



## ORIGINAL ARTICLE

## Formulation, Physical Characteristics, and Irritation Test of Soothing Gel Combination from *Aloe vera* gel and Dragon Fruit Juice

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### ABSTRACT

Dry skin is often causes of several problems in skin health. People pay less attention to symptoms caused such as redness, roughness, scaling, cracking, and itching. Factors that cause dry skin include temperature, air humidity, and exposure to ultraviolet light. Soothing gel that contains of high concentration active ingredients is one of cosmetic products that are trending in Korea. In this study, the combination of aloe (*Aloe vera*) and dragon fruit (*Hylocereus polyrhizus*) was used as active ingredients. The aim of this study was to determine the phytochemical screening of active ingredients, physical characteristic, and measuring irritation index on animal test. Formulation of soothing gel preparation was made by varying concentration of active ingredients, that is, FI (85%), FII (90%), and FIII (95%). The data obtained were analyzed by statistical with a different 95% confidence level a significant difference between treatment groups. Phytochemical screening confirmed the presence of alkaloid, flavonoid, terpenoid, and saponin (negative results in dragon fruit juice) in each juice. The result of physical characteristic showed that the concentration of active ingredient affect pH, spreadability, and adhesion power ( $P < 0.05$ ). Meanwhile, the result of measuring irritation index was showed that none of the formulas caused erythema and edema at 24, 48, and 72 h observed time.

**Keywords:** Dragon fruit juice, Irritation index, Physical properties, Soothing gel combination.

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### INTRODUCTION

The skin is the outermost part of the human body that functions to protect the body from the surrounding environment. Based on the water and oil content contained in the skin, the skin is generally divided into three, namely, normal skin, dry skin, and oily skin. Normal skin is skin that has high water content and low oil content, while oily skin has high water and oil content.<sup>[1]</sup> Dry skin is skin that contains low water content, causing skin moisture to decrease.<sup>[2]</sup> The problem that is often encountered by people, especially in tropical countries like Indonesia, is dry skin. Dry skin is caused by several factors including temperature and humidity, exposure to chemicals, aging, physiological, and genetic stress.<sup>[3,4]</sup> Dry skin can reduce the body's defense performance against infections and the effects of free radicals that occur due to ultraviolet (UV) which is a source of free radicals and can be prevented by compounds classified as antioxidants. Antioxidants are chemical compounds that can neutralize free radicals that were initially active to become relatively stable reactive so that it can protect biological components such as lipids, proteins, vitamins, DNA, and inhibit or prevent oxidation of the substrate caused by free radicals.<sup>[5]</sup>

One of the medicinal plants that thrive in tropical countries has antioxidant properties, namely, aloe (*Aloe vera*). *A. vera* contains secondary metabolite compounds

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such as anthraquinone, lignin, tannins, saponins, sterols, and flavonoids.<sup>[6,7]</sup> *A. vera* plant has therapeutic potential in topical use, namely, for anti-inflammatory, antioxidant, anti-antibiotic, antimicrobial, burns and wound healing, skin hydration, protecting the skin from UV rays, and radiation.<sup>[8-10]</sup>

Other plants original from tropical climates and have antioxidant activities, namely, dragon fruit (*Hylocereus polyrhizus*).<sup>[11]</sup> Dragon fruit (*H. polyrhizus*) often referred to as red pitaya has a red skin surrounded

by green fins with red flesh, and has its own advantages because the flowers of this dragon fruit plant always appear at any time so that production each season is always abundant.<sup>[12]</sup> Dragon fruit (*H. polyrhizus*) contains ascorbic acid compounds, anthocyanins, flavonoids, and polyphenols. These compounds have antioxidant activity to bind to free radicals and can be used as basic ingredients (active substances) of anti-aging cosmetics.<sup>[13-15]</sup>

