

Effect of Antioxidant Activity of Red Dragon Fruit (*Hylocereus polyrhizus*) Peel on Fibroblast Proliferation in the Healing Process of Oral Ulcers in Wistar Rats

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ABSTRACT

The purpose of this study is to understand effect of antioxidant activity of red dragon fruit (*Hylocereus polyrhizus*) peel on fibroblast proliferation in the healing process of oral ulcers in wistar rats. This type of research is a quasi-laboratory experiment with a randomized post test only control group design. This research will be carried out from May to June 2022, including the preparation of red dragon fruit (*Hylocereus polyrhizus*) peel extract, antioxidant activity tests, making wounds until the time for wound healing, as well as histopathological examination. The population of are wistar rats bred at Eldwin Laboratory is 300 individuals. Based on the calculation, the total sample in this study is 10 multiplied by 3 so there are 30 samples. The data obtained is not normally distributed then the statistical test is continued with Kruskal Willis test to determine differences in the effectiveness of red dragon fruit (*Hylocereus polyrhizus*) peel extract in all groups. The results show that there is an effect of antioxidant activity of red dragon fruit (*Hylocereus polyrhizus*) peel extract on fibroblast proliferation in the healing process of oral ulcers in wistar rats.

Keywords: Antioxidant Activity, Red Dragon Fruit, Peel, Fibroblast Proliferation

INTRODUCTION

The prevalence of ulcers in the oral reaches 15-30% and tends to be found in women aged 16-25 years, the frequency of

occurrence varies from four to ten times a year (Sunarjo et al., 2015). The 2018 Riskesdas stated that the prevalence of cases of recurrent canker sores was at least 4 times as much as 8% and the prevalence of canker sores that persisted and never recovered for a maximum of 1 month reached 0.9% of all dental and oral health cases (Kementerian Kesehatan, 2019). A wound in the oral called an ulcer is an abnormal condition in the form of a break in cellular continuity in the tissues of living things, generally having a picture of a break in the epithelial tissue and damage to the underlying tissue to form a yellowish-white depression accompanied by an erythema halo when experiencing inflammation (Kang and Kim, 2018).

Ulcer manifestations in the oral can include recurrent aphthous stomatitis (SAR), traumatic ulcers, angular cheilitis, and acute necrotizing ulcerative gingivitis (ANUG) (Sarwono and Suniarti, 2017). Ulcers in the oral are common and commonly encountered in everyday life.

According to the Regulation of the Minister of Health Number 89 of 2015 concerning Dental and Oral Health Efforts, dental and oral health is a state of health of the hard and soft tissues of the teeth and related elements in the oral that allows individuals to eat, speak and interact socially without dysfunction aesthetic disturbances, and

discomfort due to disease, occlusion deviation and loss of teeth so as to be able to live productively socially and economically. Disorders of dental and oral health, such as ulcers/SARs can have a negative impact on a person's quality of life in everyday life such as having difficulty eating and speaking to a decrease in general health, lowering the level of self-confidence, and interfering with performance and attendance at school or work. Noviana conducted research on quality of life with inflammation of the oral mucosa (SAR) and obtained results that SAR had an impact on functional dimensions, psychological dimensions, social dimensions and pain dimensions (Noviana et al., 2018).

Wound healing, for example in ulcers, is a survival mechanism that provides an effort to maintain normal anatomical structure and function (Shetty, 2013). Local factors that can affect the wound healing process are oxygenation, infection, the presence of foreign substances and the presence of blood vessels. While systemic factors that can affect the wound healing process include age, gender, sexual hormones, stress, ischemia, systemic disease, obesity, consumption of drugs, consumption of alcoholic beverages, smoking, immunocompromised conditions and nutrition. The oxygenation factor is a condition that explains oxygen levels needed in the process of wound healing. Oxygen is very important for cell metabolism, especially in producing energy (ATP) which plays a role in almost all wound healing processes (Guo and Dipietro, 2010).

Various kinds of drugs such as antibiotics, immunosuppressants, antiseptics are often used to speed up the wound healing process. Research on the process of wound healing is growing rapidly, including its relation to the role of antioxidants. Antioxidants are compounds that can inhibit oxidation reactions, by binding to free radicals and highly reactive molecules so that cell damage can be inhibited (Darwis and Lubis, 2016).

Scientists continue to try and develop drugs from natural sources such as plants. Plants in nature have secondary metabolites such as alkaloids, flavonoids, tannins, saponins and others which function as a defense mechanism for the plant itself against various unfavorable conditions. These secondary metabolites are reported to have beneficial effects on humans such as antioxidants, antibacterials, antidiabetics and others (Fidrianny al., 2017).

