International Journal of Health Sciences
Available online at www.sciencescholar.us
E-ISSN: 2550-696X
Int. J. of Health Sci.
DOI: 10.53730

How to Cite:
Mayorga, A. H., Kuncahyo, I., & Saptarini, O. (2025). Optimization of gel formula from active fraction of manggost fruit (Garcinia mangostana. L) and antibacterial activity test against Staphylococcus epidermidis. *International Journal of Health Sciences*, *9*(S1), 120–160.
https://doi.org/10.53730/ijhs.v9nS1.15577

Optimization of gel formula from active fraction of manggost fruit (Garcinia mangostana. L) and antibacterial activity test against *Staphylococcus epidermidis*

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***Abstract*---**The purpose of this study was to determine the antibacterial activity of the ethyl acetate fraction of mangosteen peel and the effect of the combination of Carbopol, HPMC, and Propylene glycol as humectants on physical properties and antibacterial activity. The results of the fractionation of the extract were tested on Staphylococcus epidermidis bacteria using the diffusion method, the ethyl acetate fraction which had antibacterial activity with a concentration of 10% was made into a gel preparation with the composition of carbopol, HPMC, propylene glycol with run 14 obtained by the Simplex Latice Design method. The physical quality test of the preparation was carried out, namely organoleptic test, homogeneity,

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Submitted: 09 November 2024, Revised: 27 January 2025, Accepted: 18 February 2025

pH, adhesion, spreadability, viscosity, and antibacterial activity. Test data for physical quality and antibacterial activity analyzed using the Simplex Latice Design method, after which the analyzed using the Simplex Latice Design, and statistics using SPSS with the One Way Anova test. The results of the study stated that the ethyl acetate fraction of mangosteen peel can be made into mangosteen peel gel preparations for concentrations of Carbopol 94 1.5 g, HPMC 1000DB 2.5 g, propylene glycol 5 g with a spreadability value of 4.35 cm, viscosity 433.33, antibacterial 21, 4mm.

***Keywords*---**Ethyl Acetate Fraction, Optimum Formula, Antibacterial, Simplex Lattice Design

Introduction

Acne is an abnormal skin condition caused by excessive production of sebaceous glands. Acne can often cause skin irritation (swelling and redness of the skin), acne is also a skin disease that often occurs in adulthood. The sebaceous glands are very active in this area so that the formation of acne is caused by sebum hair follicles on the head and upper body.Blocked pilosebaceous follicles When blocked sebum does not come out, sebum accumulates, and hair follicles swell (Tranggono, 2007). The main factors involved in the formation of acne are bacterial growth, inflammation, keratinocyte release, and increased sebum production. Microorganisms or bacteria involved in the pathogenesis of this disease are bacteria such as Staphylococcus epedermidis and Propionibacterium acne by producing metabolites that can react with sebum to increase the inflammatory process. So far, there are several very useful methods, but there is no complete cure for acne. Acne treatment can also use antibiotics as a solution for acne treatment which is still widely prescribed. However, although this prescription drug has side effects such as irritation when used as an anti-acne drug, long-term use of antibiotics can cause not only immunosensitivity but also organ damage and resistance (Joshita, 2009).

There are two types of treatments that can be used to treat acne, namely, use topical treatments that can be applied directly to the acne area and produce local effects, and use oral methods to treat acne in the acne area. The use of topical acne medication is considered less effective because it only treats the area treated with anti-acne medication. The mechanism of action of local drugs only reduces the lesions caused (Dinar and Mita, 2017). Natural ingredients can be used as a substitute for antibiotics for acne treatment.

One of the natural ingredients that is an antibiotic for treating acne caused by Staphylococcus epidermidis bacteria is mangosteen. The use of mangosteen as a traditional medicine has been studied by scientists. One example is a study conducted by Chomnawang et al., (2005), which showed that mangosteen has antibacterial activity against Propionibacterium acnes and Staphylococcus epidermidis. Chomnawang et al.'s research, in 2007, conducted research on various tropical plants in Thailand, one of which was mangosteen (Garcinia mangostana L.). This study showed that ethanol extract of mangosteen rind

reduced and inhibited inflammation caused by Propionibacterium acnes and Staphylococcus epidermidis. Research from Pothitirat, et al in 2008 proved that ethanol extract of mangosteen rind has effective antibacterial activity against Staphylococcus epidermidis bacteria. Phytochemical examination of mangosteen peel chemical compounds shows that this part contains alkaloids, saponins, tannins, xanthones and flavonoids and is able to produce inhibition zones against Staphylococcus epidermidis.

According to research conducted by Valmai (2019), ethyl acetate extract of mangosteen peel has antibacterial properties against Staphylococcus epidermidis, with an average inhibition zone diameter of 12 mm at 4%, 12 mm at 6%, 12.5 mm at a concentration of 8%, 13.5 mm at a concentration of 10%. Qualitative results of ethyl acetate extract of mangosteen peel showed the presence of polyphenols, namely flavonoids.

Needssociety in acne treatment is to use topical preparations that can penetrate quickly into the skin, therefore one of the right preparations for acne problems is a gel preparation. Gel is also a preparation that has transparent and clear characteristics and has a structure that is resistant to environmental changes and has a viscoelastic flow (Ismail, 2013). The advantages of gel include being non-sticky, high water content in the gel so that a large amount of water can hydrate the horny layer and there is a change in the permeability of the horny tissue to be more permeable to active ingredients that can increase the permeases of active ingredients (Lieberman, 1997).

Gelling agent (base) is a polymer component that has a high molecular weight and is a combination of several molecules and polymer coils that provide viscous properties to the gel. Base is a substance derived from inorganic materials that have hydrophilic properties. HPMC, and Carbopol are gelling agents and propylene glycol is a Humectant used in research with a concentration of HPMC as a gelling agent of 2-10% and carbopol 0.2-2.0% (Tambunan et al., 2018) while for the concentration of propylene glycol 13.5-15% (Rowe, RC, Paul JS, and Marian, 2009). In a study conducted by Suryani (2018) it was stated that the combination of HPMC and Carbopol can increase the spread and adhesion power. The prediction results with Simplex lattice design provide a solution of 1 optimum formula according to the desired criteria, namely the combination of HPMC 4.0%, propylene glycol and carbopol 1.0 with a desirability of 0.506. The desirability value ranges from 0-1, where the higher the desirability value (approaching 1) means that the optimum formula produced is increasingly achieving the desired response. According to Hasyim (2011), by comparing the carbopol and HPMC bases in gel preparations, the results obtained are that the HPMC gel base with a concentration of 8% has the most optimal physical stability compared to carbopol. HPMC is easily soluble in distilled water and several organic solvents such as ethanol, propyl alcohol and ethylene chloride. Gels that use HPMC usually have good spreadability, are easy to wash off, provide a cooling effect, and do not clog pores (Afianti and Murrukmihadi, 2015).

Formulation optimization can be obtained by using the Design Expert application with the Simplex lattice design (SLD) method. This method can determine the ideal optimum formula of the materials used for the preparation. The advantage

of simplex lattice design is a (relatively) simple optimization model compared to other optimization models and avoids trial and error formulas (Suryani et al., 2017).

Based onBased on the above information, this study aims to create a gel formulation from mangosteen peel extract and fractions which are effective as an antibacterial for acne-causing agents.With a combination of HPMC, carbopol, and propylene glycol and determining the optimum formula with the Design expert application using the simplex lattice design method and conducting physical stability tests and can be used as an antibacterial against S. epidermidis bacteria in acne. The purpose of this study was to determine the antibacterial activity of the most active fraction and optimization of mangosteen peel gel preparations with a composition of carbopol, HPMC, and propylene glycol.

Method

The sample used in this study was a mangosteen peel gel preparation made with a combination of carbopol 940, HPMC, and propylene glycol with different concentrations using the Simplex Lattice Design method.

The main material used in this study is mangosteen peel (Garcinia mangostana. L), the chemicals used are 95% ethanol, the chemicals used are 96% ethanol, the test medium used in this study is Nutrient Agar (NA) medium, MHA, carbopol 940, HPMC 1000DB (PT Aneka kurnia), Triethanolamine (Merck), Propylene glycol (DOW), Methyl Paraben (DOW), N-hexane (Merck), Ethyl acetate (Merck), ether (Merck), concentrated sulfuric acid (Merck), acetic acid (Merck), NaOH.

The tools used in this study were analytical scales with a minimum reading accuracy of 0.1 mg, and a maximum capacity of 100 grams (OHAMS), inkas, platinum ose, petri dishes (Normax), Erlenmeyer flasks (Pyrex), test tubes (Pyrex), measuring cups (Iwaki), droppers, analytical scales (OHAUS), tweezers, incubators, flannel cloth, cotton (selection), glass funnels, borer props, micropipettes (dragon), sterile cotton buds, autoclaves, filter paper, oven binders (Binder ED 53), spirit lamps, blenders (cosmos), maceration bottles, rotary evaporators (IKA RV 10), gel containers, mesh sieves number 60, spreadability testers, adhesiveness testers, pH meter testers (starter 3100), viscometers (viscotester vt-03f).

Analysis has used Experimental data from the spreadability, viscosity and antibacterial of the ethyl acetate fraction gel preparation of mangosteen peel will be analyzed in the Design Expert Software with the Simplex Lacticce Design method to obtain one optimum formula, the optimum formula obtained will be processed again using the T-test method, to determine whether the data obtained from the results of the experiment is normally distributed is said to be normally distributed if the significant value is ($p>0.05$). Normally distributed data ($p>0.05$).

Work scheme

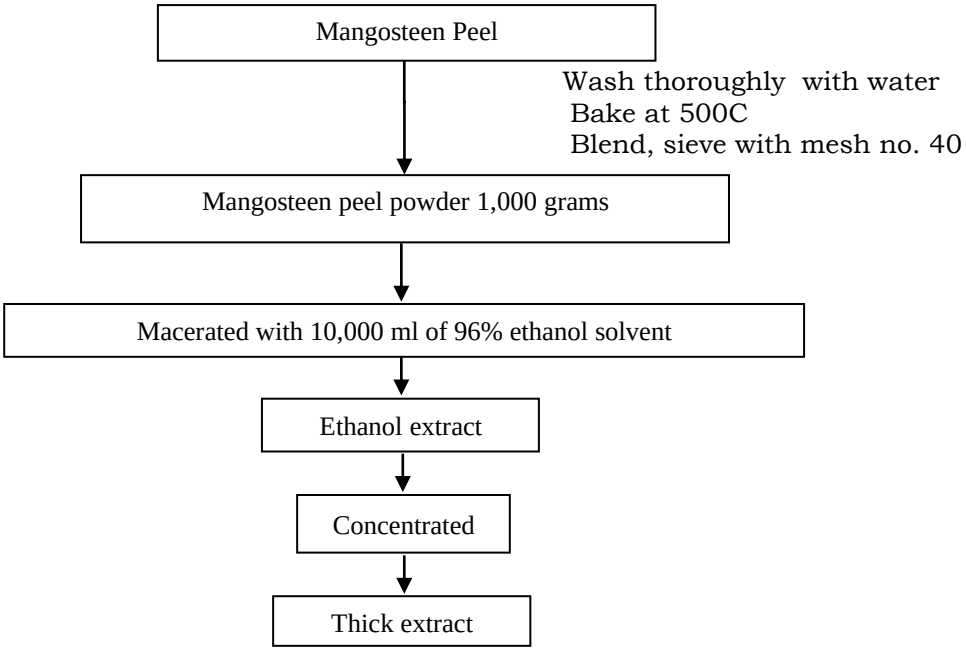


Figure 1. Scheme for making ethanol extract from mangosteen peel

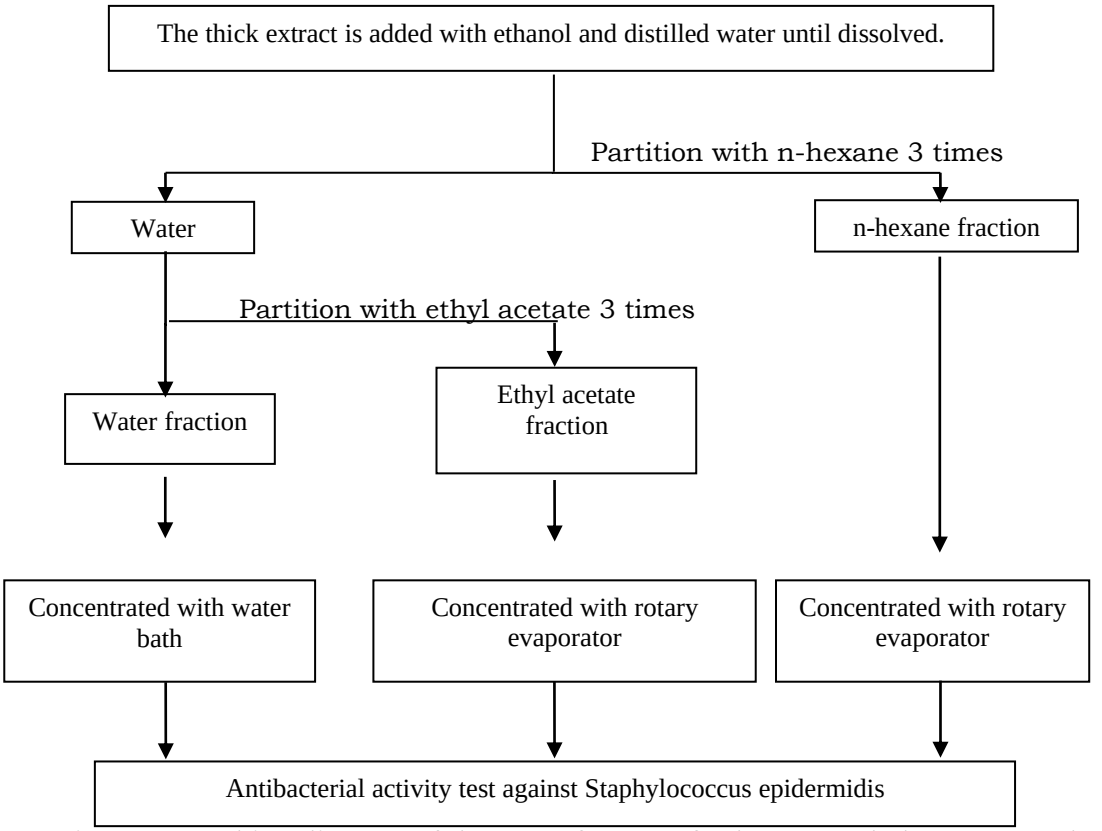


Figure 2. Working diagram of the manufacture of n-hexane, ethyl acetate, and water fractions from mangosteen peel extract