Soothing gel is a form of semi-solid pharmaceutical preparation and is used topically or applied to the surface of the skin. Soothing gel is formed by a hydrophilic polymer network that has the ability to swell by absorbing water or biological fluids but do not dissolve due to the presence of cross.<sup>[16-18]</sup> Soothing gel is widely used in pharmaceutical preparations because it has a good dispersion on the skin, besides that soothing gel has a cold effect when used because of the slow evaporation of water on the skin, does not inhibit the skin pores, easily washed with water, and allows it to be used on hairy skin.<sup>[19]</sup>

An important parameter that needs special attention is the possibility of skin irritation. Irritable skin can be characterized by erythema and edema. Erythema or redness is caused due to dilatation of blood vessels in the irritated area, whereas edema is caused due to enlargement of plasma which is frozen in the injured area and is accelerated by the presence of fibrous tissue.<sup>[20]</sup> In addition, the parameter that is no less important is the physical nature of the preparation. The choice of gelling agent will affect the physical properties of the preparation. Gelling agents are various types, which are generally used, namely, hydroxypropyl methylcellulose (HPMC) and carbomer.<sup>[21]</sup>

Based on this background, this study was conducted to determine the characteristics of the preparation by formulating a combination of *A. vera* and dragon fruit using HPMC and carbomer as a gelling agent. The combination of aloe and dragon fruit was chosen because both plants have the same content, namely, flavonoids so that the antioxidant activity produced is more optimal. This formulation aims to make a soothing gel and to know the effect of the preparation on the potential irritation that occurs such as erythema (redness) and edema (swelling) that arise on the skin of mice used as experimental animals.

## MATERIALS AND METHODES

The ingredients used in this research were *A. vera* leaf (*A. vera*) and dragon fruit meat (*H. polyrhizus*) and other suitable excipients for soothing gel preparation such as carbomer, HPMC, propylenglicol, glycerin, carbomer, HPMC, propylenglicol, glycerine, TEA, and methylparaben.

### Preparation of *A. vera* and Dragon Fruit Juice

The leaves of *A. vera* plant and dragon fruit are obtained in Tulungagung region East Java. To obtain *A. vera* juice, *A. vera* leaves were collected, washed with water, skinned, then removed the inner gel and separated with a spoon, minced and mashed using a blender then filtered to resemble a gel. Dragon fruit juice was obtained by collected, washed dragon fruit with water, taken the flesh of fruit by separating between the flesh and the skin of fruit, minced, and mashed using a blender and filtered to obtain the juice.

### Phytochemical Screening on *A. vera* and Dragon Fruit Juice<sup>[22]</sup>

*A. vera* juice and dragon fruit juice were analyzed for the presence of alkaloids, flavonoids, saponins, tannins, and terpenoids using standard procedures of analysis.

#### Phytochemical screening of alkaloid

To each 1 mL of juice is added with a few drops of Wagner reagent, a positive reaction if brown deposits are formed and negative if a color change occurs. A sample of 1 mL was added with two drops of Mayer reagent solution, a positive reaction marked by the formation of white or yellow lumpy deposits.

#### Phytochemical screening of flavonoids

To each 2 mL of juice was added to Mg powder and five drops of concentrated HCl. The presence of flavonoid compounds is indicated by the formation red or orange.

#### Phytochemical screening of saponins

To each 3 ml of juice is put into a test tube, and then added 10 mL of hot water, cooled, and shaken vigorously for 10 s. If the foam formed as high as 1–10 cm, which is stable for not <10 min indicates the presence of saponins.

#### Phytochemical screening of tannins

To each 1 mL of juice added two drops of FeCl<sub>3</sub> 1% drop by 3 mL. If there is a blackish blue or blackish green indicates tannin.

#### Phytochemical screening of terpenoids

To each 2 ml of juice was added with three drops of concentrated HCl and one drop of concentrated H<sub>2</sub>SO<sub>4</sub>. If each solution is formed red or purple, then positively contains terpenoids.

