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Jackfruit Leaf as a Natural Sun Stick Protector Through the Inhibition of the MMP-1 Receptor

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Abstract

Sunlight contains ultraviolet radiation, which can cause the formation of free radicals. One of the plants that has the potential to be used as sunscreen is *jackfruit*. This study used two methods, namely in vitro and in vivo. In vitro method was carried out using a spectrophotometric method to analyze the value of the Sun Protection Factor and the in vivo one used the Balb/c strain male white mice, which were divided into three treatment groups. From the research results, it can be reported that the in vitro SPF value at a concentration of 2,500 ppm is 36.62; 5,000 ppm is 38.66; 7,500 ppm is 38.85, and the 10,000 ppm is 38.33, indicating that the average SPF value at each concentration belongs to the ultra-protection category. The in vivo research showed that sticks gave the lowest levels of MMP-1; the results were 3.713 ng/ml of mouse blood serum, lower when compared to other brands of sun sticks with MMP-1 levels of 3.86 ng/ml. The highest MMP-1 level was shown by the results of treatment on a sun-stick basis, namely 4.737 ng/ml. This research aimed to determine the potential of sun stick jackfruit leaf extract as a UV-Protector exposed to UV-B radiation. The results shown above indicate that the *jackfruit*.leaf extract sun stick can inhibit the expression of MMP-1, reflecting its ability as a UV protector because the active compound components.The compound inhibits MMP-1 expression by inhibiting the mitogenic-activated protein kinase (MAPK) pathway.

Keywords: Jackfruit leaves, Natural Sun Stick Protector, MMP-1, UV-Protector

Introduction

Sunlight does not always have a good impact because it can cause various disorders of the skin, and it is known that the spectrum of sunlight that can adversely affect the skin is the ultraviolet (UV) one. Excessive exposure to ultraviolet rays can cause sunburn, erythema, hyperpigmentation, premature aging, and even skin cancer[1,2]. On the surface of the earth, sunlight consists of several spectrums, namely infrared rays (>760 nm), visible rays (400-760 nm), ultraviolet rays (UV) A (315-400 nm), UVB rays (290-315 nm), and UVC rays (100-290 nm), which are very dangerous, have very high energy and are carcinogenic[3]. UV rays make up a small part of the sun's spectrum, but they can be said to be the most harmful to the skin when exposed to them. Due to the reactions they cause, some skin disorders adversely affect human skin in the form of acute changes such as erythema, pigmentation, and photosensitivity, as well as long-term effects in the form of premature aging and skin cancer. Preventing the adverse effects of sunlight can be done by using sunscreen. This compound protects human skin's health from the negative influence of UV rays due to sunlight radiation.

One of the plants that have the potential to be used as a sunscreen ingredient is the jackfruit plant (*Artocarpus heterophyllus* Lamk.). Jackfruit plants are traditionally used to protect farmers from sun exposure by rubbing the leaves directly on their bodies when they plant rice. This practical experience is the basis that jackfruit leaves can act as a UV protector. Some research also says that jackfruit leaves contain nutritious compounds, namely phenols, flavonoids, tannins, saponins, gallic acid, kaempferol, quercetin, morin, tannins in the form of cyanomaclurins and tannins[4–6] which have a role as UV-protectors. Phenolic compounds present in plants can function to protect tissues against damage caused by solar radiation. In a study by Adrianta[7], 4% jackfruit leaf extract cream has almost the same activity as vitamin C in protecting the skin from UV rays. Currently, sunscreens in the form of sticks available in the market are still limited. A stick dosage is an innovative form developed to increase convenience and practicality in its use.

Sun Protection Factor (SPF) is a universal indicator that explains the effectiveness of a product or substance that is UV protective; the higher the SPF value of a product or active sunscreen, the more effective it is at protecting the skin from the adverse effects of UV rays. By knowing and testing this SPF value, the effectiveness of sun stick products can be assessed, which can later be related to MMP-1 levels.