Research on wound healing using natural ingredients derived from plants was also carried out on ulcers in the oral. Apriasari et al. (2015) conducted a study on the effect of 25% Mauli banana stem extract on epithelial thickness in wound healing in the oral of Dawley rats, the results showed that samples treated with 25% Mauli banana stem extract had the same epithelial thickness as the positive control, this was due to the tannins that has antibacterial properties and flavonoids as anti-inflammatory which are contained in Mauli banana stems.

In Indonesia, many studies have investigated natural sources as complementary materials in the wound healing process. Indonesia has a lot of natural resources in the form of plants that can be used as alternative medicinal ingredients, such as red dragon fruit (*Hylocereus polyrhizus*) which is often consumed directly or in the form of juice or other food preparations. Red dragon fruit (*Hylocereus polyrhizus*) is reported to contain several compounds such as flavonoids, phytoalbumin, betacyanin and β -amyryn which have high antioxidant activity. Red dragon fruit can be divided into two parts, namely skin and flesh, with the proportion of skin \pm 22% and flesh \pm 65% (Jamilah et al., 2011). Both parts are reported to contain many polyphenolic and antioxidant compounds, where the red dragon fruit skin is stated to have more content than the fruit flesh.

Several studies using red dragon fruit in the wound healing process include Tahir et al. (2017), they conducted research on the

effect of red dragon fruit extract on granulation tissue and epithelialization in the groin of Wistar rats. The results showed that red dragon fruit extract with a concentration of 7.5% could improve granulation tissue and better epithelialization.

The purpose of this study understands effect of antioxidant activity of red dragon fruit (*Hylocereus polyrhizus*) peel on fibroblast proliferation in the healing process of oral ulcers in wistar rats.

RESEARCH METHODS

This type of research is a quasi-laboratory experiment with a randomized post test only control group design. Laboratory experiments are experimental activities that aim to reveal a symptom or effect that arises as a result of certain treatments (Sugiyono, 2013). The posttest scores are then compared to determine their effectiveness (Afrizal, 2014).

This research will be carried out from May to June 2022, including the preparation of red dragon fruit (*Hylocereus polyrhizus*) peel extract, antioxidant activity tests, making wounds until the time for wound healing, as well as histopathological examination.

The population of are wistar rats bred at Eldwin Laboratory is 300 individuals. Based on the calculation, the total sample in this study is 10 multiplied by 3 so there are 30 samples.

The research ethics in this study include (Tanzeh, 2004):

1.Ethical Clearance

The researcher submitted an approval sheet for conducting research to the health research ethics commission based on international and national ethical provisions.

2.Informed Consent

Consent given to the patient or guardian on the basis of information and explanation regarding the medical action to be performed on the patient.

3.Confidentiality

The data collected in the research will be guaranteed confidentiality by the researcher, therefore the data displayed is in the form of the subject's personal data.

Data analysis is done computerized. The analysis performed is univariate to determine the mean and standard deviation (SD). Sugiyono (2013) furthermore, bivariate analysis, namely Shapiro Wilk test to determine the normality of data distribution, if the data obtained is normally distributed, then the statistical test is continued with one-way ANOVA test, but if the data obtained is not normally distributed then the statistical test is continued with Kruskal Willis test to determine differences in the effectiveness of red dragon fruit (*Hylocereus polyrhizus*) peel extract in all groups.

RESULT

Antioxidant Activity Test of Red Dragon Fruit (*Hylocereus polyrhizus*) Peel Extract
Antioxidant activity testing is carried out by testing the ability of red dragon fruit (*Hylocereus polyrhizus*) peel extract to capture free radicals, namely DPPH solution and compared with a comparison solution in the form of vitamin C.

1.Preparation of 0.5 mM DPPH Solution (200 ppm)

Weighed 9.8 mg of DPPH powder dissolved in methanol up to 50 mL. Obtained DPPH solution with a concentration of 200 ppm.

2.Measurement of the Maximum Absorption Wavelength of DPPH

Pipette 5 mL of the standard dpph solution, put it into a 25 mL volumetric flask, then add methanol up to the mark limit to obtain a solution with a concentration of 40 ppm. The maximum wavelength was measured using a UV-Vis spectrophotometer (400 nm–800 nm). Obtained maximum wavelength 515 nm.