### Preparation of Soothing Gel Combination from *A. vera* gel and Dragon Fruit Juice Preparations

The soothing gel combination of *A. vera* and dragon fruit was made in three formulations with different concentrations of active substances, namely, formulation

I (85%), formulation II (90%), and formulation III (95%). The formulation of soothing gel is shown in Table 1.<sup>[24]</sup>

### Preparation of Soothing Gel Combination from *A. vera* gel and Dragon Fruit Juice<sup>[23,24]</sup>

To prepare soothing gel, the gel base is made by developing carbomer with a mixture of *A. vera* juice and distilled water and HPMC using a mixture of dragon fruit juice and distilled water, then mixed with other ingredients such as glycerin, propylene glycol, TEA, nipagin, nipasol, and slowly crushed to form a gel base.

### Physical Characteristic Test of Soothing Gel Combination from *A. vera* Gel and Dragon Fruit Juice

#### Organoleptic test

Organoleptic characterization is carried out using the five senses. The samples from the preparations are taken, and then the shape, color, and odor are observed.

#### Homogeneity test

Soothing gel is applied to a piece of glass, and then observed that is not mixed. Homogeneity is indicated by the absence of coarse grains.<sup>[24]</sup>

#### pH test

PH characterization was carried out using a pH meter. The pH meter is dipped in a diluted gel. The pH of the preparation meets the standard if it meets the skin's pH criteria, which is 4.5–6.5.<sup>[20,24]</sup>

**Table 1:** Formulation of soothing gel combination from *Aloe vera* gel and dragon fruit juice

Material	Concentration (%)		
	F1	F2	F3
<i>Aloe vera</i> extra	42.5	45	47.5
Dragon fruit juice	42.5	45	47.5
Carbomer	1	1	1
HPMC	2	2	2
Propylene glycol	0.6	0.6	0.6
Glycerin	0.4	0.4	0.4
TEA	0.1	0.1	0.1
Nipagin	0.05	0.05	0.05
Nipasol	0.05	0.05	0.05
Essence	qs	qs	qs
Aquadest	ad 100	ad 100	ad 100

HPMC: Hydroxypropyl methylcellulose

#### Adhesion test

Weighed a dosage of 0.5 g soothing gel placed on top of the slide and then covered with other slide, was given a 50 g load for 1 min, then pulled with a weight of 80 g, recorded the time until both of the slides were released. Adhesion requirements for topical preparations are not <4 s.<sup>[25]</sup>

#### Spreadability test

A total of 0.5 g of soothing gel was placed on a glass with a diameter of 7 cm; the other glass was placed on it and left for 1 min. The diameter of the spread of the soothing gel was measured after 1 min, then a load of 50 g, 100 g, 150 g, 200 g, and 250 g was allowed to stand for 1 min then a constant diameter was measured.<sup>[26]</sup> Good spreadability is used for semi-solid preparations ranging in diameter from 3 cm to 5 cm.<sup>[27]</sup>

#### Experimental Animals

Test animals used in this study were using male white rats (*Rattus norvegicus*) with ± BB 200 g, 6–8 weeks old; there were no anatomical or physiological abnormalities. The institutional ethical committee of Institut Ilmu Kesehatan Bhakti Wiyata (No: 130/PP2M-KE/II/2019) approved method of this study for handling and care experimental animals. This protocol for handling and care was according to the international guidelines of the National Research Council.<sup>[28]</sup>

#### Irritation test

The irritation test was carried out using three mice as experimental animals. The gels tested are gels containing bases, F I, F II, and F III. The acclimated mice each had their hair shaved on the back. After 24 h, the test material is applied, covered with gauze and plaster, allowed to stand for 24 h. After 24 h, open and rinse with water. The parameters observed were erythema and edema by Draize Test.<sup>[27]</sup> The surface of the skin is observed for any visible changes such as erythema (redness) and edema (swelling) after 24, 48, and 72 h of application formulation.<sup>[28]</sup> The data obtained were analyzed to obtain a primary irritation index (PII). PII value is used to determine the level of irritation, presented in Table 2. Categories skin values after observation are seen based on Table 3.<sup>[29]</sup> The following formula for PII is as follows:

$$PII = \frac{\text{The sum of all erythema and edema values at the time of observation}}{\text{The number of animals tested} \times \text{The amount of time observed}}$$

#### Statistical Analysis

The result of pH test, spreadability test, and stickiness test obtained in this study was analyzed using the Shapiro–Wilk normality test and homogeneity with the Levene Test first.