The metalloproteinase matrix constitutes a family of enzymes that can degrade almost every extracellular matrix component. Although some MMP is expressed on the skin of mammals, only three collagenolytic enzymes are MMP-1 (interstitial collagenase) and MMP-8 (neutrophil

collagenase). MMP-1 is the primary mediator against the onset of collagen degradation in photoaging skin. Exposure to ultraviolet light, especially excessive ultraviolet B (UV-B) light, can cause the formation of a free radical, namely Reactive Oxygen Species (ROS), which contributes a lot to the aging process[8]. Activation of the ROS signaling pathway will further affect the secretion of matrix metalloproteinases (MMPs) due to the formed ROS, particularly the synthesis of matrix metalloproteinase-1 or MMP-1, which is responsible for collagen degradation in the skin[8]. MMP-1 is a collagenase enzyme that is most affected by the induction of UV rays from the sun on human skin. The MMP-1 expression will degrade collagen fibrils that maintain skin strength, and elastin fibrils, which maintain skin elasticity. Thus, inhibiting the expression of MMP-1 is one way to prevent premature aging due to exposure to UV rays[9].

This research aimed to determine whether jackfruit leaf extract (*Artocarpus heterophyllus* Lamk.) sun sticks have the potential to act as a UV-Protector in male mice (*Mus musculus*) exposed to UV-B radiation.

Materials and Methods

Materials

The materials used in this study were the leaves of the jackfruit plant (*Artocarpus heterophyllus* Lamk.), 96% ethanol (Bratachem, Indonesia), male mice (*Mus musculus*) aged 6-9 weeks with a body weight of 15-25 grams, and healthy, mice feed. Materials used to make the sun sticks were carnauba wax (Bratachem, Indonesia), cera alba (Bratachem, Indonesia), castor oil, olive oil, BHT (butylated hydroxytoluene) (Bratachem, Indonesia), and methylparaben (Bratachem, Indonesia). All other chemical reagents and solvents were of analytical grade and were used for this research without further purification.

Methods

Preparation of the Jackfruit Leaf Extract

Fresh jackfruit leaves (*Artocarpus heterophyllus* Lamk.) were picked from Bona Village, Blahbatuh District, Gianyar Regency, Bali, Indonesia. The jackfruit leaves were sorted, chopped, and weighed and then dried in a tray covered with a black cloth and not exposed to direct sunlight. Drying was done until the leaves appeared brown and the texture became crunchy. After the leaves were dry, they were sorted and crushed using a blender. The resulting leaf powder was weighed and then put into a glass jar.

The extraction process used 96% ethanol solvent with a ratio of 1:4 in a glass jar and then stirred. The glass jar was tightly closed and wrapped in black plastic. The soaked jackfruit

leaves were stirred after 24 hours, closed again, and wrapped in a dark cloth, protected from light. The soak was stirred again after 24 hours, and filtering was carried out using filter paper. The filtrate obtained was stored in dark glass bottles or wrapped in black plastic. The macerate obtained was added to the solvent again, then the extraction process was repeated for up to two repetitions. The filtrate obtained was concentrated using a rotary evaporator (BUCHI Rotavapor^{TM} R-300) with a temperature of 30-40^{o}C. The thick extract obtained was stored in a tightly closed container and protected from sunlight.

Procedure for Making the Jackfruit Leaves Natural Sun Stick Protector

The ingredients were weighed first according to the formula in Table 1 (made 20 grams). Carnauba wax was put into a vaporish dish and melted over a water bath with Cera alba to a temperature of 80°C (Mixture I). Castor oil and half a portion of olive oil were melted in a water bath at 80°C (Mixture II). BHT and methylparaben were mixed with the remaining half of the olive oil and then poured into mixture II. Then, mixture II was mixed with mixture I while in the water bath. Jackfruit leaf extract was added to the mixture while stirring for approximately 5 minutes. The mixture was removed from the water bath, and stirring continued until the temperature decreased. Then, the mixture was poured into the mold and kept at room temperature for approximately 30 minutes until it hardened to be packaged in a proper container.