Results and Discussion

Identification results of Mangosteen plants (Garcinia mangostana L.)
Plant determination

The purpose of this determination is to establish the truth of the plants related to the morphological characteristics of the mangosteen plant against the literature, and is proven in the Plant Systematics Laboratory, Faculty of Pharmacy, Setia Budi University.

Determination Results according to Steenis, CGGJV, Bloembergen, H, Eyma, PJ 1992: 1b – 2b – 3b – 4b – 6b – 7b – 9b – 10b – 11b – 12b – 13b – 14b – 16a. group 10. 239b – 243b – 244b – 248b – 249b – 250a – 251b – 253b – 254a. family 80. Guttiferae 1a. 1. Garcinia. 1b. Garcinia mangostana L.

Plant description

Tall tree, taproot system. Round, woody stem, monopodial branching. Has single leaves, elongated to oval-elongated, base pointed to blunt, tip pointed to pointed,

flat edges, pinnate leaf veins, like bones, shiny dark green. Length 12.5 - 20.2 cm, width 5.1 - 8.9 cm, pinnate leaf veins. Regular flowers, female flowers at the end of the twigs, outermost petals green yellow, 2 innermost smaller, crown leaves oval inverted, thick fleshy, green yellow, staminodia often in groups, ovary bears 4-8, pistil head has 4-8 fingers. Fruit is a depressed ball shape, diameter 3.5-7 cm, dark purple, thick fruit wall, fleshy, purple, with yellow sap. Seeds 1-3 cm, covered by a thick and juicy seed membrane, white.

Based on the determination results, it can be ascertained that the plant used in this study is the plant (Garcinia mangostana L.). The image can be seen in attachment 1.

Results: Collecting ingredients, drying and making mangosteen peel powder

Mangosteen plants were picked randomly in the Tawangmangu area, Central Java in November 2021. Peeled mangosteen skin was washed, collected, with running water, and cut into pieces then dried using an oven at a temperature of 65°C for 40 minutes. The dried simplicia that had been obtained from the drying results was powdered using a blender, the simplicia powder obtained was sieved using mesh no. 40, the simplicia powder from the sieve was stored in a jar (Satongaun et al., 2011).

The results of the percentage of dry weight to wet weight can be seen in table 2 showing the results of the percentage of dry weight to wet weight. Furthermore, the wet weight of mangosteen peel up to 10,000 grams was dried to obtain a dry weight of 1,056 grams, with a dry weight yield to wet weight of 10%. The calculation of the percentage of wet weight to dry weight can be seen in table 2.

Table 1. Percentage of dry weight to wet weight of mangosteen peel

Wet weight (grams)	Dry weight (grams)	Yield (% w/w)
10000	1056	10%

Identification of mangosteen peel powder

Identification of powdered herbal medicines according to the Indonesian Herbal Pharmacopoeia, II edition of 2017 for mangosteen rind herbal medicines includes organopleptic identification, drying shrinkage test, total ash, acid-insoluble ash, water-soluble essence, ethanol-soluble essence (FHI, 2017).

Organoleptic identification

Organoleptic tests are conducted to describe the smell, color, taste and texture of the herbal medicine using the five senses, so that objective results will be obtained (Directorate General of POM, 2000: 31). The results of the organoleptic test of mangosteen herbal medicine are that it has an aromatic smell, purplish red color, has a bitter astringent taste, and has a fairly rough and thick texture.

Drying shrinkage

Determination of drying shrinkage of mangosteen peel using a moisture balance tool. The results of determining the drying shrinkage of mangosteen peel powder using a moisture balance tool are listed in the table below:

Table 2. Results of determining the drying shrinkage of mangosteen peel

No	Powder weight (grams)	Drying loss (%)
1	2.00	3.43
2	2.00	2.98
3	2.00	2.47
	Mean±SD	3.12±0.26

Drying loss is one of the non-specific parameters that aims to provide a maximum limit (range) on the amount of compounds lost in the drying process. The results of determining the average drying loss for mangosteen peel were 2.96%, where the drying loss has met the requirements that the drying loss of simplicia powder should not exceed 10%. This is because if the drying loss is less than 10%, the substances contained in the plant will die, the enzymes will not be active, and the bacteria and fungi will not be active. and bacteria and fungi do not grow so that the material is more durable (Katno et al., 2008).

Determination of total ash content

Determination of ash content is a method of measuring materials heated at a certain temperature where organic compounds and their derivatives are destroyed and evaporated so that only mineral and inorganic elements remain with the aim of providing a picture of internal and external minerals originating from the initial process until the extract is formed (Ministry of Health of the Republic of Indonesia, 2000). The purpose of testing the total ash content is to provide a picture of the internal and external mineral content originating from the initial process until the extract is made (Ministry of Health of the Republic of Indonesia, 2000). The results of determining the total ash content can be shown in table 4 and the calculation of the total ash content is shown in appendix 8.

Table 4**.** Testing the total ash content of mangosteen peel

Weight of residual ash	Simple weight	Calculation results
63,112	65,122	0.96%
64,213	66,135	0.97%
62,314	64,212	0.97%
	Mean±SD	0.96%±0.005

The results of the total ash content of mangosteen rind in this study were 0.96% ± 0.005. The total ash content value indicates the content of inorganic compounds obtained from the mangosteen rind plant or obtained from outside the plant. A total of 2 grams of mangosteen rind powder obtained inorganic compounds of 0.96% ± 0.005. The results of the total ash content value have met the requirements for total ash content, which is not more than 2.9% (Indonesian

Herbal Pharmacopoeia, 2017) ash content should have a small value because inThis parameter indicates the presence of heavy metal contamination that is resistant to high temperatures (Isnawati and Arifin, 2006). Examples of internal and external mineral content are calcium, phosphorus and magnesium for bone growth (Yuriah et al., 2024). Sodium and chloride for body fluids, iron for the formation of hemoglobin and red blood cells (Bonato et al., 1987). This is different from toxic minerals (heavy metals) such as mercury, lead, copper, cadmium and strontium. Accumulation of heavy metals in the human body over a long period of time can interfere with the circulatory system, nerves and kidney function (Widaningrum et al., 2007). The results of the total ash content in this study were 0.96% ± 0.005 which is in accordance with the Indonesian herbal pharmacopoeia where the total ash content is less than 2.9%.

Determination of acid insoluble ash content

Determination of acid insoluble ash content aims to determine the amount of ash content obtained from external factors, originating from impurities originating from sand or soil (Ministry of Health of the Republic of Indonesia, 2000). The results of the determination of total ash content can be shown in table 5 and the calculation of acid insoluble ash content is shown in appendix 8.

Table 5**.** Ash content insoluble acid of mangosteen fruit skin powder

Weight of residual ash	Simple weight	Calculation results
63,095	65,122	0.96%
64,175	66,135	0.97%
62,231	64,212	0.96%
	Average	0.96%±0.005

The results of the insoluble ash content of mangosteen rind acid in this study were 0.96% ± 0.005. A total of 2 grams of mangosteen rind powder obtained inorganic compounds of 0.96% ± 0.005. The acid-insoluble ash content reflects the presence of mineral or metal contamination that is not acid-soluble in a product. The resulting value does not meet the requirements in the Indonesian Herbal Pharmacopoeia where the acid-insoluble ash content is not more than 0.7%, and the acid-insoluble ash content in this study was more than 0.7% with an acid-insoluble ash content value of 0.96% ± 0.005 (FHI, 2017). The high acid-insoluble ash content indicates the presence of silicate content originating from soil or sand, soil and metal elements silver, lead and mercury (Guntarti et al., 2015). Determination of acid-insoluble ash content to determine the content of compounds that are quite high, the content of sand, silica and mud in the simplicia (Awaliyah & Yuriah, 2024). Soil conditions for growing processes during washing, drying, and storage can also affect the size of organic matter in the simplicia (Kartikasari et al, 2017).

Determination of water soluble extract levels

Determination of water-soluble essence content was carried out to determine the water-soluble essence content in mangosteen rind powder. The purpose of determining the water-soluble essence content is to estimate the amount of polar

compounds that are soluble in water (Saifudin et al., 2011). The results of determining the water-soluble essence content can be shown in table 6 and the calculation of the water-soluble essence content is shown in appendix 9.

Table 6. Water soluble content of mangosteen peel

No	Powder weight (grams)	Water soluble content (%)
1	2.00	5.5
2	2.00	4.4
3	2.00	5.9
	Mean±SD	5.2±0.7

The results of 2 grams of simplistic powder used in determining the water-soluble extract content obtained a value of 5.2% ± 0.7, this value has met the requirements of the Indonesian Herbal Pharmacopoeia (2017) namely that the water-soluble extract content should not exceed 47%. The size of the results of determining the extract content is influenced by biological factors including the location of the plant, the harvest period and the age of the plant. Storage and harvesting that are not on time can also affect the content of chemical compounds (Ministry of Health of the Republic of Indonesia, 2000: 7). The water-soluble extract content provides an initial picture of the amount of compound content in the simplicia that can be dissolved by solvents that have polar properties (Ministry of Health of the Republic of Indonesia, 200)

Determination of ethanol soluble extract content

Determination of ethanol soluble essence content is carried out to determine the content of ethanol soluble essence in mangosteen rind powder according to herbal pharmacopoeia or not. The purpose of determining the content of ethanol soluble essence is to estimate the amount of polar and non-polar compounds that are soluble in ethanol (Saifudin et al., 2011). The results of determining the ash content of ethanol soluble essence can be shown in table 7 and the calculation of ethanol soluble essence content is shown in appendix 9.

Table 7. *Ethanol soluble extract content of mangosteen peel*

No	Powder weight (grams)	Ethanol soluble extract content (%)
1	2.00	7.2
2	2.00	9.5
3	2.00	4.9
	Mean±SD	7.2±2.3

The value of the results of the determination of the ethanol soluble extract of the mangosteen rind simplex obtained a value of 7.2% ± 2.3, the results of the rough test of the ethanol soluble extract of the mangosteen rind simplex have met the requirements of the Indonesian Herbal Pharmacopoeia (2017) namely the ethanol soluble extract content of the mangosteen rind powder is not less than 10%. The value of the ethanol soluble extract content is less than the provisions indicating

low solubility of the simplex to the ethanol solvent so that the chemical compound is not optimal. The value of the results of the determination of the ethanol soluble extract content is greater than the value of the water soluble extract content. This states that a good solvent for mangosteen rind is an ethanol solvent because with an ethanol solvent you will get a higher extract content than with a water solvent.This shows that the polar compounds contained in mangosteen skin are greater than the non-polar compounds..

Results of making mangosteen peel extract

In this study, the preparation of ethanol extract used the remaceration method. Remaceration is the easiest extraction method. The advantage of the remaceration process lies in the processing method and equipment used which are simple and easy to use. Because the remaceration process does not involve heating, so that components that are not heat resistant such as flavonoids remain in the extract (Marjoni, 2016). The results of making thick extracts of mangosteen rind remaceration can be seen in table 4

Table 8. Results of making mangosteen peel maceration extract

Powder weight (grams)	Extract weight (grams)	Yield (%b/b)
1056	122	12.2

The weight of the powder obtained as much as 1056 gr will be remacerated, the results of the remaceration will be evaporated to obtain a thick extract of 122 gr with a yield of 12.2%, according to Pustiari 2014 the percentage yield of mangosteen peel extract is 12.61%.