Data that are normally distributed, variations between homogeneous samples, and unrelated variables need to be done with the one-way ANOVA method (one-way analysis of variance) and *post hoc* LSD, whereas if the data are not normally distributed the Kruskal–Wallis method are used. The statistical significance of differences among groups formulation of soothing gel was evaluated.  $P < 0.05$  was considered as significant difference. Meanwhile, organoleptic test, homogeneity test, and phytochemical screening result were carried out by qualitative descriptive analysis. The irritation index test was analyzed by calculating the scoring of erythema and edema in test animals.<sup>[29]</sup>

## RESULTS AND DISCUSSION

### Extraction of *A. vera* and Dragon Fruit Juice

*A. vera* and dragon fruit juice which is used as active ingredients in soothing gel preparation was obtained by mesh and blend then squeeze.<sup>[30]</sup> These method was chosen because this method does not involve heating so there is no temperature factor that affects the active compounds in *A. vera* plants and dragon fruit and is also an easy method to do and uses relatively simple equipment.

### Phytochemical Screening of *A. vera* and Dragon Fruit Juice

Phytochemical screening of *A. vera* juice and dragon fruit was carried out to determine the compound

content of *A. vera* juice and dragon fruit by conducting alkaloid, flavonoid, tannin, saponin, and terpenoid tests. Phytochemical screening results on positive *A. vera* extract contain alkaloids, flavonoids, saponins, and terpenoids, and dragon fruit shows positive results containing alkaloids, flavonoids, and terpenoids [Table 4].

### Result of Physical Characteristic of Soothing Gel Combination from *A. vera* and Dragon Fruit (*H. polyrhizus*)

#### Organoleptic test

Organoleptic test of the soothing gel combination of *A. vera* and dragon fruit FI (85%), FII (90%), and FIII (95%) was performed visually, including the shape, color, and smell of the preparation. The results of the organoleptic test FI (85%) preparations were semi-solid, pink, and distinctive odor of dragon fruit, FII (90%) preparations were semi-solid, red, and distinctive odor of dragon fruit, and FIII (95%) dosage form semi-solid, deep red color, and the characteristic smell of dragon fruit [Table 5]. The results obtained show that the higher the concentration of the active substance, the dosage form becomes rather runny, the dosage color will be more concentrated, and the odor of the preparation is more typical of dragon fruit.

#### Homogeneity test

Homogeneity test of the soothing gel combination of *A. vera* and dragon fruit FI (85%), FII (90%), and FIII (95%) was carried out using glass slide to determine the components of the preparation [Table 6]. The results of the homogeneity test FI (85%), FII (90%), and FIII (95%) did not show any coarse grains that were seen visually so that the soothing gel FI (85%), FII (90%), and FIII (95%) has a homogeneous arrange. Homogeneous soothing gel preparations will give good results when applied to the skin and produce an optimal therapeutic effect.

#### pH test

The pH test of the soothing gel combination of *A. vera* and dragon fruit FI, FII, and FIII was carried out using

**Table 2:** Response and irritation categories

Category	Primary irritation index
Does not mean	0–0.4
Slight irritations	0.5–1.9
Medium irritation	2–4.9
Severe irritations	5.0–8.0

**Table 3:** Skin state value categories

Erythema		Edema	
Type	Value	Type	Value
There is no erythema	0	There is no edema	0
Little erythema	1	Very mild edema	1
Erythema is evident	2	Mild edema (edge and clear enlargement)	2
Moderate to strong erythema	3	Medium edema (thickness ± 1 mm)	3
Severe erythema	4	Severe edema (thickness > 1 mm)	4