Table 1. The formula of Jackfruit Leaf Natural Sun Stick Protector

Ingredient Name	Function	Concentration (%)
Jackfruit leaves extract	Active ingredient	4
Carnauba Wax	Stabilizing agent	5
Cera Alba	Stabilizing agent	10
Castor Oil	Emollient	50
Olive Oil	Emollient	30.85
Butylated hydroxytoluene	Antioxidant	0.05
Methylparaben	Preservatives	0.1

Physical evaluation of the sun stick dosage form

The tests carried out were organoleptic, homogeneity tests, and pH tests. The organoleptic test was carried out by observing the physical appearance in the form of shape, color, and aroma of the sun stick dosage form[10]. The homogeneity test was observed by applying a dose to the object glass to see a homogeneous arrangement and if any coarse particles were visible[10]. The pH test was carried out on a small sample placed on a glass slide. The pH of the dosage form was measured using pH paper at room temperature. The results were compared with color indicators (Macherey-Nagel, Germany) to determine the pH value[11].

Sun Protection Factor (SPF) Analysis Procedure

The method used in this study involved in vitro testing and then continued to in vivo testing. In vitro testing was conducted to analyze the dosage form's Sun Protection Factor (SPF) using the Shimadzu UV 1800 Double Beam Spectrophotometer. Furthermore, in vivo testing was carried out to analyze the Matrix Metaloprotein-1 (MMP-1) levels using the ELISA Smart reader accouris MR9609 T.

Analysis of the SPF value was carried out as follows[12,13]. Samples were weighed for a concentration of 2,500 ppm as much as 250 mg, for a concentration of 5,000 ppm as much as 500 mg, for a concentration of 7,500 ppm as much as 750 mg, and for a concentration of 10,000 ppm as much as 1,000 mg. Each sample was dissolved in 100 ml of 96% ethanol with the help of ultrasonic waves for 5 minutes at room temperature. Then, each solution was filtered and transferred into a 50 ml measuring flask and 96% ethanol was added until the calibration mark. Then 1 ml of solution was transferred thoroughly into a 10 ml measuring flask and diluted with 96% ethanol until the calibration mark. This solution was then filtered, and its absorbance was measured at 290-320 nm wavelength with an interval of 5 nm. The difference in absorption between samples was measured by UV light at a wavelength of 290-320 nm. The absorbance results were recorded, and then the SPF value was calculated. The determination of this SPF value uses the Mansur equation[14], namely:

$$SPF = CFx \sum_{290}^{320} EE\ (\lambda) xI(\lambda) xAbs(\lambda)$$

Information:
CF = Correction factor (10)
EE = spectrum of erythema effect caused by UV rays at wavelengths λ nm.
I = UV light intensity spectrum on wavelength λ nm
Abs = Sample absorbance at wavelengths λ nm.

The EE x I are a constant determined by Sayre et al.[15] and is shown in Table 2.

Table 2. EE × I constant value

Wavelength (λ nm)	EE x I
290	0.0150
295	0.0817
300	0.2874
305	0.3278
310	0.1864
315	0.0839
320	0.0180
Total	**1**

(EE= the spectrum of the effectiveness of erythema; I= UV light intensity spectrum)

Table 3. Sunscreen Effectiveness Based on SPF Value

SPF	Sunscreen Protection Categories
2-4	Minimal protection
4-6	Medium protection
6-8	Extra protection
8-15	Maximum protection
≥15	Ultra-protection

MMP-1 testing procedure

The in vivo test using mice was done considering ethical issues and obtaining a license from the ethics committee of Udayana University, Bali, Indonesia, with the ethical clearance number B/78/UN14.2.9/PT.01.04/2021. Mice were acclimatized to the research environment for seven days.