The solvent in the maceration method in Puspitasari's (2014) study used 96% ethanol and produced a yield of 12.61%. The results of this study from the extraction of 1056 grams of filtrate obtained a thick extract of 122 grams with the calculation of the extract yield of 12.2%, the results of the yield value obtained have met the requirements. The requirement for a good yield of mangosteen peel extract is that the value is not less than 8.2%, so the yield from maceration on mangosteen peel is declared good because the yield is> 8.2%. The difference in the amount of yield is due to differences in environmental factors such as light intensity, nutrients, temperature and humidity.

Results of identification of extracts and ethyl acetate fractions of mangosteen peel

Organoleptic identification.
Identification of mangosteen rind extract is done visually, which includes the color of the extract from the mangosteen rind, which is purple, and the distinctive smell of the mangosteen plant.

Chemical content of mangosteen peel.
The results of the identification of the chemical content of mangosteen peel extract can be seen in table 5.

Table 9. Results of identification of chemical content of mangosteen peel extract

Compound	Results	Library	Note
Flavonoid	The yellow color of the amyl alcohol layer.	A positive reaction is indicated by the presence of a red, yellow or orange color on the amyl alcohol layer (Alamsyah et al. 2014).	(+)
Alkaloid	Tube 1 → Yellowish white precipitate (Mayers reagent). Tube 2 → Brownish red precipitate (Dragendorff reagent)	There is a yellowish white coagulated precipitate in Mayer's reagent and a red to brownish orange precipitate is formed in Dragendroff's reagent (Alamsyah et al. 2014).	(+)
Saponins	Stable foam is formed + 1 drop of 2N HCl the foam does not disappear.	Stable foam is formed + 1 drop of 2N HCl, the foam does not disappear (Ramyashree et al. 2012).	(+)

The results of research by Putri in 2019 for the identification of the chemical content of the ethyl acetate fraction of mangosteen peel are tests for the content of flavonoid, alkaloid, and saponin compounds. Testing of flavonoid compounds in the ethyl acetate fraction of mangosteen peel was declared positive due to the presence of intense yellow fluorescence, testing of alkaloid compound content was carried out using 2 tubes where the positive alkaloid results with tube 1 formed a yellowish white precipitate for Mayer's reagent and for tube 2 formed a brownish red precipitate in the dragendroff reagent, testing of saponin compounds in the ethyl acetate fraction was declared positive because foam was formed as high as 1.3 cm for 30 seconds.

The purpose of adding powdermagnesium and HCL in the flavonoid test is to reduce the benzopyrone core contained in the flavonoid structure to form a red or orange flavylium salt. Most flavonoid groups are soluble in hot water, which causes heating. Flavonoids are compounds containing two aromatic rings with several hydroxyl groups. Phenolic compounds with high hydroxyl groups are very soluble or polar in water and can be extracted with polar solvents. Figure 9 shows the reactions that occur between flavonoid compounds, including HCL and Mg powder.

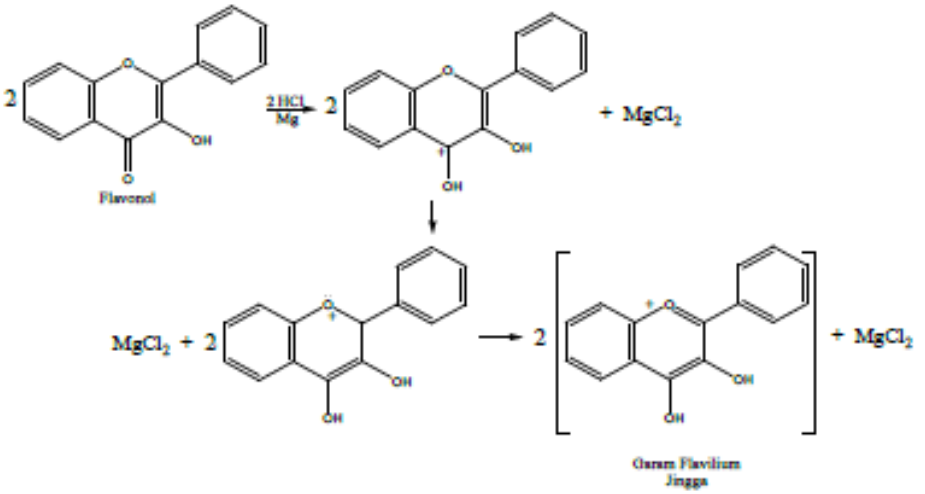


Figure 3. Reaction of Flavonoids with Mg Metal and HCl (Septyangsih 2010)

The principle of the alkaloid test is a precipitation reaction.caused by ligand exchange. Positive alkaloid results in the Mayer test are indicated by the formation of a white precipitate. The precipitate is believed to be a potassium alkaloid complex. Alkaloids contain nitrogen atoms with lone pairs of electrons and can be used to form coordinate bonds with metal ions (Sangi et al., 2008). In the alkaloid test using Meyer's reagent, it is estimated that nitrogen in the alkaloid reacts with the metal ion K + from potassium tetraiodide mercurate (II) to form a precipitated potassium alkaloid complex. Figure 10 shows the response that occurs in the Mayer test.

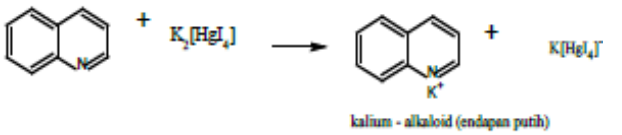


Figure 4. Mayer test reaction (Marliana et al., 2005)

Positive results for alkaloids in the Dragendorff test alsoindicated by the formation of a light brown to yellow (orange) precipitate. The precipitate is a potassium alkaloid. The alkaloid test with Dragendorff's reagent uses nitrogen to form a coordinate covalent bond with the metal ion K +. The response from the Dragendorff test can be seen in Figure 11.

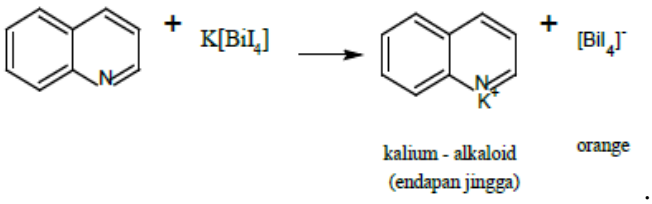
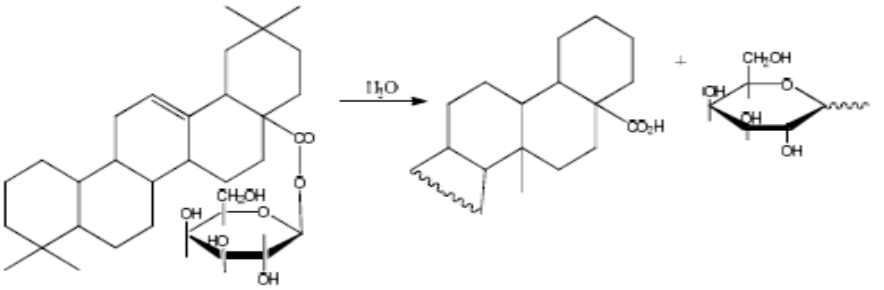


Figure 5. Dragendorff Test Reaction

The appearance of foam in the saponin test indicates the presence of glycosides that can form foam in water that is hydrolyzed into glucose and other compounds. Figure 12 shows the reactions that occur during the saponin test.



I-Arabinopyriosyl-3β-acetyloleanolate Glucose Aglycone
Figure 6. Hydrolysis Reaction of Saponin in Water

The results of the chemical compound identification of ethanol extract of mangosteen skin (Persea americana Mill.) can be seen in the attachment.

Determination of water content

Determination of the water content of mangosteen rind extract was carried out to determine the water content of the mangosteen rind extract is in accordance with the Indonesian herbal pharmacopoeia. The results of the study of the water content of mangosteen rind are 0.16% where the results of the water content of the mangosteen rind extract are in accordance with the Indonesian herbal pharmacopoeia of less than 0.25% page 310 in FHI edition II in 2017.

Table 10. Water content of mangosteen peel extract

No	Powder weight (grams)	Water content (%)
1	2.00	0.14
2	2.00	0.16
3	2.00	0.18
	Mean±SD	0.16±0.02

Determination of total ash content

Determination of total ash content was carried out to determine whether the total ash content of mangosteen rind is in accordance with the Indonesian herbal pharmacopoeia. The results of the total ash content test of mangosteen rind were 0.96%, meeting the requirements of the Indonesian herbal pharmacopoeia, which is not less than 4.4%. The purpose of testing the total ash content is to provide an overview of the internal and external mineral content originating from the initial process to the formation of the extract (Ministry of Health of the Republic of Indonesia, 2000). Examples of internal and external mineral content are calcium, phosphorus and magnesium for bone growth. Sodium and chloride for body fluids, iron for the formation of hemoglobin and red blood cells (Bonato et al., 1987).

Table 11. Total ash content of mangosteen peel extract

Weight of residual ash	Simple weight	Calculation results
64,613	66,637	0.96%
62,423	64,435	0.97%
66,424	68,412	0.97%
	Average	0.96%±0.005

Determination of acid insoluble ash content

Determination of total ash content conducted in this study to determine the acid-insoluble ash content in mangosteen rind extract. The results of the acid-insoluble ash content test in mangosteen rind extract, which is 0.96%, do not meet the Indonesian herbal pharmacopoeia, which is less than 0.2. High acid-insoluble ash content indicates the presence of dirt or sand that may be found on the ash filter paper.

Table 12. Acid insoluble ash content of mangosteen peel extract

Weight of residual ash	Simple weight	Calculation results
64,609	66,637	0.96%
62,411	64,435	0.96%
66,412	68,412	0.97%
	Average	0.96%

Mangosteen leaf extract fraction results

Fractionation is the process of separating groups of compounds found in plants. Fractionation is carried out for the purpose of separating the main compound content from other groups of compounds. Separation of fractions is carried out with the aim of considering the properties of the desired compounds. Fractionation is generally carried out using different polarity solvents, so that polar compounds penetrate polar solvents while semi-polar compounds enter semi-polar solvents and non-polar compounds enter nonpolar solvents (Alam and Tayeb, 2003).

n-hexane fraction

Hexane is widely used as a solvent because it is inert and does not react with the synthesized components (Kastianti and Amalia, 2008). Compounds that can be dissolved in n-hexane solvent are non-polar compounds such as alkaloids, terpenoids, triterpenoids, and phenylpropanoids (Tiwari et al, 2011). The yield of n-hexane fractions can be seen in table 13.

Table 13. Yield of n-hexane fractionation results from mangosteen peel

Extract weight (grams)	Fraction weight (grams)	Yield (%)
10	1.14	11.4
10	1.13	11.3
10	1.12	11.2
	Mean±SD	11.3±0.1

The results of the calculation of the yield of the n-hexane fraction of mangosteen peel powder can be seen in Appendix 12. Based on Table 13, it can be seen that the calculation of the percentage of the yield of the n-hexane fraction of mangosteen peel powder obtained an average percentage of 11.3%.

Ethyl acetate fraction

Ethyl acetate is a semi-polar solvent and is flammable and volatile, so store it in a closed container and avoid heat. Ethyl acetate can be used as a solvent because it can attract alkaloids, flavonoids, saponins, and polyphenols (Putri et al, 2013).
The yield of ethyl acetate fraction can be seen in table no. 14.

Table 14. Yield of ethyl acetate fractionation results from mangosteen peel

Extract weight (grams)	Fraction weight (grams)	Yield (%)
10	1.38	13.8
10	1.37	13.7
10	1.38	13.8
	Mean±SD	13.75±0.05

From Table 14 it can be seen that the calculation of the yield of ethyl acetate fraction of mangosteen rind powder gives an average percentage of 13.8%. The calculation of the yield of ethyl acetate fraction from mangosteen rind is presented in Appendix 13.

Water fraction

he residue of the ethyl acetate extract was then concentrated to produce a thick extract. Ethanol 96% is a multifunctional solvent that can dissolve polar, semi-polar and non-polar compounds. Table 15 shows the results of the water fraction of the mangosteen peel fraction.

Table 15. Yield of water fraction from mangosteen peel

Extract weight (grams)	Fraction weight (grams)	Yield (% w/w)
10	2.68	26.8
10	2.68	26.8
10	2.67	26.7
	Average±0.05	26.8±0.05

From Table 15, it can be seen the calculation of the water fraction yield, it can be seen that the average obtained is 27.8%. The calculation of the water fraction yield of mangosteen leaf skin can be seen in Appendix 14.

The results of the fraction weight against the extract weight obtained from each fractionation using solvents are very small. This is because when conducting fractionation, an emulsion process occurs during testing, so that the resulting compound is not optimal. The compounds contained in the fraction evaporate a lot and are lost during the separation process.

The total fractionation result of n-hexane, ethyl acetate and water is 51.9% w/w from 10% w/w. The total fractionation value is less than 10% because there are several things that cause it, namely in the fractionation process such as imperfect separation in the separating funnel and the large amount of fractionation residue stuck to the tool but not taken.

