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Antimicrobial Activity of Ethanol Extract of Cucumber (*Cucumis Sativus* L.) Peels and Formulation as Anti-Acne Cream

Nadya Wulan Ramadhani[1]*, Siti Harnina Bintari[1]

[1]Department of Pharmacy, Universitas Negeri Semarang, Semarang, 50229, Indonesia

*Correspondence to: *nadyawulanramadhani02@students.unnes.ac.id*

Abstract: Background: Cucumber is proven to have pharmacological activities as antimicrobial. Some of the secondary metabolites contained in cucumber fruit have antimicrobial activity. **Aim:** This study aims to determine the antibacterial activity of ethanol extract of cucumber peels against *Staphylococcus epidermidis* and to make anti-acne cream using cucumber skin extract. **Material and Methods:** The extraction of cucumber peels extract with maceration using 96% ethanol solvent. Phytochemical screening to determine the compounds contained in the extract. The antibacterial activity test of the extract was carried out through liquid and solid dilution methods to determine the MIC and MBC values. The extract was then made into a cream with varying concentrations of stearic acid and TEA as an emulsifier and then evaluated and tested for antibacterial activity using the agar diffusion method. **Results:** Cucumber peels extract contains steroids, alkaloids, flavonoids, phenols, and saponins that have antibacterial activity against *Staphylococcus epidermidis* with an MIC value of 2.5% and an MBC value of 5%. The results of the cream evaluation test show that formula F(3) is the most optimal formula for inhibiting *Staphylococcus epidermidis* bacteria with a cucumber skin concentration content of 4.5%. The antibacterial activity test has an inhibition zone of 33-52.70 mm with a very strong category.

Keywords: Cucumber peels, antibacterial, *Staphylococcus epidermidis*, anti-acne cream

INTRODUCTION

Indonesia had 60% of patients suffering from acne in 2006 which then increased to 80% of patients and increased again in 2009 to 90% of patients (Saragih et al., 2016). Bacteria that cause acne work by producing lipase that will break down free fat from skin lipids that will harden so that inflammation is triggered by one of the bacteria *Staphylococcus epidermidis* (Mulqie et al., 2015). So far there are several ways to treat acne, one of which is with antibiotic therapy. he use of antibiotics itself has the side effect of causing irritation and can increase bacterial resistance, thus reducing its effectiveness (Madelina & Sulistiyaningsih, 2018). An alternative acne therapy with relatively minimal side effects is needed by utilizing natural ingredients, one of which is the use of cucumber fruit peel (*Cucumis sativus* L.).

Cucumber (*Cucumis sativus* L.) is proven to have several pharmacological activities such as antioxidant, antidiabetic, hypolipidemic agent, and antimicrobial (Mukherjee et al., 2013). Cucumber fruit (*Cucumis sativus* L.) contains secondary metabolites such as alkaloids, phenols, flavonoids, terpenoids, and saponins that have antimicrobial activity (Agustin & Gunawan, 2019). According to research Anjani et al., (2023) states that cucumber (*Cucumis sativus* L.) peels extract has KHM against Escherichia coli, Streptococcus mutans and Pseudomonas aeruginosa bacteria at concentrations of 1.87; 3.75; and 7.5 mg/ml. aside from the meat, cucumber (*Cucumis sativus* L.) peels also has potential as an antimicrobial agent but is still rarely studied, so in this study, antimicrobial activity testing will be carried out against *Staphylococcus epidermidis* bacteria and formulation of cream that contains cucumber (*Cucumis sativus* L.) peels extract.

Topical treatment is usually one of the acne treatment routes because topical drugs are intended for use on the skin and produce local effects (Fitriani, Lubis, Yuniarti, & Rahayu, 2022). One of the topical treatments for acne treatment is cream which is an appropriate preparation because it is easier to apply and is not fatty (Hadisoebroto & Budiman, 2019). Cream is a semi-solid preparation containing dissolved or dispersed medicinal ingredients in a suitable base (Depkes RI, 2014). There are two types of cream preparations, namely oil-in-water cream type (M/A) and water-in-oil type (A/M). Oil-in-water (M/A) cream type is a type of cream that is easily washed with water, so it is often intended for cosmetic use (Hasniar, 2015). Therefore, this study aims to look at the antibacterial activity of peel off mask preparations of cucumber (*Cucumis sativus* L.) peels extracted with 96% ethanol against *Staphylococcus epidermidis and* This is intended to optimize the utilization of cucumber peels into a useful and valuable product.

METHODS

Extraction

Fresh cucumber peels were obtained from MSMEs sellers around the author. The cucumber skin was peeled manually and dried in the sun and then pulverized with a blender. To make the extract, 500 g of cucumber skin simplicial powder was macerated using 96% ethanol (1:10 ratio) in a closed container for 24 hours while stirring occasionally. Remaceration was carried out for 2x24 hours. The extract was filtered through filter paper and concentrated at 60°C using a rotary evaporator machine at 100rpm.