The mice were randomly divided into three groups, each with ten mice. All groups of mice were shaved on the back. Only the base of the sun stick dosage form was applied to Group 1 (P1), which served as the negative control group. The second treatment group (P2) was a positive control, namely the mice group was smeared with other brands of sunscreen sticks. The third treatment group (P3) was smeared with jackfruit leaf extract sun stick. The sun-stick base, another brand of sunscreen, and jackfruit leaf extract sun stick were applied twice a day, about 20 minutes before UV-B exposure and 4 hours after exposure. All treatment groups were exposed to UV-B light three times a week (Monday, Wednesday, and Friday), wherein the first-week exposure of 50 mJ/cm^2 was given, the second-week exposure of 70 mJ/cm^2 was given, and the third-week exposure of 80 mJ/cm^2 was given. After the last 48 hours of irradiation, the effect of acute irradiation was reduced. All mice were checked for the number of MMP-1 levels as post-test data. A million MMP-1 levels were measured in serum. The serum extraction of mice was carried out by taking blood through the orbital sinuses and then collecting them in Eppendorf tubes. The blood taken was then put into a blood tube containing EDTA and placed at room temperature for 1-2 hours until the blood clotted. Then, the serum (supernatant) was centrifuged for 10 minutes at 3,000 rpm[16]. The results of this study were then analyzed. The test used an enzyme-linked immunosorbent assay (ELISA) colorimetric test kit.

MMP-1 Content Measurement

The microtiter plates provided in this kit have been coated with antibodies specific to MMP-1. The sample was then added to the microtiter plate holes corresponding to the conjugated antibodies specific to MMP-1. Next, the reagent was added to each microplate well and incubated. After the reagent substrate solution was added, only wells containing MMP-1, conjugated biotin antibodies, and conjugated avidin enzymes would show discoloration. The

enzyme-substrate reaction ended with adding a sulfuric acid solution. The discoloration was measured spectrophotometrically at a wavelength of 450nm ± 10nm. The concentration of MMP-1 in the sample was then determined by comparing the sample to a standard curve[17].

Results and Discussion

Natural ingredients contain secondary metabolites known for their antioxidant activity and absorb UV. The resulting side effects are lower than sunscreens that use synthetic active ingredients. In formulations using synthetic ingredients, the problem often faced is allergic reactions on the skin, for example, to amino benzoic acid, which triggers photosensitivity reactions on the skin. In addition, synthetic materials that work by absorbing UV radiation sometimes undergo photodegradation and trigger the formation of free radicals that will cause skin damage. Photoactivation of metal oxides by UV radiation can lead to the formation of ROS, which can be cytotoxic[18]. The formulation of natural sun stick protector with the active ingredient of jackfruit leaf extract was made to be practically used as a sunscreen that has protection activities from UV rays or UV-protector which can help prevent photoaging with inhibition activity of MMP-1.

The physical evaluation result of the sun-stick dosage form

The dosage form was first tested for its physical quality through organoleptic, homogeneity, and pH tests. The result of the dosage form was solid with a dark green color and a smell of jackfruit leaves. This organoleptic observation (Figure 1) is essential to ensure that the pharmaceutical dosage forms follow the original formulation design. In addition, a change in color, smell, and shape indicates the possibility of chemical, physical, or microbiological instability due to microbial activity[19].

The homogeneity test was carried out by looking for the presence or absence of fine and coarse particles. The homogeneity test results on the dosage form of jackfruit leaf extract sun stick concluded that there were no visible particles, both fine and coarse, so they were declared homogeneous (Figure 2). Drug content uniformity is essential to confirm the homogeneity of dispersed drugs throughout the formulation. Homogeneous dosage forms will give good results because the active ingredients are evenly dispersed in the base ingredients, so each part of the dosage form contains the same amount of active ingredients. In the case where the active ingredients are not evenly dispersed in the base ingredients, the active ingredients will not provide a continuous therapeutic effect[19,20].

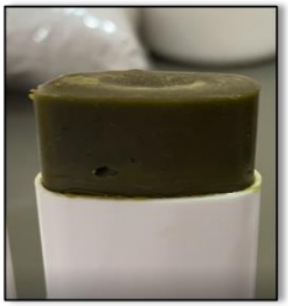

Figure 1. Organoleptic Test Results

Figure 2. Homogeneity

Topical pharmaceutical dosage forms must be manufactured in such a way as to have an appropriate pH, as this may affect the solubility and stability of the active ingredients. It is also essential to know the pH value of the dosage form to see the formula's potential to cause skin irritation because if the dosage form has a pH that is too alkaline, it can cause dry skin. In contrast, if the pH is too acidic, it will cause skin irritation[19-21]. The pH test aimed to determine the safety of the dosage form when used so that it does not irritate the skin[22]. The pH of the dosage form was six, corresponding to the pH range for topical dosage forms, which is between 4.5 - 6.5.