Research conducted by Pratiwi, 2016 obtainedThe ethyl acetate fraction obtained in this study weighed 5.9352 g or had a yield value of 5.9352% from 70% ethanol extract and the n-hexane fraction obtained in this study weighed 0.3174 g or had a yield value of 0.3174% from 70% ethanol extract. The amount of extract fractionated by ethyl acetate and n-hexane solvents had a relatively small yield. This is possible due to the small amount of non-polar content that can be extracted by ethyl acetate and n-hexane from 70% ethanol extract.This is not much different intotal yield of mangosteen peel fraction.

Results of identification of test bacteria
Identification of Staphylococcus epidermidis bacteria by Gram staining

Identification of Staphylococcus epidermidis bacteria in Gram staining aims to determine the morphology of Staphylococcus epidermidis bacterial cells. The results of Gram staining of Staphylococcus epidermidis bacteria can be seen in Figure 13.

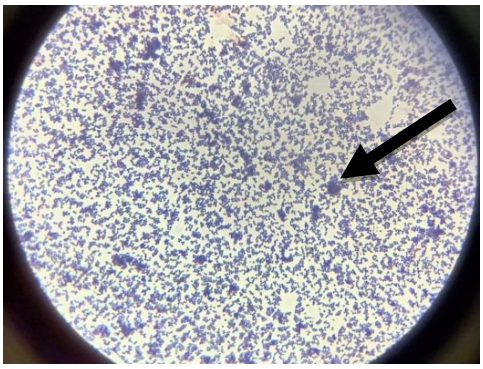


Figure 7. Gram staining of Staphylococcus epidermidis bacteria

The results of the bacterial cells are purple and coccus-shaped (round). These results indicate that the Staphylococcus epidermidis bacteria tested are included in Gram-positive bacteria that have a grape-like arrangement in the form of cocci,

clustered, in groups and purple. Gram-positive bacteria have purple or violet characteristics because the dye from crystal violet is maintained even though it is given a bleaching solution or lugol. The outermost cell wall of Gram-positive bacteria consists of thick peptidoglycan (Retnowati, Bialangi, & Posangi 2011), without a lipoprotein or lipopolysaccharide layer like in Gram-negative bacteria (thin peptidoglycan), so that when given a crystal violet solution followed by a bleaching solution, a complex of purple crystals and iodine will form which adheres strongly to the cell wall (Bogut et al. 2014). The function of giving crystal violet is as the main dye (primary) which is used as a histological dye and a method for classifying Gram bacteria (Yuriah et al., 2023). Acidic microorganisms will bind to basic Crystal violet, so that transparent microorganism cells will appear purple (violet 2018). Giving iodine solution to strengthen the binding of color to bacteria, and giving acetone for primary dye solution.

Gram staining is done to observe the morphology of bacteria and the Gram properties of bacteria. Gram staining uses four types of paint, namely Gram A (Crystal violet), Gram B (Lugol's iodine), Gram C (96% ethanol) and Gram D (Safranin). Bacteria that have gram-positive properties will be purplish blue while bacteria that have gram-negative properties will be red (Wulandari et al., 2019).

Identification of catalase of Staphylococcus epidermidis bacteria. Identification of catalase from Staphylococcus epidermidis bacteria is to determine the presence of bubbles produced in the process of planting a suspension of test bacteria added with H2O2 on a glass object. Staphylococcus epidermidis bacteria are bacteria that have the catalase enzyme where the catalase enzyme can catalyze the decomposition of Hydrogen peroxide into H2O and O2 (Juniarti et al., 2024). Hydrogen peroxide is toxic to cells because it can inactivate enzymes in cells. The results of the identification of catalase in Staphylococcus epidermidis bacteria show the presence of bubbles after H2O2 is dripped. The catalase enzyme or perixodase plays a very important role in the survival of microbes (Karimela et al. 2017). This catalase test detects the catalase enzyme in several facultative anaerobic bacteria and aerobic bacteria containing cytochrome except for bacteria classified as Streptococcus and Enterococcus (Services 2015). Catalase test is useful in identifying certain groups of bacteria. Catalase test on coccus-shaped bacteria is used to differentiate Staphylococcus and Streptococcus (Karimela et al. 2017).

The function of catalase in bacteria is to break down hydrogen peroxide into other harmless compounds because hydrogen peroxide is a poison that can damage the bacterial metabolism system.Catalase Test is a test used to identify bacteria that produce the catalase enzyme. The catalase enzyme in bacteria is an enzyme that functions to break down hydrogen peroxide (H2O2) which is formed from the aerobic respiration process of bacteria, into water (H2O) and oxygen (O2).

Identification of mannitol sugar of Staphylococcus epidermidis bacteria

Identification of Staphylococcus epidermidis bacteria using mannitol salt media so that the use of mannitol salt media in this study is to determine whether it inhibits the growth of other bacteria from Staphylococcus epidermidis bacteria.

The results of the mannitol sugar test are that Staphylococcus epidermidis bacteria form white and relatively small colonies (Radji, 2010).

Figure 8. Mannitol sugar test of Staphylococcus epidermidis bacteria on MSA media

The results of this study showed positive results in Staphylococcus epidermidis bacteria as evidenced by the absence of color changes in the MSA media from red to yellow and marked by the growth of white or pink colonies of Staphylococcus epidermidis bacteria in the research results. There was no change in the color of the media from red to yellow because Staphylococcus epidermidis bacteria cannot ferment mannitol and produce lactic acid which causes changes in the media from red to yellow, this can distinguish Staphylococcus epidermidis and Staphylococcus aureus bacteria. The change in color of the medium to yellow is due to the presence of the Phenol red indicator in the medium (Kateete et al. 2010). Where the addition of the Phenol red indicator to the medium that undergoes carbohydrate fermentation into acid in aerobic conditions, the pH will drop and finally the Phenol red indicator will change color to yellow (Dewi 2013). Staphylococcus aureus bacteria can form lipochrome pigments which cause colonies to appear yellow on MSA media, whereas Staphylococcus epidermidis bacteria cannot form lipochrome pigments which cause colonies to appear white or pink (Todar, 2005).

Identification of Staphylococcus epidermidis bacterial coagulase

Coagulase identification was carried out in this study to determine the presence or absence of coagulase enzymes, where coagulase enzymes are extracellular proteins produced by Staphylococcus aureus bacteria which are used to distinguish the genus of Staphylococcus aureus and Staphylococcus epidermidis bacteria. The coagulase enzyme produced by Staphylococcus aureus bacteria can clot plasma. Plasma clotting can occur due to the presence of proteins that resemble enzymes which, if added with oxalate or citrate, can cause clots. Serum factors react with coagulase, namely to form esterase, clotting activity and activate prothrombin into thrombin. Thrombin will form fibrin which affects plasma clotting (Boerlin, 2003). Staphylococcus aureus bacteria have the ability

to clot plasma which is one of the virulence factors that is quite important in the pathogenesis of Staphlococcus aureus bacteria themselves.

Coagulase testing on bacteria*Staphylococcus epidermidis*In this study, negative results were obtained, which were indicated by the absence of lumps such as sand or gel. The observation results can be seen in Figure 15. The results of coagulase identification are in accordance with the research conducted (Ely et.al, 2018). The research conducted by Ely et al. stated that coagulase testing on Staphylococcus epidermidis bacteria did not show lumps, which means that the coagulase test results were negative.

Figure 9. Staphylococcus epidermidis bacterial coagulase test

Results of antibacterial activity testing of mangosteen peel.
Antibacterial test results by diffusion

The results of antibacterial activity tests on extracts, n-hexane fractions, ethyl acetate fractions, and mangosteen rind water fractions that have been carried out indicate the inhibition of the growth of Staphylococcus epidermidis bacteria, indicated by the presence of an inhibition zone around the paper disc where the test solution has been placed.

The results of the antibacterial activity test on the extract, n-hexane fraction, ethyl acetate fraction, and mangosteen rind water fraction against Staphylococcus epidermidis bacteria showed that the ethyl acetate fraction had the largest inhibition zone with an inhibition zone of 28.6 mm.

Table 16. Diameter of inhibition zone of antibacterial activity test of mangosteen peel extract and fraction against Staphylococcus epidermidis FNCC 0048

Contents	Concentration	Inhibitory diameter (mm)			Mean (mm)±SD
		1	2	3	
Extract	10%	15	13.6	14	14.2±0.5
n-hexane	10%	10.6	14.6	14.3	12.7±2
Ethyl acetate	10%	25.6	30.3	30.3	28.7±2.7
Water	10%	16.3	19	19.6	18.3±1.7
Positive Control (+)	10%	36.3	37.6	37.6	37.1±0.7
negative control (-)	_	-	-	-	-

Information
+ : positive control (antibiotic clindamycin)
- : negative control (DMSO 1%)

The purpose of the data normality test is to determine whether the data is normally distributed or not. This study uses the Shapiro-Wilk test as a data normality test because the number of samples is less than 50. The value of the Shapiro-Wilk test results prove that the antibacterial n-hexane fraction is normally distributed with a significant value of 0.129 (> 0.05), the antibacterial ethyl acetate fraction is normally distributed with a significant value of 0.319 (> 0.05), the antibacterial water fraction is normally distributed with a significant value of 0.328 (> 0.05), and the antibacterial extract is normally distributed with a significant value of 0.287 (> 0.05). The value of the Shapiro-Wilk test can be concluded that the data above is normally distributed because p> 0.05, so all data in table 16 is normally distributed. The normality results will be continued with a homogeneity test (Lavene test) which is then carried out by the Posthoc Tukey test to obtain the results of the homogeneity of the subsets. In the homogeneity column of subsets, it shows that the results of the antibacterial test on the extract and ethyl acetate fraction are close to the positive control. The results of the Anova test using Shapiro-Wilk, homogeneity, posthoc Tukey and homogeneity of subsets against antibacterials in the n-hexane fraction, ethyl acetate fraction, water fraction, extract and negative control are in appendix 36.

The antibacterial activity of the ethyl acetate fraction of mangosteen rind in inhibiting the growth of Staphylococcus epidermidis bacteria is thought to be due to the influence of the content of several secondary metabolite compounds contained in the fraction. Based on phytochemical examination, it is known that mangosteen rind extract contains secondary metabolites in the form of flavonoids, alkaloids, and saponins.

Each secondary metabolite compound found in mangosteen rind has a different mechanism of bacterial growth inhibition. Active ingredients that act as antibacterials can interfere with physiological processes and prevent the formation of bacterial cell components such as cell wall synthesis, cytoplasmic membrane protein synthesis and nucleic acid synthesis (Subandrio, 1995). From

the table above, it can be seen that the ethyl acetate fraction has the greatest inhibitory power of the n-hexane fraction and the water fraction. According to Huliselan et al. (2015), ethyl acetate can extract a total phenolic compound content of 36.25 mg/L in each plant used in the extraction. Compared to other polar solvents such as ethanol (5.795 mg/L) and non-polar solvents such as n-hexane (14.659 mg/L), ethyl acetate can extract more phenolic compounds than other semi-polar or non-polar solvents. Thus, ethyl acetate is an effective solvent for extracting phenolic compounds in mangosteen rind.

Flavonoids, saponins and alkaloids are compounds in plants that have antibacterial activity. The mechanism of flavonoids in inhibiting bacterial growth is causing damage to the permeability of bacterial cell walls, bacterial microsomes and bacterial lysosomes as a result of the interaction between flavonoids and bacterial DNA, flavonoid compounds are able to release transduction energy to the bacterial cytoplasmic membrane, flavonoids can also inhibit bacterial motility. The hydroxyl group found in the structure of flavonoid compounds causes changes in organic components and nutrient transport which will eventually result in toxic effects on bacteria (Sabir 2005). Flavonoids are a group of phenol compounds that have a tendency to bind proteins, thereby disrupting the metabolic process. Flavonoid compounds are related to biogenesis and have a close relationship with xanthone compounds. The antibacterial activity of xanthone compounds is related to the reaction of xanthone carbonyl groups that interact with non-ionized amino acid groups such as the ε-amino group of lysine residues or the terminal α-amino group of a bacterial cell membrane protein, causing the function of the bacterial cell membrane protein to be lost (Putra, 2010).

Saponin compounds can damage the cytoplasmic membrane of bacterial cells. Damage to the cytoplasmic membrane of bacterial cells can reduce the permeability of the bacterial cell membrane so that the transport of substances into and out of bacterial cells becomes uncontrolled. Substances in bacterial cells such as organic ions, enzymes, amino acids and nutrients can exit bacterial cells. If these enzymes exit bacterial cells together with substances such as water and nutrients, metabolism can be inhibited, resulting in a decrease in ATP needed for the growth and reproduction of bacterial cells, and bacterial cell growth is inhibited and causes bacterial cell death (Retnowati 2011). Alkaloid compounds have antibacterial activity by disrupting the peptidoglycan composition of bacterial cells, so that the bacterial cell wall layer is not formed completely and causes the death of the bacterial cells (Amalia 2014).