3.Preparation of Test Solution for Red Dragon Fruit (*Hylocereus polyrhizus*) Skin Samples

25 mg of condensed red dragon fruit (*Hylocereus polyrhizus*) skin extract is weighed and dissolved with methanol up to 50 mL, a solution with a concentration of 500 ppm is obtained. Taken 0.35 mL; 0.7 mL; 1.05 mL; 1.4 mL; 1.75 mL of the 500 ppm extract solution, then 1 ml of DPPH solution (200 ppm concentration) is added and methanol is added to the mark limit (5 mL volumetric flask), concentrations of 35, 70, 105, 140, 175 ppm are obtained. Incubated for 30 minutes, then the absorbance was measured using a UV-Vis spectrophotometer at a maximum wavelength of 515 nm.

Figure 1. DPPH Solution and Sample Test Solution



4.Determination of the DPPH Free Radical Trapping Process

Determination of the free radical entrapment process by the test sample using the DPPH free radical entrapment method.

5.Calculation of IC₅₀ Value

Calculation of the results of the DPPH trapping method is to calculate IC₅₀, this value indicates that plant extracts can cause attenuation of as much as 50% of DPPH activity, this can also be seen from the color change of the test sample which is deep purple when added DPPH will turn yellow if the extract has damping. The calculation results are entered into the regression equation with sample concentration (ppm) as the abscissa (X axis) and the percent damping activity value as the ordinate (Y axis).

Figure 2. UV Vis Spectrophotometer Tool



The value of the antioxidant activity of red dragon fruit (*Hylocereus polyrhizus*) peel extract and the IC₅₀ value category as an antioxidant can be seen in Tables 1 and 2:

Table 1. Antioxidant Activity Value of Red Dragon Fruit (*Hylocereus polyrhizus*) Peel Extract

Red Dragon Fruit (<i>Hylocereus polyrhizus</i>) Peel Extract	IC ₅₀ (ppm)	Category
I	140.5836	Currently
II	140.8946	Currently
III	140.7264	Currently
Mean ± SD	140.7349±0.1557	Currently

Table 2. Categories of IC₅₀ Value as Antioxidant

Category	Concentration (ppm)
Very Strong	<50
Strong	50–100
Currently	101-150
Weak	151–200
Very Weak	>200

Differences in the Mean of Fibroblast between Groups on each Treatment Day

Table 3. Differences in the Mean of Fibroblast between Groups on each Treatment Day

Day	Group	Mean ± SD	p-Value
4	I (Red Dragon Fruit Peel Extract 1.9%)	96.33 ± 0.577	0.009*
	II (Red Dragon Fruit Peel Extract 3.2%)	100.33 ± 4.041	
	III (Red Dragon Fruit Peel Extract 7.5%)	114.67 ± 6.351	
	IV (Aloclair Gel)	125.00 ± 2.646	
	V (Base Gel)	82.00 ± 6.245	
7	VI (Red Dragon Fruit Peel Extract 1.9%)	101.67 ± 2.517	0.010*
	VII (Red Dragon Fruit Peel Extract 3.2%)	138.33 ± 14.742	
	VIII (Red Dragon Fruit Peel Extract 7.5%)	155.67 ± 8.505	
	IX (Aloclair Gel)	201.00 ± 32.047	
	X (Base Gel)	114.00 ± 5.196	

*Significant, $p < 0.05$

The results of Shapiro-Wilk test show that some data on mean fibroblast is not normally distributed ($p > 0.05$). Therefore, differences in mean fibroblast between groups on each treatment day are analyzed using Kruskal Wallis test. Table 3 shows that on days 4 and 7, aloclair gel (group) showed the highest mean fibroblast, followed by red dragon fruit peel extract group at 1.9%, 3.2%, 7.5%, and control group negative. The statistical test results showed that there is a significant difference in mean fibroblast between all treatment groups, both on day 4 and day 7 ($p < 0.05$). So in general, the results show that there is an effect of antioxidant activity of red dragon fruit (*Hylocereus polyrhizus*) peel extract on fibroblast proliferation in the healing process of oral ulcers in wistar rats.

CONCLUSION AND SUGGESTION

The results show that there is an effect of antioxidant activity of red dragon fruit (*Hylocereus polyrhizus*) peel extract on fibroblast proliferation in the healing process of oral ulcers in wistar rats. From the results of the research above, the following suggestions can be taken:

1. The results of this study are expected to be the basis for further research.
2. Red dragon fruit (*Hylocereus polyrhizus*) peel extract can be used as an alternative to oral ulcer treatment.
3. It is necessary to carry out further research on variations in the concentration of red dragon fruit (*Hylocereus polyrhizus*) peel extract for a more optimal ulcer healing process.

Declaration by Authors

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