Phytochemical Screening

Phytochemical screening can be done in a qualitative way through the addition of certain reagents to the extract.

a. Steroid test. Add 1-3 drops of anhydrous acetic acid and concentrated H2SO4 to 2mg of extract, a blue color will form.
b. Alkaloid test. Add 1-3 drops of mayer reagent to 2mg of extract. A white precipitate will form if the extract contains Alkaloids.
c. Phenol test. Add 1-3 drops of FeCl3 1% on 2mg of extract. A blackish color will appear if the extract contains phenolics.
d. Flavonoid test. Add 1-3 drops of 10% AlCl3 to 2mg of extract. A red color will appear if the extract contains flavonoids.
e. Saponin test. 2 mg of extract was added to distilled water until the entire snippet was submerged and then boiled for 2 minutes and cooled and shaken. A stable froth will form if the extract contains saponin compounds.

Antibacterial Activity of Cucumber Peel Extract

Antibacterial activity test of cucumber peel extract was carried out by liquid dilution and liquid dilution methods. The solid dilution method is used to calculate MBC, while the liquid dilution method is used to calculate Minimum Inhibitory Concentration (MIC) (Sari, Apridamayanti, & Pratiwi, 2022). To measure the minimum inhibitory concentration (KHM) is done through the liquid dilution method by inserting 4 ml of cucumber skin extract (*Cucumis sativus* L.) into each test tube with a concentration variation of 5%; 2.5%; 1.25%; and 0.625% along with positive control and negative control. After that, each test tube containing the extract and control was added with 1 ml of bacterial suspension. Then all test tubes were incubated at 37°C for 18-24 hours and observed for turbidity (Fitriyanti, Ridha, & Ramadhan, 2023). Meanwhile, to calculate the minimum kill concentration (KBM), each test concentration and control was inoculated to NA media using an ose then incubated at 37˚C for 18-24 hours and observed the number of bacteria that grew (Fitriyanti et al., 2023).

Formulation of Anti-Acne Cream Base

This formulation consist of stearic acid, cetyl alcohol, dan TEA as emulsifier. Glycerin and propylene glycol as moisturizer. Methylparaben and propylparaben as preservatives and distilled water as solvent

Table 1. Formulation of Anti-Acne Cream Base

Materials	F1	F2	F3	F4
Stearic Acid	8%	9%	10%	12%
Cetyl Alcohol	2%	2%	2%	2%
Glycerin	5%	5%	5%	5%
Propylene Glycol	10%	10%	10%	10%
Triethanolamine	2%	2%	3%	4%
Methylparaben	0,18%	0,18%	0,18%	0,18%
Propylparaben	0,02%	0,02%	0,02%	0,02%
Aquades ad	100%	100%	100%	100%

The cream was prepared by melting stearic acid in a water bath at 70-80°C. Triethanolamine, methylparaben, and propylparaben were dissolved into propylene glycol (Mixture 1). Mixture 1 was added to glycerin (Mixture 2), then stirred until homogeneous. It was then heated with stearic acid in a saucer on a water bath (Mixture 3). The remaining water was also heated to boiling. Mixture 3 and the remaining water were put into a hot mortar and stirred at a constant speed to form a creamy mass.

Evaluation Test of Cream Base

This evaluation includes organoleptic, pH, homogeneity, spread-ability, adhesion, and emulsion type. Organoleptic tests were carried out by applying the cream to the preparation glass and then observing the texture, color, and smell of the cream. The pH was carried out by diluting 1 gram of cream using 10 ml of distilled water and then measured using a pH meter. The homogeneity test was carried out by spreading 1 gram of cream on the preparation glass and then observe the preparation whether it still contains unmixed particles. The spreadability test was carried out by applying 1 gram of cream on the preparation glass and then observe the preparation whether it still contains unmixed particles. The spread-ability test was carried out by applying 1 gram of cream on the preparation glass and then observing the preparation whether it still contains unmixed particles. The adhesion test was carried out by applying 250 mg to the adhesion test device and crushed with a 1 kg load for 5 minutes and then counted the time until the two object glasses separated. The emulsion type test was carried out by dissolving the cream using distilled water.

Antibacterial Activity Test of Cucumber Peels Extract Cream.

The analysis of antibacterial activity of cucumber peels extract cream was carried out using the well diffusion agar method by making holes using a cork borer on agar and putting cucumber peels extract cream preparations and Medi-Klin cream as a positive control into the well that had been prepared earlier and then incubated in an incubator for 18-24 hours at 37^{o}C then the inhibition zone formed was measured using a caliper (Trisuci et al., 2020). The media used for this method is Nutrient Agar media which is prepared by dissolving 11.5 grams of nutrient agar using 500 ml of distilled water then sterilized using an autoclave at a pressure of 1 atm and a temperature of 121˚ C for ± 15 minutes and then allowed to solidify. Then the bacterial inoculum was streaked using a sterile ose needle and then incubated for 18-24 hours at 37^{o}C.