**Table 4:** Result of phytochemical screening

Phytochemical	<i>Aloe vera</i> juice	Dragon fruit juice
Alkaloid	+	+
Flavonoids	+	+
Saponins	+	–
Tannins	–	–
Terpenoids	+	+

**Table 5:** Result of soothing gel organoleptic test

Formulation (%)	Shape	Color	Smell
I (85)	Semi-solid	Pink	Dragon fruit
II (90)	Semi-solid	Red	Dragon fruit
III (95)	Semi-solid	Deep red	Dragon fruit

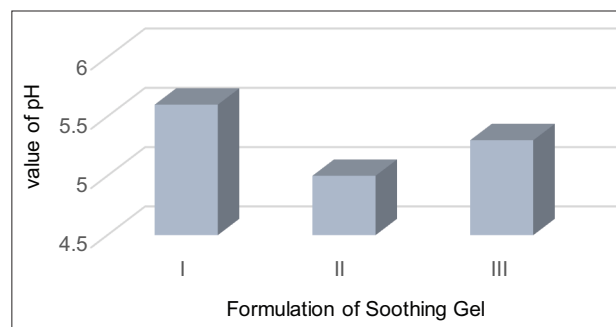
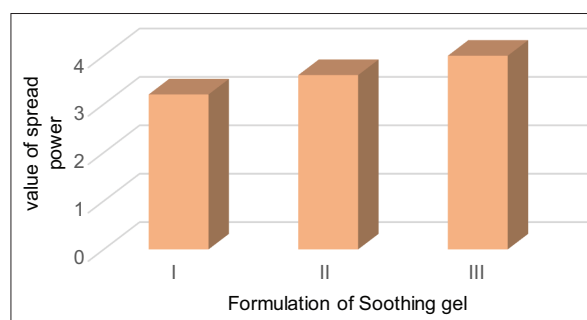
**Table 6:** Result of soothing gel homogeneity test

Formulation (%)	Homogeneity
I (85)	Homogeneous
II (90)	Homogeneous
III (95)	Homogeneous

a pH meter. The results of the pH FI test (85%) obtained an average of 5.6 out of three repetitions, FII (90%) obtained an average of 5.0, and FIII (95%) obtained an average of 5.3 [Figure 1]. Based on statistical analysis showed that significance level is 0.006 when  $P < 0.05$  it's mean that different concentration of active ingredients in each formula affect pH of soothing gel. The pH value of the soothing gel FI (85%), FII (90%), and FIII (95%) is still in the normal skin pH range of 4.5–6.5 so that the soothing gel combination of *A. vera* and dragon fruit meets the requirements and does not cause irritation, thereby increasing the comfort of the preparation when used.<sup>[20,24]</sup> The pH test aims to determine and adjust the acid-base properties of the soothing gel with the pH of human skin for topical use, because this is related to the safety and comfort of the preparation when used, if it is not in accordance with the pH of the skin, the preparation can cause irritation, other than that the pH also must be in accordance with the active substance, if the pH is too acidic or too alkaline it will affect the active substance which causes the active substance to be damaged so that the desired effect cannot be achieved.

#### Spreadability test

The results of the measurement of the distribution of FIs (85%) obtained an average of 3.2 out of three repetitions, FII (90%) obtained an average of 3.6, and FIII (95%) obtained an average of 4.0 [Figure 2]. The spread test results of the formulas were meet the requirements. All formulas show significant difference in spreadability test based on statistical analysis ( $P < 0.05$ ). It means concentration of active ingredients influence spread power of soothing gel.