The results of antibacterial activity tests on the extract, n-hexane fraction, ethyl acetate fraction, and water fraction of mangosteen peel against Staphylococcus epidermidis bacteria showed that the best antibacterial activity was the ethyl acetate fraction.

Based on the standard reference of the Ministry of Health of the Republic of Indonesia regarding the sensitivity of test bacteria to antimicrobial compounds from plants which states that the sensitive category of test bacteria if they have a diameter of the resulting inhibition zone ranging from 12-24 mm (Ministry of Health of the Republic of Indonesia, 1998), then the study of antibacterial activity

against Staphylococcus epidermidis bacteria sensitive to the ethyl acetate fraction of mangosteen rind with a concentration of 10% has antibacterial activity with an inhibition zone of 28.6 mm which has met the provisions issued by the Ministry of Health of the Republic of Indonesia 1998. The strength of the extract in inhibiting the growth of test bacteria is classified based on the diameter of the inhibition zone according to Monks et al. with the following criteria: the diameter of the inhibition zone is less than 7 mm categorized as no antibacterial activity, the diameter of the inhibition zone is 7-11.99 mm categorized as weak antibacterial activity, the inhibition zone is 12-16.99 mm categorized as moderate antibacterial activity, the inhibition zone is more than or equal to 17 mm categorized as strong antibacterial activity.

Results of testing the gel preparation of ethyl acetate fraction of mangosteen rind

The ethyl acetate fraction made in gel preparation will be designed or entered using the design expert application using the Simplex lattice design method by entering 3 variables, namely variable A as Carbopol 940, variable B HPMC 1000DB and variable C Propylene glycol, these three variables provide 14 formulas with different concentration variants in the 14 formula variables, the formula results can be seen in table 18.

Table 17. Design of optimum run formula

No	Material name	Formula													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	Carbopol 940	1	2	1.6	1	1.5	1.5	2	1	1	1.5	1.16	1.3	1.16	1
2	HPMC	2	2	2.16	2	2	2.5	2	3	3	2.5	2.16	2.3	2.6	2.5
3	Propylene Glycol	6	5	5.16	6	5.5	5	5	5	5	5	5.6	5.3	5.16	5.5

After getting 14 formulas with the design expert application, the 14 formulas will be observed for their physical properties, including organoleptic, homogeneity, pH, spreadability, adhesiveness, and antibacterial. Observations of the gel preparation will be carried out to determine which gel preparation is good from the 14 formulas. To obtain the optimum formula, 3 parameters will be taken, namely adhesiveness, spreadability, and antibacterial in the gel preparation, where these 3 parameters will be processed using the design Expert application with the Simplex Latice Design method and will obtain 1 optimum or best formula.

Organoleptic test results of the gel

Organoleptic testing of gel preparations was carried out by observing the gel preparation without using any aids by observing the shape, color, and odor of the gel preparation. The results of the organoleptic testing can be seen in table 18. Based on the table below, it can be seen that the gel preparation has a yellow color caused by the ethyl acetate fraction of mangosteen rind when mixed with

the pure gel preparation that has been made so that it can affect the color of the preparation on the gel.

Table 18. Organoleptic test results of gel preparations

Formula	Form	Color	Smell
1	Semi solid	Yellow	Odorless
2	Semi solid	Yellow	Odorless
3	Semi solid	Yellow	Odorless
4	Semi solid	Yellow	Odorless
5	Semi solid	Yellow	Odorless
6	Semi solid	Yellow	Odorless
7	Semi solid	Yellow	Odorless
8	Semi solid	Yellow	Odorless
9	Semi solid	Yellow	Odorless
10	Semi solid	Yellow	Odorless
11	Semi solid	Yellow	Odorless
12	Semi solid	Yellow	Odorless
13	Semi solid	Yellow	Odorless
14	Semi solid	Yellow	Odorless

Information:

F1 : Formula 1	F2 : Formula 2	F3 : Formula 3	F4 : Formula 4
F5 : Formula 5	F5 : Formula 5	F6 : Formula 6	F7 : Formula 7
F8 : Formula 8	F9 : Formula 9	F10: Formula 10	F11 : Formula 11
F12: Formula 12	F13 : Formula 13	F14 : Formula 14	

Gel homogeneity test results

Homogeneity testing is carried out to determine whether the gel preparation is homogeneous or not, homogeneity testing is carried out by placing 0.5 grams of gel preparation on a glass object and pressing it with a deg glass. The gel preparation is said to be homogeneous if the gel preparation does not separate and is solid, the results of the gel preparation test can be seen in appendix 28. Based on observations of the homogeneity of the gel preparation, it can be seen that the gel preparation has homogeneous physical properties, and is proven by the absence of separation during the homogeneity test,

Table of physical properties testing of mangosteen rind ethyl acetate fraction gel

The results of the physical properties testing of the gel including pH testing, adhesion testing, and critical parameters including spreadability, viscosity, and antibacterial can be seen in table 19.

Table 19. Results of testing the physical properties of the mangosteen rind ethyl acetate fraction gel

Formula	pH	Adhesion	Spread power	Viscosity	Antibacterial
1	6.3±0.08	3±0	4.1±0.1	423±10.01	21.5±3.05
2	6.49±0.13	3±0	3.26±0.01	544±1	22±1
3	6.6±0.02	3.3±0.57	3.38±0.01	743±17.77	22±1
4	6.43±0.03	4±1	4.46±0.01	414±1	21.3±2.08
5	6.46±0.03	3.3±0.57	4.21±0.05	432±0	21±1
6	6.6±0.02	6±3.6	4.15±0.13	524±10	21.3±2.08
7	6.78±0.02	4±1	3.24±0.01	564±1	22±1
8	6.42±0.06	4±1	4.23±0.30	664±10	24±1
9	6.45±0.02	4±1	4.51±0.05	608±1	23±2
10	6.53±0.03	3±0	4.65±0.13	300±0	20.6±1.52
11	6.35±0.03	4.3±0.57	3.45±0.13	800±0	20.8±1.40
12	6.43±0.04	3.3±0.57	3.41±0.05	715±10	20.3±3.05
13	6.3±0.01	3±0	3.53±0.1	759±10	20.9±1.27
14	6.3±0.04	3.6±0.57	4,470.31	425±10	21.3±2.08

Information :

F1 : Formula 1	F2 : Formula 2	F3 : Formula 3	F4 : Formula 4
F5 : Formula 5	F5 : Formula 5	F6 : Formula 6	F7 : Formula 7
F8 : Formula 8	F9 : Formula 9	F10: Formula 10	F11 : Formula 11
F12 :Formula 12	F13 : Formula 13	F14 : Formula 14	

Table 20. Simplex Lattice Design equation for the response of mangosteen rind gel preparation

	Simplex Lattice Design Equation
Spread power	Y= +3.25 (A) + 4.37 (B) + 4.29 (C) + 2.33 (AB) + 2.29 (AC) – 9.32 (BC)
Viscosity	Y = + 554.00 (A) + 615.88 (B) + 429.83 (C) –737.09 (AB) – 213.18 (AC) + 2651.62 (BC)
Antibacterial Activity	Y = 2.20 (A) + 2.35 (B) + 2.14 (C) – 0.7314 (AB) – 0.2345 (AC) – 0.6142 (BC)

Description:
Y = Response
A = Carbopol 940
B = HPMC 1000DB
C = Propylene glycol

pH gel test results

Observation of the pH test on the gel preparation was carried out using a pH meter by inserting the pH meter into the gel preparation and then looking at the numbers listed on the pH meter to 14 formulas, the pH results were obtained with an average of 6.3-6.7, if the pH of the formula increases or is high, this is

due to the presence of Triethanolamine content with a large concentration which can increase the pH of the formula, in addition to Triethanolamine carbopl 940 will form a suspension at pH 3, and the viscosity will increase so that it forms a gel preparation at pH 6-8 (Dewi and Saptarini, 2016). The level of comfort of using the gel will decrease if the viscosity is too high because the gel is difficult to remove from the packaging and does not spread easily when applied to the skin (Sumule, Kuncahyo and Leviana, 2020). The results of the pH test of the gel preparation can be seen in table 20.

pH or acidity level also affects bacterial growth (Pelczar and Chan, 2007). The pH generally preferred by microbes is neutral pH, which is pH 7. Some bacteria grow at pH 6, but there are also microbes found growing at pH 4 or pH 5. It is very rare for a microbe to grow well at pH 4, except for certain autotrophic bacteria because bacteria produce metabolic products that are acidic or basic (Volk and Wheeler, 1993).

The effect of pH on bacterial growth is related to enzyme activity. Enzymes are needed by bacteria to catalyze reactions related to bacterial growth. If the pH in a medium or environment is not optimal, it will interfere with the growth of the bacteria themselves. When the pH decreases or increases, the nature of the amino acid groups will change, causing bacteria to not be able to grow optimally and will affect the metabolic products that will be produced (Pelczar and Chan, 2007).

Gel adhesion test results

The gel preparation adhesion test was conducted to determine the time required by the gel preparation to adhere to the skin, the longer the gel preparation's ability to adhere to the skin, the longer the therapeutic effect given. The gel adhesion was conducted to determine the bond between the gel and the skin. The higher the gel adhesion indicates the stronger the bond between the gel and the skin, allowing for higher drug absorption by the skin. Conversely, if the bond between the gel and the skin is less than optimal, the drug will be easily removed from the skin (Nevi, 2006). The results of the gel preparation adhesion test from 14 formulas showed that formula 11 had the highest inhibition time with a time of 4.3 seconds with variations in humectants in formula 11 Carbopol 940 1.16667, HPMC 1000DB 2.16667, propylene glycol 5.66667. The results of the gel preparation adhesion test can be seen in table 19.

Critical parameter optimization based on Simplex Lattice Design
Data from observations of mangosteen rind gel preparations covering 3 critical parameters, namely spreadability, viscosity, and antibacterial activity, were entered into the software.*Simplex Lattice Design*.

Gel spread power test results

Spreadability testing of gel preparations is carried out to determine the spreadability of a preparation on the skin surface, the wider the spreadability of the preparation, the better the spreadability of the active preparation on the skin surface, the spreadability value is inversely proportional to the viscosity value so that the higher the viscosity value, the lower the spreadability value. Spreadability

is the ability of the preparation to spread when used on the skin, the greater the spreadability, the wider the active substance will be distributed properly. The smaller the spreadability, and the antibacterial activity decreases, good spreadability causes contact between the drug and the skin to occur quickly, the wider the spreadability will affect the contact between the active substance and the skin surface, the wider the contact surface of the efficacious substance with the skin, the greater and the absorption of the drug will be more optimal (Sholichah et al, 2019). The results of the spreadability test showed that formula 10 had the best spreadability with a value of 4.65 cm and with variations of humectants carbopol 940 1.5%, HPMC 1000DB 2.5%, and propylene glycol 5% from this data, it will be continued by entering the values into the Design Expert application with the aim of determining the effect of the three humectants in the gel preparation. The results of the gel preparation spreadability test can be seen in table 19.

The data obtained will be processed using the Design Expert application, the results of data processing obtained the equation shown in table 20. The difference in the data obtained is not significantly different which is stated in the insignificant model parameters and the lack of fit parameters which have insignificant values, which means that the replication formula on the same component has the same response. Based on the above spreading power equation, it can be concluded that the three variables get positive results which means that carbopol 940, HPMC 1000DB, and propylene glycol can cause an increase in the gel spreading power value and the interaction between carbopol and HPMC 1000DB gives a positive value (+2.33) which means that the addition of carbopol 940 and HPMC 1000DB is predicted to increase the spreading power of the gel preparation, the interaction that occurs between carbopol 940 and propylene glycol gives a positive value (+2.29) which means that the addition of carbopol 940 and propylene glycol can increase the spreading power of the gel preparation, and the interaction between HPMC 1000DB and propylene glycol gives a negative value (-9.32) which means that the addition of HPMC 1000DB and propylene glycol will reduce the spreading power of the gel preparation. The equation that has been discussed above, it can be seen that the interaction that occurs between carbopol 940 and HPMC 1000DB is a good interaction to increase the spreadability of the gel preparation. Research by Nursiah et al. (2011) shows that the HPMC gelling agent has hydrophilic properties and has advantages by producing good spreadability, cooling effect, does not clog pores, is easily washed with water and has good drug release. Based on the data above, it can be seen that the addition of HPMC 1000DB can increase the spreadability of the results of the equation that has been discussed can be seen in the Counter plot of spreadability in Figure 14

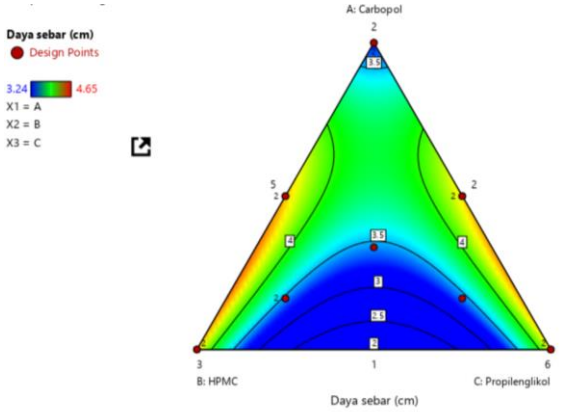


Figure 10. Counter Plot Spread Power

In the picture*Counter plot*From the above spreading power, it can be seen that from the three factors, namely carbopol 940, HPMC, and propylene glycol, there is an interaction as evidenced by the presence of waves in the triangle.*Counter plot*spreading power, from*Counter plot*above, it can be seen that HPMC 1000DB has an important role in increasing the spreadability of the gel, which is seen in the orange color of HPMC 1000DB and according to the equation above, HPMC 1000DB has a higher coefficient value than carbopol 940 and propylene glycol, this is in accordance with research conducted by (Sukmawati 2013) which states that HPMC 1000DB affects the spreadability of the preparation. In addition to HPMC 1000DB, propylene glycol can also have an effect on increasing the spreadability because propylene glycol has water properties that can affect the consistency of the gel preparation (Ayorbaba, 2020).