Testing of the SPF Value of the Jackfruit Leaf Extract Natural Sun Stick Protector

The highest SPF value, as shown in Table 4, was at a concentration of 5,000 ppm, which belongs to the ultra-protection category. Nevertheless, according to the sunscreen effectiveness based on the SPF value listed in Table 3, the SPF values of other concentrations also belong to the ultra-protection category. The average SPF value at each concentration was obtained based on the study's results. Namely, at a concentration of 2,500 ppm, an SPF value of 36.62 was obtained (ultra-protection category); for a concentration of 5,000 ppm, an SPF value of 38.66 (ultra-protection category) was obtained; for a concentration of 7,500 ppm an SPF value of 38.35 (ultra-protection category) was obtained; and for a concentration of 10,000 ppm, an SPF value of 38.33 (ultra-protection category) was obtained. The results shown indicated that the jackfruit sun stick protector has the potential to be a UV protector. By having an SPF value, the jackfruit leaf extract sun stick can effectively protect the skin from the adverse influence of UV rays. This is in line with the research of Dutra et al. that the higher the SPF, the more influential the product will be in preventing sunburn[14]. At high concentrations of jackfruit leaf extract sun stick (*Artocarpus heterophyllus* Lamk.), it can be categorized as having ultra-protection. For example, the study of SPF values of lotion dosage forms with a combination of cinnamon extract and pomegranate peel extract in the previous study showed an SPF value of 20.15 at a

concentration of 200 ppm. From the results of the research screening above, cinnamon extract and pomegranate bark extract also contain almost the same secondary metabolites as shown by the jackfruit leaf extract, such as flavonoids which have the potential to be sunscreen. The difference in SPF values obtained is thought to be due to differences in the amount of secondary metabolite content contained in each extract.

Table 4. SPF Value Measurement Results

Dosage Concentration (ppm)	Sun Protection Factor (SPF) value			Average	Sunscreen Protection Categories
	R I	R II	R III		
2,500	36.716	36.44	36.73	36.62	Ultra-protection
5,000	38.71	38.26	39.01	38.66	Ultra-protection
7,500	38.32	38.36	38.38	38.35	Ultra-protection
10,000	38.65	37.99	38.37	38.33	Ultra-protection

Description:
RI, RII, RIII: 1st, 2nd, and 3rd replication

Jackfruit has many beneficial secondary metabolites, and jackfruit leaves are rich in phenolic compounds, such as flavonoids, with good antioxidant properties[23]. Active antioxidant compounds such as flavonoids can increase photoprotective activity. The ability of flavonoids to penetrate human skin is also excellent, so the topical use of flavonoids is believed to increase photoprotection on the skin. In another study conducted earlier[7], it was said that a 4% jackfruit leaf 96% ethanol extract in cream has almost the same activity as vitamin C in protecting the skin from UV rays. The flavonoid group has the potential to be a sunscreen due to the presence of a chromophore group (conjugated single, double bond) which can absorb UV rays, both UV A and UV B, to reduce their intensity on the skin[24]. The characteristic of an ultra-violet (UV) absorbent of flavonoids has long been considered evidence of flavonoids' role in UV protection. Flavonoids are often present in the epidermis skin layer and tissues susceptible to UV rays. About 8% of epidermal cells are melanocytes that produce the pigment melanin (yellow-red or brown-black pigment). This pigment contributes to skin tone and absorbs damaging ultraviolet (UV) rays. Once inside the keratinocytes, the melanin granules cluster to form a protective sheath above the nucleus, in addition to towards the surface of the skin. In this way, they protect the core DNA from UV light damage.

Sunscreen prevents and minimizes the damaging effects of UV rays from sun exposure. Sunscreen works through the absorption of UV energy by converting it into thermal energy, thereby reducing the harmful effects and the depth of UV rays' penetration into the skin[25]. A good sunscreen should be able to absorb the UV spectrum to protect the skin from the adverse effects of UV rays as measured by SPF values.

