vitamin C as

antiinflammatory agents will reduce excess immune response and allow the next phase of wound healing to occur, so that the inflammatory phase can be completed optimally. [19] This is evidenced by the insignificant mean reduction in the area of second degree burns on the 4th day measurement. The results of the 4th day measurement presented the role of dragon fruit peel extract gel in the inflammatory phase, because the alkaloids, vitamin C, flavonoids, and steroids in the red dragon fruit peel extract gel act as antibacterial and anti-inflammatory, thus supporting the inflammatory phase of the wound. [20]

Gelling agents or gel base ingredients and vitamin C will support the angiogenesis process. [11,12,20] Tannins and saponins, which each act as astringent agents and stimulators of collagen production, will help the epithelialization process. [22-24] Tannins and saponins will have a synergistic effect in the proliferation phase. This is evidenced by a significant decrease in the mean area of second degree burns on the 7th and 14th day measurements. Day 7 and 14 represent the role of red dragon fruit peel extract gel during the proliferation phase. [20]

Red dragon fruit peel extract gel with a concentration of 15% and 20% gave a significant difference in the mean area of second degree burns on day 14. The active compound content of red dragon fruit peel extract gel with a level of 20% was able to significantly reduce the average area of second degree burns compared to burnazin plus cream. This shows that the active compound of red dragon fruit peel extract gel with a level of 20% has the ability to reduce the area of second degree burns which is much better than the standard drug. Meanwhile, the active compound content in the red dragon fruit peel extract gel with a level of 15% is more able to reduce the average area of burns, but not significantly compared to standard drugs.

Red dragon fruit peel extract gel with a concentration of 10% did not give a significant difference compared to the standard drug, even the mean area of second degree burns on the 4th and 7th days was still greater than the average wound area treated with burnazin plus cream. This indicates that the active compound content in the 10% concentration of red dragon fruit peel extract gel is not as good as burnazin plus cream in reducing the average wound area in the inflammatory phase and early proliferation phase. Meanwhile, the average wound area treated with red dragon fruit peel extract gel was smaller than the group given burnazin plus cream on the 14th day. This indicated that the 10% concentration of active compound extract gel had more influence on the wound area in the final proliferation phase. This is in line with the theory that second-degree burns begin to heal within 10-14 days. [25]

Previous studies compared red dragon fruit peel extract gel with a concentration of 5%, 10%, and 15% with bioplacenton. The results of his research, red dragon fruit peel extract gel concentrations of 10% and 15% are effective in healing burns on the 10th day. [26] The difference between the results of Mayefis, 2019 and this research is possible because the positive controls used are different. Mayefis, 2019 research used bioplacenton which is not the gold standard drug for burns, while this study used the gold standard drug for burns, namely burnazine plus cream which contains silver sulfadiazine. Bioplacenton only contains placenta extract which triggers the formation of new tissue and neomycin sulfate which acts as an antibiotic, so that only 10% and 15% concentration of red dragon fruit peel extract gel has made a significant difference compared to Bioplacenton in reducing the area of second degree burns. While burnazin plus cream contains silver sulfadiazine (a broad spectrum antibiotic) and hyaluronic acid which can stimulate tissue regeneration, cellular migration, and angiogenesis, so that the 10% and 15% concentration of red dragon fruit peel extract gel has not been able to produce a significant difference and requires a concentration of 20% to produce a significant difference in the reduction in the mean IIA degree burn area.

4. CONCLUSION

Red dragon fruit peel extract gel with a concentration of 20% affected the area of second degree burns the most and the difference was significant compared to the mean area of second degree burns in the positive control group that was given silver sulfadiazine (burnazin plus cream) with a large effect of 0.820 which was included in the strong category.

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