Gel viscosity test results

Gel preparation viscosity testing is carried out to determine the thickness of the gel preparation, gel preparation testing is carried out using a viscometer, testing is carried out on 14 gel preparation formulas. The higher the viscosity, the higher the level of viscosity of the substance and the greater the resistance of the preparation to flow which will affect the antibacterial activity of the viscosity of the preparation will increase so that its antibacterial activity will be lower, this happens because the bonds between the base formula with high viscosity become tighter so that the active substance will be more difficult to diffuse out (Intan et al, 2017). The results of the gel preparation viscosity test can be seen in table 19.

The results of the viscosity test showed that formula 11 had a high viscosity of the other 13 formulas with a value of 800 dPas and with variations in humectants formula 11 Carbopol 940 1.16667, HPMC 1000DB 2.16667, propylene glycol 5.66667, high viscosity values can be caused by carbopol where carbopol 940 can increase viscosity in the preparation. While the higher the viscosity, the more difficult the active substance that comes out of the drug compound will be (Madan & Singh, 2010). The increase in high viscosity values can be influenced by carbopol 940 and the viscosity value is also influenced by the concentration of HPMC 1000DB and propylene glycol. HPMC 1000DB is a neutral gelling agent and can form a clear gel and can maintain the viscosity of the resulting gel (Rowe,

2009). Research conducted by Rupal et al. (2010), on the release of drugs from gels with gelling agents HPMC 1000DB and carbomer found that the results of the study showed that propylene glycol affects the ability to release drugs. The conclusion that can be drawn is that HPMC 1000DB and propylene glycol can cover the shortcomings of carbopol 940 where carbopol 940 can increase high viscosity which will cause difficult drug release therefore HPMC 1000DB has the property to neutralize, and produce physical characteristics that meet the requirements of gel preparations with good and acceptable results. HPMC 1000DB and propylene glycol can affect the ability to release drugs.

HPMC 1000DB can increase viscosity compared to carbopol 940 and propylene glycol because HPMC 1000DB is a cellulose derivative. In cellulose derivative polymer dispersions, primary molecules will enter the cavity (*cavities*) formed by water molecules so that hydrogen bonds occur between the hydroxyl groups (-OH) of the polymer and water molecules. This hydrogen bond plays a role in hydration in the development process of a polymer so that increasing the content of HPMC 1000DB causes more hydroxyl groups and higher viscosity (Kibbe, 2004)

The data obtained will be processed using the Design Expert application, the results of data processing obtained the equation shown in table 21. The difference in the data obtained is significantly different which is stated in the model parameters that have significant values and the lack of fit parameters that are not significant, meaning that the replication formula with the same components has a different response. Based on the equation in table 20, it can be concluded that the three variables show positive results or values, which means that by increasing the three variables, the viscosity value can be increased and the interaction between carbopol 940 and HPMC 1000DB gives a negative value (-7.37.09) which means that the addition of carbopol and HPMC 1000DB is predicted to reduce the viscosity of the gel preparation, the interaction between carbopol 940 and propylene glycol gives a negative value (-213.18) which means that the addition of carbopol 940 and propylene glycol is predicted to reduce the viscosity of the gel preparation, and the interaction between HPMC 1000DB and propylene glycol gives a positive value (+ 2651.62) which means that the addition of HPMC 1000DB and propylene glycol can increase the viscosity of the gel preparation. The equation that has been discussed above, it can be seen that the interaction between HMPC 1000DB and propylene glycol is a good interaction in increasing the viscosity of the gel preparation. This shows that the greater the proportion of HPMC 1000DB used in the formula will increase the viscosity value. Conversely, if the greater the proportion of carbopol 940 and propylene glycol used, the viscosity response will decrease. Based on the data above, it can be seen that the addition of HPMC 1000DB can increase the viscosity of the gel preparation.

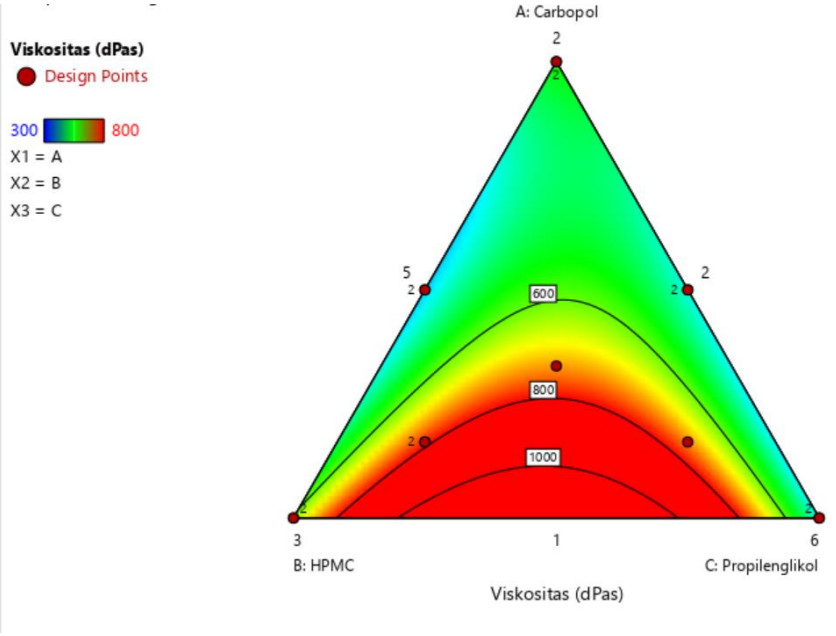


Figure 11. Viscosity Counter Plot (dPas)

Based on *Counter plot* above, it can be seen that there is an interaction between two factors, namely HPMC 1000DB and propylene glycol. This is proven by the presence of waves on*Counter plot*triangle and based on*Counter plot*above, it can be seen that HPMC 1000DB and propylene glycol may have an important role in increasing viscosity. This is indicated by the red color located on HPMC 1000DB and propylene glycol and is proven by the equation value that HPMC 1000DB has the highest value, followed by propylene glycol.

Results of antibacterial activity testing of ethyl acetate fraction gel from mangosteen rind

Antibacterial activity testing of the ethyl acetate fraction gel preparation of mangosteen rind was carried out to determine whether the ethyl acetate fraction of mangosteen rind in the gel preparation has activity to inhibit the growth of Staphylococcus epidermidis bacteria. The results of the antibacterial activity test of the ethyl acetate fraction gel preparation of mangosteen rind can be seen in table 19.

The antibacterial activity data of the gel preparation obtained will be entered and processed using the Design Expert application to obtain an equation as in table 20. Based on the equation above, it can be seen that the interaction of the three variables has a significant influence, in the interaction of carbopol 940 and HPMC 1000DB getting a negative value (-0.7314), carbopol 940 and propylene glycol (-0.2345), and HPMC 1000DB and propylene glycol (-0.6142) which means that the addition of carbopol 940 and HPMC 1000DB, carbopol-propylene glycol, and the addition of HPMC-propylene glycol do not affect antibacterial activity. HPMC 1000DB has an important role in increasing viscosity so that by increasing the viscosity of a preparation, and the greater the viscosity of a food preparation, the

greater its resistance (Sinko, 2011) so that it can inhibit the release of the active substance and result in a decrease in inhibition of the gel formulation against Staphylococcus epidermidis bacteria. Based on the data above, the Counter plot of the inhibition test for Staphylococcus epidermidis bacteria based on SLD can be seen in Figure 16.

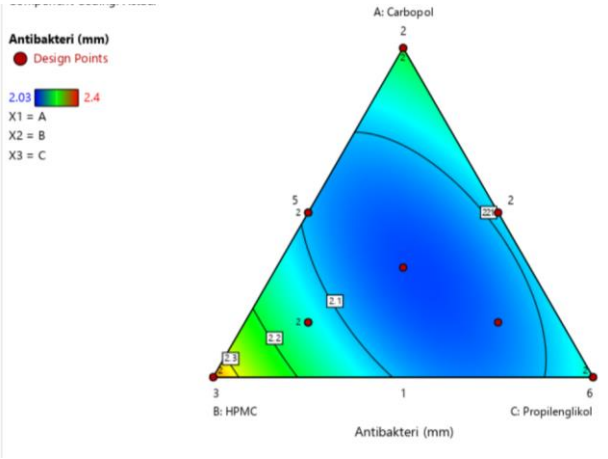


Figure 12. Counter plot of inhibition test for Staphylococcus epidermidis bacteria

Based on the Counter plot image above, it can be seen that there is no interaction between the three factors, namely carbopol 9940, HPMC, propylene glycol. This is proven by the presence of waves on the Counter plot and the blue color found in HPMC and propylene glycol, which is different from HPMC. 1000DB which has an important role to increase antibacterial activity, this can be shown by the presence of orange color located in HPMC 1000DB and proven by the equation above where the coefficient value of HPMC 1000DB is greater than carbopol 940 and HPMC 1000DB. Research conducted by Rowe et al., (2009) stated that HPMC 1000DB can inhibit microbial growth.

Optimum formula for mangosteen rind ethyl acetate fraction gel preparation

Determination of the optimum formula using the SLD method by entering the target response to be obtained and entering the degree of importance. The selected response targets include minimize, maximize and in range. The degree of importance is the level of how important each response is to determine an optimum formula, the degree of importance can be determined with values ranging from less important (+) to very important (++++).

The determination of the optimum formula will be entered data from the results of the physical properties of the mangosteen rind ethyl acetate fraction gel preparation, and the critical factors that will be used are the spreadability, viscosity, and antibacterial properties of the mangosteen rind ethyl acetate fraction gel preparation. The degree of importance of the spreadability is (++++) with a target response in the range of determining this degree of importance because the spreadability is an important factor in the gel preparation, the spreadability can help the gel preparation work on the skin surface. The degree of

importance for viscosity is (++++) with a target response in the range so that the viscosity value will be at the expected minimize and maximize values. The degree of importance for antibacterial activity is (++++++) with a maximize response determining the degree of importance at the highest antibacterial activity because the inhibitory power for bacterial growth in the gel preparation is the most important factor in the research conducted, especially to see the ability of the compound activity of the active substance so as to obtain maximum results. The results will be shown in table 21.

Table 21. Optimization data of the optimal formula for the preparation of ethyl acetate fraction gel from mangosteen rind using the Design Expert application

Name	*Goal*	*Lower limit*	*Upper limit*	*Importance*
Carbopol 940	*Is in range*	1	2	1
HPMC1000DB	*Is in range*	2	3	1
Propylene Glycol	*Is in range*	5	6	1
Spread power	*Is in range*	3.08	4.4	1
Viscosity	*Is in range*	300	800	1
Antibacterial activity	*Maximize*	2	2.3	1

After the response data has been entered into the Design Expert application with the SLD method, it will obtain the results of material variation solutions and good response value predictions. The results of the analysis, composition and prediction of the optimum formula physical properties are shown in table 22.

Table 22. Kcomposition and prediction of physical quality test of optimum gel preparation formula

Carbopol 940	HPMC	Propylene glycol	Spread power	Viscosity	Antibacterial activity	*Desirability*
1,500	2,500	5,000	3,779	439,610	2.116	1,000

Based on the data prediction, it can be concluded that the formula produces a desirability value of 0.872. and Super improsed obtained by showing the yellow area that provides the optimum response, the desirability value approaching 1 indicates the desired formula but the desirability value approaching 0 indicates the formula is not as desired, the results of the Counter plot of the desirability value are shown in Figure 19.