However, the effectiveness of natural sunscreens is still lagging compared to synthetic sunscreens. The next plan that can be developed is how to process the available natural materials

by specific methods so that natural materials can compete with synthetic materials in terms of their effectiveness. For example, using nanotechnology because of its high efficiency and can increase skin permeability[26]. Another technology that may be able to be developed is *phytosomes*. The word *phytosome* comes from the words "*Phyto*," which means "plant," and "*some*," which means "like a cell." The principle of this technology is that plant extracts are introduced into phospholipids to create complexes of molecules compatible with lipids. It leads to an increase in UV-A and UV-B absorption ability, with high SPF values even though the amount of extract used is small[27].

MMP-1 Level Measurement Results

This research was conducted to determine the UV-protector potential of a natural sun protection dosage form of jackfruit leaf extract (*Artocarpus heterophyllus* Lamk.) as the active ingredient. The mechanism of protecting the skin from UV-B rays is measured by inhibiting matrix metalloprotein-1 (MMP-1) expression in male mice (*Mus musculus*) exposed to UV-B radiation. After treatment for 21 days, an examination of MMP-1 levels in mice (*post-test*) was carried out, and the following results (Figure 3) were obtained.

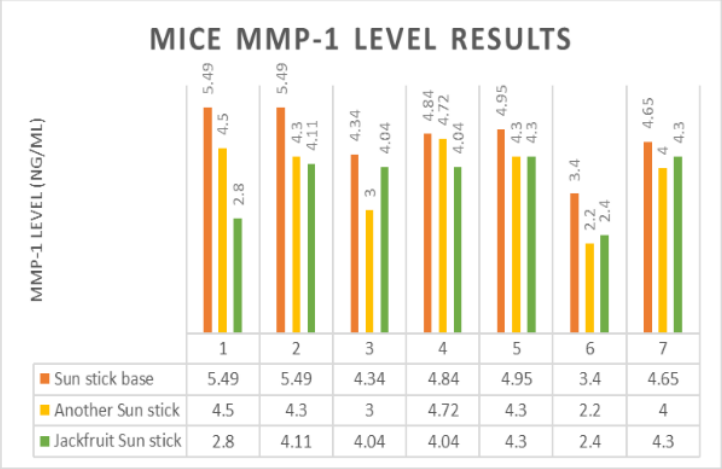

Figure 3. Mice MMP-1 Level Result

The administration of jackfruit leaves indicates the lowest average MMP-1 level, natural sun stick protector dosage forms, which obtained results of 3.713 ng/ml of mice blood serum, lower than other brand sticks with MMP-1 levels of 3.86 ng/ml. The highest MMP-1 levels were indicated by the results of treatment with a placebo base sun stick which was 4.737 ng/ml (Figure 4).