**Figure 1:** Result of soothing gel pH test**Figure 2:** Result of soothing gel spreadability test

The spread test aims to determine the ability of the spread of aloe gel and dragon fruit soothing gel at the location of use when applied to the skin. Good spreadability is used for semi-solid preparations ranging in diameter from 3 cm to 5 cm.<sup>[26]</sup> The results obtained indicate that the higher the concentration of the active substance, the greater the dispersal power of the preparation, because the water content is greater so that the preparation is thinner and has a wider spread range. The dispersion power affects the diffusion rate of active substances in through the membrane. The wider the membrane where the preparation is spread, the greater the diffusion coefficient resulting in increased drug diffusion, so the greater the spread of the preparation, the better.<sup>[31,32]</sup>

#### Result of Adhesion Test

Adhesion test aims to find out how long the preparation sticks to the skin in a certain time so that it can function optimally in the delivery of active substances. The ability of adhesion is inversely proportional to the ability of spreadability; soothing gel preparations with low spreadability have high adhesion. High adhesion affects the absorption of the preparation because the longer the contact with the skin, the maximum absorption will be so that the expected therapeutic effect can be achieved. There are no specific requirements regarding the adhesion

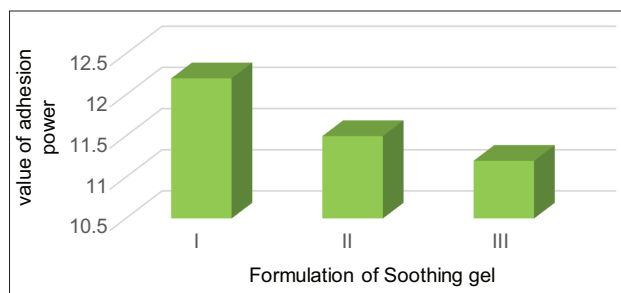


Figure 3: Result of soothing gel adhesion test

of semisolid solids, but the good adhesion requirements for topical preparations are not  $<4$  s.<sup>[25]</sup> The results of the FI adherence test (85%) obtained an average of 12.22 from three repetitions, FII (90%) obtained an average of 11.48, and FIII (95%) obtained an average of 11.23 [Figure 3]. Based on analysis by one-way ANOVA showed significance level is  $0.000 < 0.05$  it's mean that that there are significant differences in each formula. The results of the adhesion test of the formulas meet the requirements. The results obtained show that the higher the concentration of the active substance the smaller the stickiness of the preparation, because the water content is greater so that the time to attach to the preparation is shorter. The higher sticking power will increase viscosity but decrease the spreadability because the soothing gel preparation is more restrained to flow and spread on the skin.<sup>[28]</sup>

The relationship between spreadability and sticking power, that is, the greater the sticking power, the lower the spread power, because both of them have the ability to be inversely proportional. The greater the value of the dispersal power, the more surface area that can be reached by the preparation, but it reduces the ability of adhesion so that the ability of the soothing gel to adhere to the skin does not last long.

#### Result of irritation test

The irritation test is used to determine the soothing *A. vera* gel and dragon fruit irritate or not when used. Irritation is characterized by the emergence of erythema and edema.<sup>[20]</sup> The irritation test was carried out using three white rat animals. Each animal was given five treatments including base control (+), control (-), FI (85%), FII (90%), and FIII (95%). The test results did not cause irritation in three white rats that were given a sample of soothing gel for 24 h that were covered with plaster and observed for 72 h [Table 7]. The level of irritation is calculated based on the PII.

The results of the calculation of PII can be concluded that the preparation of soothing gel combination of *A. vera* and dragon fruit does not cause irritation because of the calculation of PII obtained results 0 which are included in

Table 7: Result of soothing gel irritation test

Test group	Result of irritation index		Average±SD
	Erythema value	Edema value	
Control (-)	0	0	0
Base control (+)	0	0	0
FI (85%)	0	0	0
FII (90%)	0	0	0
FIII (95%)	0	0	0

the category of irritation response is not significant (does not cause irritation).

#### CONCLUSION

From the results of the research that has been carried out, we concluded that concentration active ingredients of combination of *A. vera* and dragon fruit in all formulas influenced on the physical characteristic of soothing gel preparations. Physical characteristic of FI, FII, and FIII already has range that meets the requirements for the preparation of semi-solid. Soothing gel combination of *A. vera* and dragon fruit does not provide any potential irritation to the skin; because the irritation index score results are 0.

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