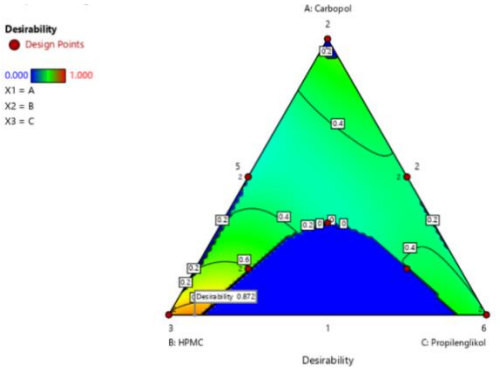


Figure 1. Counter plot Desirability

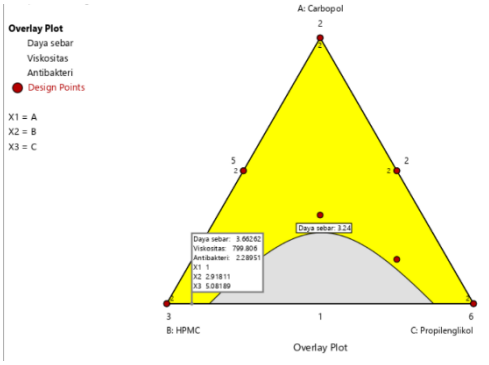


Figure 2. Counter plot superimposed mangosteen skin gel

Verification of optimization results and statistical analysis

The optimum formula predicted by the Simplex Lattice Design method was tested for its accuracy by making a gel preparation formula again and conducting physical quality tests including adhesive power, spread power, viscosity, and antibacterial. The results obtained showed that the prediction and experimental data were not much different, the results are shown in table 23.

Table 23. Prediction value and experiment of ethyl acetate fraction gel of mangosteen rind

Response	Prediction value	Trial value	Conclusion
Spread power	3,779	3.7	No significant difference
Viscosity	439,610	436.66	No significant difference
Antibacterial	2.116	2.14	No significant difference

Results of physical stability testing of optimum formula

The optimum formula of ethyl acetate fraction gel preparation with a humectant composition of carbopol 940 1,500%, HPMC 1000DB 2,500%, and Propylene glycol 5,000% was then tested for physical quality again with accelerated storage for 3 cycles. This method is called the freeze thaw method, namely by placing the

gel preparation at a temperature of ± -10 ° C for 24 hours and at room temperature around 25-29 ° C for 24 hours (1 cycle), observations were made on the viscosity, spreadability, adhesiveness, pH, and organoleptic of the ethyl acetate fraction gel preparation of mangosteen rind in the 0th and 3rd cycles.

Organoleptic and Homogeneity

Organoleptic observations conducted on the mangosteen rind ethyl acetate fraction gel preparation during cycle-0 and cycle-3 storage did not show any changes in color, odor, shape and homogeneity. From these results, it can be seen that the mangosteen rind ethyl acetate fraction gel preparation is stable. The results of organoleptic observations are seen in table 24.

Table 24. Organoleptic observations of the optimum formula for mangosteen rind gel preparation

Cycle	Color	Smell	Form	Homogeneity
0	Yellow	Odorless	Semi solid	Homogeneous
3	Yellow	Odorless	Semi solid	Homogeneous

pH

Observation of pH on the optimum formula of mangosteen rind ethyl acetate fraction gel preparation was carried out in cycles 0 to 3. The pH value results can be presented in table 25.

Table 25. The optimum pH value of the formula for the ethyl acetate fraction gel preparation from mangosteen rind

Replication	Cycle-0	Cycle-3
Replication-1	6.75	6.23
Replication-2	6.54	6.37
Replication-3	6.67	6.43
Average	6.65	6.34

Based on the test data above, it can be seen that the pH in the preparation is stable as evidenced by the absence of any pH values that experience significant changes and fall into the category of pH that is safe for the skin, a pH that is safe for the skin is 4.5-7 (Pranawati, et al 2016). The results of the analysis using Shapiro-Wilk showed that the pH data in cycle-0 was normally distributed with a significant value of 1>0.05 and cycle-3 was normally distributed with a value of 1>0.05. Normally distributed data will be continued with T-test testing of the test results from the T-test with the results in cycle-0 the p-value is greater than the alpha value 129.904> 0.05 which means H0 is accepted and Ha is rejected, while the results of the T-test in cycle-3 the p-value is greater than the alpha value 64.086> 0.05 which means Ho is accepted and Ha is rejected, if Ho is accepted and Ha is rejected then it can be concluded that there is no influence between the independent variable and the dependent variable.

Adhesion

Observation of the adhesive power of the optimum formula of mangosteen rind ethyl acetate fraction gel was carried out in cycle 0 and cycle 3, for the results of this test will be processed with Shapiro-Wilk to determine the data obtained is normally distributed or not normally distributed, the adhesive power data entered into the Shapiro-Wilk software obtained adhesive power in cycle-0 with a significant value of 0.637> 0.05 and in cycle-3 with a significant value of 0.637> 0.05.Normally distributed data will be continued with T-test testing, the test results from the T-test with the results in cycle-0, the p-value is smaller than the alpha value -287.253 <0.05 which means Ho is rejected and Ha is accepted, the results of the T-test in cycle-3, the p-value is smaller than the alpha value -322.404 <0.05 which means H0 is rejected and Ha is accepted, based on the data above, it can be concluded that there is an influence between the independent variable and the dependent variable., the results of the adhesion test can be seen in table 26. The SPSS data for viscosity can be seen in appendix 33.

Table 26. Stability testing of adhesive power of gel preparations

Cycle	Adhesion (seconds)
0	3.42
3	3.15

Spread power

Observation of the spreadability of the optimum formula of the mangosteen rind ethyl acetate fraction gel preparation was carried out in cycle 0 and cycle 3, for the value of the results of this test will be processed with Shapiro-Wilk to determine the data obtained is normally distributed or not normally distributed. The spreadability data in cycle-0 obtained in Shapiro-Wilk is normally distributed with a significant value of 0.812> 0.05 while in cycle-3 it is normally distributed with a value of 0.910> 0.05. The test is continued by using the T-test where in cycle-0 the p-value is smaller than the alpha value -32.007 <0.05 which means Ho is rejected and Ha is accepted and in cycle-3 the p-value is smaller than the alpha value -32.742 <0.05 which means H0 is rejected and Ha is accepted, with the data above it can be concluded that there is an influence between the independent variables on the dependent variables, the results of the adhesion test can be seen in table 27, the spss data from the spread power can be seen in appendix 34.

Table 27. Stability testing of gel preparation spreadability

Cycle	Spread power (cm)
0	3.99
3	3.76

Viscosity

Observation of viscosity on the optimum formula of mangosteen rind ethyl acetate fraction gel preparation was carried out in cycle 0 and cycle 3, for the value of the

results of this test will be processed with Shapiro-Wilk to find out the data obtained is normally distributed or not normally distributed, the test results using Shapiro-Wilk to find out the viscosity test data is normally distributed or not then the results in cycle-0 are 0.780> 0.05 normally distributed while in cycle-3 with a value of 0.637> 0.05 normally distributed. The results of the viscosity test above will be continued with the T-test where in cycle-0 the p-value is greater than the alpha value 59.281> 0.05 which means H0 is accepted and Ha is rejected and in cycle 3 the p-value is greater than the alpha value 46.754> 0.05 which means H0 is accepted and Ha is rejected. If H0 is accepted and Ha is rejected, then there is no influence between the independent variable and the dependent variable, meaning that there is no difference in the experimental viscosity values during the storage period in cycle 0 and cycle 3. The results of the adhesive strength test can be seen in table 28. The SPSS data for viscosity can be seen in appendix 35.

Table 28. Stability of viscosity testing of gel preparations

Cycle	Viscosity
0	436.66
3	418.33

Antibacterial activity

Antibacterial activity test on the optimum formula of mangosteen rind ethyl acetate fraction gel preparation using the well diffusion method. In the antibacterial activity test on the optimum formula, namely by observing the clear zone around the well. Antibacterial activity testing was carried out using the optimum formula, positive control using clindamycin antibiotics and negative control using the optimum gel formula preparation without ethyl acetate fraction. Antibacterial activity testing was carried out with 3 replications, testing was carried out 3 replications aimed at getting good results. The results of the antibacterial test can be seen in table 29.

Table 29. Results of antibacterial test of optimum formulation

Contents	Replication (mm)			Average ± SD
	1	2	3	
Optimum formula	1.9	2.2	2.3	2.13±0.20
Positive control (+)	3.3	3.2	3.4	3.3±0.08
Negative control (-)	-	-	-	-

The results of the antibacterial activity test of the optimum formula of the ethyl acetate fraction gel preparation showed that it had an inhibition zone of 21.3 mm, for the positive control it had an inhibition zone of 3.3 mm, and for the negative control there was no inhibition zone, which means that the gel preparation without the ethyl acetate fraction did not have antibacterial activity.

Observation of antibacterial activity on the optimum formula of mangosteen rind ethyl acetate fraction gel was carried out in cycle 0 and cycle 3, the results of this test will be processed with Shapiro-Wilk to determine whether the data obtained

is normally distributed or not normally distributed. The results of the analysis using Shapiro-Wilk showed that the antibacterial activity data in cycle-0 was normally distributed with a significant value of 0.657> 0.05 and cycle-3 was normally distributed with a value of 1>0.05. Normally distributed data will be continued with T-test testing of the test results from the T-test with the results in cycle-0 the p-value is greater than the alpha value 41.966> 0.05 which means H0 is accepted and Ha is rejected, while the results of the T-test in cycle-3 the p-value is greater than the alpha value 41.469> 0.05 which means H0.If H0 is accepted and Ha is rejected, it can be concluded that there is no influence between the independent variable and the dependent variable, meaning that there is no difference in the experimental viscosity values during the storage period in cycle 0 and cycle 3.

Conclusion

Based on the results of the study, it can be concluded that the ethyl acetate fraction of mangosteen rind with a concentration of 10% has antibacterial activity against Staphylococcus epidermidis bacteria with an inhibition zone of 28.6 mm. The proportion of the mangosteen rind gel preparation formula to the concentration of Carbopol 940 1.5 gr, HPMC 1000DB 2.5 gr, propylene glycol 5 gr with a spreadability value of 4.35 cm, viscosity 433.33, antibacterial 21.4 mm. The optimum formula of the mangosteen rind gel preparation with a combination of carbopol 940, HPMC 1000DB and propylene glycol has antibacterial activity against Staphylococcus epidermidis bacteria.

Similar research needs to be conducted with the replaced humectant, namely HPMC 1000DB replaced with CMC, to see the stability test of the gel preparation containing HPMC 1000DB and CMC has a significant difference or not. Antibacterial activity testing can use other bacteria, namely Staphylococcus aureus and Propionicbatarium acnes, which are one of the bacteria that cause acne.

Conflict of interest statement
The authors declared that they have no competing interests.

Statement of authorship
The authors have a responsibility for the conception and design of the study. The authors have approved the final article.

Acknowledgements
The author would like to thank the Director of RSAU dr. Efram Harsana Madiun and all the staff of the Pharmacy Installation of the Director of RSAU dr. Efram Harsana Madiun for their assistance and cooperation during the research and all related parties for the permission given to the author to conduct the research.

References

Awaliyah, H. F., & Yuriah, S. (2024). Family empowerment in support of pregnancy examination: Scoping review. *International Journal of Health Sciences*, *8*(S1), 1543–1555. https://doi.org/10.53730/ijhs.v8nS1.15319

Ayorbaba, F. R. H., 2020. Optimasi CMC-Na dan Propilen Glikol dalam Sediaan Gel Ekstrak Herba Pegagan (Centalla asiatica (L.) Urban) dengan Metode Simplex Lattice Design. Skripsi. Universitas Sanata Dharma, Yogyakarta.

Badan POM. 2003. *Bahan Tambahan Pangan, Direktorat Surveilan dan Penyuluhan Pangan*. Deputi Bidang pengawasan Keamanan Pangan dan Bahan Berbahaya. Jakarta Badan POM

Badan Pengawas Obat dan Makanan Republik Indonesia (BPOM RI). 2014. Peraturan Kepala Badan Pengawas Obat dan Makanan Republik Indonesia Nomor 17 Tahun 2014 tentang Perubahan atas Peraturan Peraturan Kepala Badan Pengawas Obat dan Makanan Nomor HK.03.1.23.07.11.6662 Tahun 2011 Tentang Persyaratan Cemaran Mikroba dan Logam Berat dalam Kosmetika. Jakarta: Badan Pengawas Obat dan Makanan Republik Indonesia.

Badan Pengawas Obat dan Makanan. 2003. Keputusan Kepala Badan Pengawas Obat dan Makanan Republik Indonesia Nomor Hk.00.05.4.1745 Tahun 2003, Tentang Kosmetik, Kepala Badan Pengawas Obat dan Makanan, Jakarta.

Bahri, S., Pasaribu, F. Dan Sitorus, P. 2012. Uji Ekstrak Etanol Kulit Buah Manggis (Garcinia Mangostana ,L) Terhadap Penurunan Kadar Glukosa Darah. Journal of Pharmaceutics and Pharmacology. 1(1) : 1-8.

Barel, A.O., Paye, M., and Maibach, H.I. 2009. *Handbook of Cosmetic Science and Technology, 3rdEdition*. New York: Informa Healthcare USA, Inc.,

BPOM RI, 2014, Persyaratan Mutu Obat Tradisional, Peraturan Kepala Badan Pengawas Obat dan Makanan Republik Indonesia, Indonesia, p. 1–25.