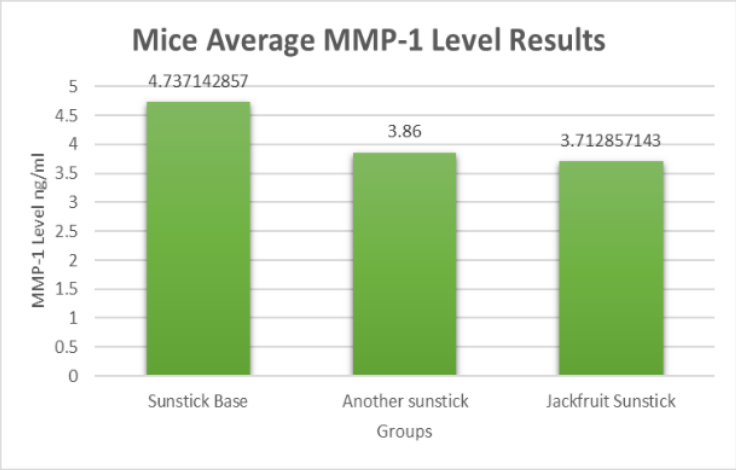

Figure 4. Mice Average MMP-1 Level Result

The analysis of observational data showed statistical results that were not normally distributed and inhomogeneous, then the One-Way Anova Test was rejected; therefore, a non-parametric test was used, namely the *Wallis Kruskal* Test (Table 5). From the analysis data carried out, a *P* value of 0.022 ($p<0.05$) was obtained. From the test results, it can be concluded that "there are significant differences in the results of observations in at least between the two treatment groups." The results of the *Kruskal Wallis* Test were followed by a *post hoc* test to determine the differences between treatment groups against the average necrosis of liver cells. The results of *the Mann-Whitney post hoc* test between treatment groups on average MMP-1 levels are the following. In the P1 group (sun stick basis) and the P2 group (another brand of sun stick), there are significant differences due to the value of $p<0.05$. In the P1 group (sun stick basis) and the P3 group (jackfruit leaf extract, natural sun stick protector), there are significant differences due to the $p<0.05$ value. The P2 group (another brand of sun stick) and the P3 group (jackfruit leaf extract sun stick) did not have any significant differences due to the $p>0.05$ value. The comparative test results in Table 6 show significant differences between several groups, namely P1 with P2 and P1 with P3. At the same time, P2 and P3 have no significant differences.

Table 5. *Kruskal Wallis* Non-Parametric Alternative Test Results

Group	N	Average Ratings	p
P1 (Sun Stick Protector Basis)	7	16.14	
P2 (Another Sun Stick Protector)	7	9.43	0.022
P3 (Jackfruit Sun Stick Protector)	7	7.43	

Table 6. Comparative Test Between Treatment Groups to MMP-1 Levels

No	Comparison Between Groups		P-value	Information
1	P1	P2	0.035	Significant differences
		P3	0.012	Significant differences
2	P2	P3	0.477	No Significant difference

Description:
P1: Sun Stick Base
P2: Another Brand of Sun Stick
P3: Jackfruit Leaf Extract Sun Stick

The Role of Natural Sun Stick Protector with Jackfruit Leaf Extract Against MMP-1 Levels

From the results of measuring MMP-1 levels in mice that have been carried out, the application of the sun stick with jackfruit leaf extract influences the inhibition of matrix metalloprotein-1 (MMP-1) production, which has been exposed to UV-B rays. Based on the data listed in Table 6, the effect of MMP-1 inhibition from jackfruit leaf extract sun sticks (P3) was not significantly different from MMP-1 inhibition by other brands of sun sticks on the market (P2) (p value> 0.05). The administration of the jackfruit sun stick indicates the lowest average MMP-1 level leaf extract, a result of 3.713 ng/ml of blood serum mice, lower when compared to other brands of sun sticks with MMP-1 levels of 3.86 ng/ml. The highest MMP-1 levels were shown by the results of treatment with a sun stick base of 4.737 ng /ml. The results show that jackfruit leaf extract sun sticks can inhibit the expression of MMP-1, reflecting the ability as a UV-Protector.

Inhibition of MMP-1 expression results in inhibition of collagen degradation so that it does not cause photoaging due to exposure to UV-B light. Matrix Metalloprotein, or MMP, is a proteinase enzyme that contains zinc and degrades matrix proteins such as collagen[8]. UV radiation from the sun can directly increase the activity of MMP. MMP-1 is most affected by the sun's UV induction in human skin. It is responsible for collagen damage to the skin of the reticular stratum in the dermis. It triggers photoaging or premature aging due to exposure to UV rays[9]. MMP-1 is the primary mediator for the onset of collagen degradation in the skin. MMP-1 degrades the fibrils of collagen and elastin, which are essential for the strength and elasticity of the skin. The activity of MMP-1 in the skin will increase even with only a short UV radiation, which will cause wrinkles on the skin which is a sign of premature aging due to UV rays or photoaging. Thus, inhibiting MMP-1 is one way to prevent skin damage due to exposure to UV rays[8].