Choma, I., & Edyta, M. 2010. Bioautography Detection in Thin-Layer Chromatography. *Journal of Chromatography.*

Chomnawang MT, Surassmo S, Nukoolkarn VS, Gritsanapan W. 2005. Antimicrobial effects of Thai medicinal plants against acneinducing bacteria. 101:330-333.

[Depertemen Kesehatan RI]. 2000. *Invertaris Tanaman Obat Indonesia.* Jakarta: Depertemen Kesehatan Republik Indonesia.

Dewanjee, S. *et.al.* 2015. "Bioautografi and its scope in the field of natural product chemistry, "*Journal of Pharmaceutical Analysis*. Elsevier, 5(2) pp. 75-84 doi: 10.1016/j.jpha.2014.06.002

Dewanti, S. dan M. T. Wahyudi. 2011. Uji Aktivitas Antimikroba Infusum Daun Salam (Folia Sygium polyanthum WIGHT) terhadap Pertumbuhan Bakteri Escherichia coli secara In Vitro. Jurnal Medika Planta 1 (4) : 78-81.

Draelos, Z.D., 2010. Cosmetic Dermatology Products and Procedures.West Sussex:Willey-Blackwell

Efendi, Z., 2003. Peranan Kulit dalam Mengatasi Terjadinya Akne Vulgaris. Available from :http://library.usu.ac.id/download/fk/histologi-zukesti3.pdf.

Emma, S, K., Iskandarsyah., Praptiwi.. 2014. Evaluasi Uji Stabilitas Sineresis Sediaan Gel yang Mengandung Minoksidil, Apigenin dan Perasan Herba Seledri (Apium graveolens L). *Jurnal Bul. Penelitian Kesehatan.* Vol 4:213-222

Fitriani. 2017. Analisis Penggunaan Rele differensial sebagai Proteksi pada Transformator Daya 16 MVA di Gardu Induk Jajar. Jurnal. Jurusan Teknik Elektro. Fakultas Teknik. Surakarta: Universitas Muhammadiyah

Gunawan D, Mulyani S. 2004. *Ilmu Obat* (*Farmakognosi)*. Jakarta: Penebar Swadaya. hlm 13.

Gunawan, I. W. A.. 2009. Potensi Buah Pare (*Momordica charantia* L)Sebagai Antibakteri *Salmonella thphimurium. Skripsi*. Fakultas Keguruan dan Ilmu Pendidikan. Denpasar: Universitas Mahasaraswati Denpasar

Hambali,)E.,)S.)Mujdalipah,)A.)H.)Tambunan,)A.)W.)Pattiwiri) dan) R.) Hendroko,)) 2008.) Teknologi) Bioenergi.) Agro) Media,)Jakarta.

Harborne. JB. 1987. *Metode Fitokimia penentun Cara Modern Menganalisa Tumbuhan,* Pandmawinata k. Soediro I. Penerjemah. Niksolihim S, editor. Bandung: ITB

Harminta RM. 2004. *Analisa Hayat.* Jakarta: Departemen Farmasi FMIPA Universitas Indonesia

Hartanti V. *Jadi Dokter di Rumah Sendiri dengan Terapi Herbal dan Pijat.* Pustaka Anggrek; 2003.

Hasyim, N. & Baharuddin, A., 2011, Formulasi Gel Sari Buah Belimbing Wuluh, Majalah Farmasi dan Farmakologi, 5–9.

Herawati, D, Nuraida, L., Sumarto. 2012. *Cara Produksi Simplisia yang Baik.* 10-11. Bogor: Seafast Center IPB.

Ismail, Isriany. Formulasi Kosmetik (Produk Perawatan Kulit dan Rambut). Makassar: AlauddinUniversity Press. 2013.

Jawetz, E., J, Melnick dan Adelberg. 2004. Mikrobiologi Kedokteran Edisi 23. EGC. Jakarta

Jawetz, M. 2005. Adelberg. Mikrobiologi Kedokteran.

Juniarti, S., Yuriah, S., & Sepriani, P. (2024). Women's empowerment model in treatment of pregnant women at risk of anemia in Indonesia: Literature review. *International Journal of Health Sciences*, *8*(S1), 1680–1689. https://doi.org/10.53730/ijhs.v8nS1.15357

Kanisius. 2003. Bibit Manggis. Penerbit Kanisius, Yogyakarta.

Katno, Kusumadewi AW, Sutjipto. 2008. Pengaruh waktu pengeringan terhadap kadar tanin daun jati Belanda (*Guazumaulmifolia* Lamk.). *Jurnal Tumbuhan Obat Indonesia* 1: 38-46.

Kastaman, R. 2007. Prospective Analysis on Development of Mangosteen (Garcinia mangostana) Processing Product in order to Improve Farmers Income (Case Study in Kecamatan Puspahiang Kabupaten Tasikmalaya). Jurnal Agrikultural. Vol 18. No. 15

Kemenkes RI. 2017. Data dan Informasi Kesehatan Profil Kesehatan Indonesia 2016

Kibbe, A. H., 2004, Handbook of Pharmaceutical Exipients, Third Edition, 18-19, 462-469, 629-631, Pharmaceutikal Press, London.

Komansilan, J. G., Christy N. M., dan Olivia W. 2015. Daya Hambat Ekstrak Kulit Manggis (Garcinia mangostana L.) terhadap Streptococcus mutans. Jurnal eGiGi (eG). 3(2) : 309-316.

Lestari, P. B, dan Hartati, T. W. 2017. *Mikrobiologi Berbasi Inkuiry*. Cet. 1, Penerbit Gunung Samudera. Malang.

Madan J. dan Singh R., 2010, Formulation and Evaluation of Aloe Vera Topical Gels, Int. J. Ph. Sci, 2 (2), 551–555.

Misnadiarly, dan Djajaningrat, Husjain. 2014. Mikrobiologi untuk Klinik dan Laboratorium. Jakarta : Rineka Cipta.

Mukhriani. 2014. Ekstraksi, Pemisahan Snyawa, dan Identifikasi Senyawa Aktif,

Muliyawan, Dewi & Suriana, Neti. 2013. A-Z Tentang Kosmetik. Jakarta: PT Elex Media Komputerindo

Mulyaningsih, S. 2004. *Mikrobiologi Dasar.* Buku FMIPA UII. Yogyakarta : UII

Nimah, S. Widodo F, dan Agus T. 2012. Uji Bioaktivitas Ekstrak Teripang Pasir (Holothuria scabra) terhadap Bakteri Pseudomonas aeruginosa dan Bacillus cereus. Jurnal Perikanan no 1. Vol.2

Pratiwi ST. 2008. *Mikrobiologi Farmasi.* Jakarta: Penerbit Airlangga.

Primadiati, R. 2001. Kecantikan Kosmetika dan Estetika. Jakarta: PT. Gramedia Pustaka Utama

Poeloengan, M., dan Praptiwi. 2010. Uji Aktivitas Antibakteri Ekstrak Kulit Buah Manggis (Garcinia mangostana Linn). Media Litbang Kesehatan. 20(2) : 65-69.

Pranawati, E., Sugihartini, N., Yuwono, T., Farmasi, F., Dahlan, U. A., & Email, C. (2016). SIFAT FISIK DAN DAYA IRITASI KRIM TIPE A / M MINYAK ATSIRI BUNGA CENGKEH (Syzigium aromaticum) DENGAN BERBAGAI VARIASI KONSENTRASI cengkeh (Syzygium aromaticum) memiliki khasiat diantaranya satu faktor pendorong untuk dikembangkannya sediaan yang prak. Jurnal Ilmiah Farmasi, 12(1), 1–7.

Putri IJ, Fauziyah. Elfita. 2013. Aktivitas antioksidan daun dan biji buah nipah (*Nypa fruticans*) asal pesisir Banyuasin Sumatera Selatan dengan metode DPPH. *Maspari Journal* 5(1): 16-21.

Putri et al, 2013, Skrining Fitokimia Ekstrak Etil Asetat Kulit Buah Manggis (Garcinia mangostana L.)

Qa'dan F., Thewani A.J., Ali D.A., Aßißi R., Elkhawad A., Matalka K.Z. The antimicrobial activities of Psidium guajava and Juglans regia leaf extracts to acne-developing organism, *Am J chin Med*, 33 (2): 197-205. 2005.

Ramdani, R., Sibero, H.T. 2015. *Treatment for Acne Vulgaris.* Lampung: Fakultas Kedokteran Universitas Lampung

Ramyashree, M., Krishna Ram, H., and Shivabasavaiah., 2012, Ethnomedicinal value of Opuntia elatior fruits and its effects in mice, Online Jurnal of Natural Science, Vol.3(3): 331 – 340.

Rijayanti, R.P. 2014. Uji Aktivitas Antibakteri Ekstrak Etanol Daun Mangga Bacang (Mangifera feotida L.) Terhadap Staphylococcus aureus Secara In-Vitro. *Skripsi*. Universitas Tanjungpura Pontianak.

Roudhatini., 2013, Uji Efektivitas Sediaan Gel Anti Jerawat Minyak Atsiri Daun Jeruk Sambal (X Citrofortunella microcarpa (Bunge) Wijnands) Terhadap Propionibacterium acnes dan Staphylococcus epidermidis, Skripsi, Fakultas Kedokteran Universitas Tanjungpura, Pontianak.

Rowe, et al. 2009. *Handbook of Pharmaceutical Excipients, sixth edition.* London: The Pharmaceutical Press

Saising, J., Hiranrant, A., Mahabusarakam, W., Ongsakul, M. and Voravuthikunchai, S. P., 2008. Rhodomyrtone from Rhodomyrtus tomentosa (Aiton) Hassk. as a Natural Antibiotic for Staphylococus Cutaneous Infections. *Journal of Health Science,* 54(5):589-595.

Sanches Neviton Rogério, Cortez Diógenes Aparício Garcia, Schiavini Michelle Simone,NakamuraCelso Vataru, Filho Benedito Prado Dias. An evaluation of antibacterial activities of Psidium guava (L.). Brazilian archieves of biology and technology, *an international journal.* 2005; 48(3): 429—36.

Sarker, Satyajit D., Zahid Latif, & Alexander I. Gray (Ed). 2006. *Natural Products Isolation.* Totowa : Humana Press

Sinko, P. J., 2011, Martin Farmasi Fisika dan Ilmu Farmasetika, diterjemahkan oleh Tim Alih Bahasa Sekolah Farmasi ITB, Edisi kelima, 706, Penerbit Buku Kedokteran EGC, Jakarta.

Sukmawati, N.M.A., 2013, Pengaruh Variasi Konsentrasi PVA, HPMC, dan Gliserin terhadap Sifat Fisika Masker Wajah Gel Peel Off Ekstrak Etanol 96% Kulit Buah Manggis (Garcinia mangostana L.), Skripsi, Fakultas Farmasi, Universitas Udayana Denpasar.

Suryani dan Teuku N.S.S. 2018. Formulasi Gel Minyak Atsiri Sereh dengan Basis HPMC dan Karbopol. Majalah Farmaseutik Vol. 14 No. 2 : 87-95 ISSN-p : 1410-590x ISSN-e : 2614-0063

Suryani. *Et al.* 2017 Optimasi Formula Gel Antioksidan Ekstrak Etanol Buah Bligo (Benincasa hispida) dengan Metode Simplex Lattice Design (SLD). Jurnal Farmasi Galenika (Galenika Journal of Pharmacy) 2017; 3 (2): 150 – 156

Tambunan, S., Sulaiman, T.N.S., 2018, Formulasi Gel Minyak Atsiri Sereh dengan Basis HPMC dan Karbopol, Majalah Farmaseutik, Vol 14(2), Fakultas Farmasi, Universitas Gadjah Mada, Yogyakarta.

Tranggono dan Latifah. 2007. *Buku Pegangan Ilmu Pengetahuan Kosmetik*, Editor: Jhosita Djadjadisastra. Jakarta: Penerbit Pustaka Utama

Tiwari P. Bimlesh K. Mandeep K., Gurpreet K., Harleen K 2011. *Skrinning Fitokimia dan Ekstrasi. Internationale Pharmaceutica Selencia.* 1 (1). Departemen Farmasi Ilmu Sekolah. Indah Ilmi Farmasi. Phagwara, punjab.

Valmai. 2019. Aktivitas Antibakteri Ekstrak Etil Asetat Kulit manggis (*Garcinia mangosta.* L) terhadap *Staphylococcus epidemidis*. Acta Pharm Indo. Vol 7 No 1 : 36-41

Winarsih, H. 2007. Antioksidan Alami dan Radikal Bebas. Yogyakarta: Kanisius.

Yuriah, S., Ananti, Y., & Nurjayanti, D. (2024). Dynamics of the experience of sexual violence and its impact on girls in Ogan Komering Ulu Regency. *International Journal of Health Sciences*, *8*(S1), 579–592. https://doi.org/10.53730/ijhs.v8nS1.14860

Yuriah, S., Juniarti, S., & Sepriani, P. (2023). Midwifery care for Mrs "Y" at BPM Soraya Palembang. *International Journal of Health Sciences*, *7*(S1), 2966–2984. https://doi.org/10.53730/ijhs.v7nS1.14631