In this study, the induction of UV-B rays was carried out using a UV lamp device. The experimental animal, namely a mouse, numbered 21, had shaved hair on the back. Then it was exposed to UV-B light three times a week, where in the first-week exposure of 50 mJ / cm^2 was given, in the second-week exposure of 70 mJ/cm^2 was given, and in the third-week exposure of

80 mJ/cm^2 was given. The experimental animal was left at room temperature after the last 48 hours of irradiation to avoid the influence of acute irradiation. Blood serum was then taken from the experimental animal to see MMP-1 levels using an enzyme-linked immunosorbent assay (ELISA) colorimetric test kit. ELISA is a technique performed to detect the presence of an antibody or antigen in a sample. In addition to detecting, it can also quantitatively calculate the level of antigens or antibodies in a sample examined by spectrophotometry methods[17]. MMP-1 expression can be measured in blood serum[28,29]. The increase in MMP-1 levels due to UV-B induction occurred indicative of the high levels of MMP-1 in the basis-only treatment group compared to other treatment groups. The group treated with another brand of sun stick and that treated with the natural sun stick protector with jackfruit leaf extract had lower MMP-1 levels. The lower MMP-1 levels reflect the inhibition of MMP-1 expression so that collagen degradation does not occur so that photoaging can be avoided. This was in line with previous research by Liliana et al. [8]. It is known that the decrease in MMP-1 levels is inversely proportional to the amount of collagen on the skin.

In the mechanism of collagen degradation, Reactive Oxygen Species (ROS) have a prominent role in increasing the expression of MMP-1. ROS is a free radical that has one or more unpaired electrons and is highly reactive. Increased ROS levels directly cause tissue damage through a series of molecular processes, such as modifying cellular proteins, lipids, and DNA. ROS is formed due to exposure to UV rays, especially UV-B, which has enormous energy and wavelength. The ROS formed will activate the mitogen-activated protein kinase (MAPK) pathway, conveying information on transcription factors in photoaging, namely nuclear factor kappa β (NF-kβ)[30]. Activation of this transcription factor will spur the expression of various metalloproteinase matrix enzymes (MMPs). One of the most expressed is the MMP-1. Increased expression of MMP-1 will specifically degrade collagen and further cause photoaging[31]. So, a compound is needed that can inhibit the expression of MMP-1.

As mentioned before, jackfruit (*Artocarpus heterophyllus* Lamk.) is a plant that has many beneficial secondary metabolites. Secondary metabolites in jackfruit leaves include phenolic compounds, flavonoids, tannins, saponins, gallic acid, kaempferol, and quercetin[32]. Jackfruit leaves are rich in phenolic compounds such as flavonoids with good antioxidant properties[23]. Flavonoids are a group of phenolic compounds that have a basic carbon framework consisting of 15 carbon atoms that form the C6-C3-C6 arrangement, which has a role as an antioxidant[33]. The antioxidant mechanism of flavonoids is to capture ROS[34]. Flavonoids can have an antioxidant effect by donating their electrons to oxidants, thus neutralizing free radicals[22].

In addition, kaempferol and quercetin inhibit MMP-1 expression by inhibiting the mitogen-activated protein kinase (MAPK) pathway. The inhibition of the MAPK path significantly inhibits the expression of MMP-1. This happens because MAPK has a function to convey information that activates photoaging transcription factors, namely nuclear factor kappa β (NF-kβ)[30]. NF-kβ is a promoter in the nucleus that spurs the expression of a wide variety of MMPs; one of the most induced by UV is MMP-1. In inhibiting MMP-1 and lowering the regulation of MMP-1, flavonoids can block collagen damage in certain pathological conditions, for example, when exposed to sunlight. Therefore, natural flavonoids in plants help treat some inflammatory skin disorders and protect the skin from premature aging. These results show that natural flavonoids have the potential to inhibit MMP-1 and decrease MMP-1 expression[35].

Conclusion

Natural sun stick protector dosage forms of Jackfruit Leaf (*Artocarpus heterophyllus* Lamk.) have potential as a UV-protector through inhibition of matrix expression of metalloprotein-1 in male Balb/c mice exposed to UV-B light radiation with MMP-1 levels of 3.713 ng/ml and has the potential as a Photoprotector with an ultra-protection category with the best SPF value of 38.66.

Conflict of interest

The authors declare there is no conflict of interest.

Authors' Declaration

The authors with this declare that the work presented in this article is original and that they will bear any liability for claims relating to the content of this article.

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