RESULT AND DISCUSSION

Extraction

Cucumber peels extract was obtained by extraction using the maceration method. This method has the main advantage of easy-to-use procedures and equipment. In this method, no heating is required so that there will be no decomposition of active compounds due to high temperatures (A. D. Puspitasari & Prayogo, 2017). Maceration was carried out using 96% ethanol because of its good absorption and good filtering ability so that non-polar, semi-polar, and polar compounds can be attracted. This is because 96% ethanol solvent is easier to penetrate into the cell wall of the sample than the ethanol solvent concentration below so that the resulting extract is more concentrated (Wendersteyt, Wewengkang, & Abdullah, 2021). The thick extract was weighed and obtained a thick extract weighing 43.78gr. The yield of the extract obtained was 8.75%.

Figure 1. Cucumber Peels Extract

Phytochemical Screening

The purpose of phytochemical screening is to determine the content of secondary metabolic compounds contained in the extract (Baharuddin, 2017). The results of phytochemical screening of cucumber skin extract can be seen in the following table.

Table 2. Phytochemical Screening

Assay	Reagent	Positive	Identification	Result
Steroid	Liebermann-Burchard	Blue-green	Formed blue-green color complex	(+)
Alkaloid	Mayer	White colored precipitate	Formed white colored precipitate	(+)

Phenolic	FeCl3 1%	Blackish	Formed blackish colored complex	(+)
Flavonoid	AlCl3 10%	Yellow	Formed yellow colored complex	(+)
Saponin	Aquadest	Bubbles	Formed stable bubbles	(+)

a. Steroid

Analysis of steroid content is done by adding Liebermann-Burchard reagent to the extract. If the extract contains steroids, a green-blue color will form. In this process there is an acetylization reaction to the -OH group between steroid compounds and anhydrous cetic acid. Steroid compounds will be oxidized by forming conjugated double bonds so that color changes occur (Sulistyarini, Sari, & Wicaksono, 2019).

b. Alkaloid

Analysis of alkaloid content is done by adding 1-3 drops of mayer reagent to 2mg of extract. A white precipitate will form if the extract contains Alkaloid (Agustin & Gunawan, 2019). In the alkaloid test using Mayer's reagent, nitrogen in the alkaloid will react with the metal ion K + from potassium tetraiodomercurat (II) to form a potassium-alkaloid complex that precipitates (Wardhani & Supartono, 2015).

c. Phenolic

Analysis of phenol content is done by adding 1-3 drops of FeCl3 1% to 2mg of extract. A blackish color will appear if the extract contains phenol (Ikalinus et al., 2015). The blackish color arises because FeCl3 can react with phenol hydroxyl groups bound to unsaturated carbon which then produces a blackish color complex (Bawekes, Yudistira, & Rumondor, 2023).

d. Flavonoid

Analysis of flavonoid content is done by adding 1-3 drops of 10% AlCl3 to 2mg of extract. A yellow color will appear if the extract contains flavonoids (Marpaung & Wahyuni, 2018). The yellow color that is formed is due to the formation of a compound complex between AlCl3 with ketone groups at C-4 atoms and hydroxy groups at C-3 or C-5 atoms in flavonoid compounds (Estikawati & Lindawati, 2019).

e. Saponin

Analysis of saponin content was carried out by adding distilled water to 2 mg of extract and then boiling for 2 minutes and cooling and shaking. A stable foam will form if the extract contains saponin compounds (Ngajow et al., 2013). Because glycosides that can form foam in water contained in the compound so that foam can be formed in the saponin test (Agustina, Nurhamidah, & Handayani, 2017).

Antibacterial Activity of Cucumber Peel Extract

To determine the antibacterial activity of cucumber peels extract, a liquid dilution test was carried out to determine the Minimum Inhibitory Concentration (MIC) which is indicated from the lowest concentration of extract in a tube that also contains bacterial culture which begins to appear clear indicating no bacterial growth (Fitriana, Fatimah, & Fitri, 2020). Nutrient Broth media and solid diffusion using Mannitol Salt Agar were used. The extracts were made in concentrations of 5%; 2.5%; 1.25%; and 0.625%. The results of the antibacterial activity test of cucumber peel extract by liquid dilution method are shown in the table.

Table 3. Antibacterial Activity of Cucumber Peel Extract

Concentration	Result
5%	Clear
2,5%	Clear (MIC)
1,25%	Turbid
0,625%	Turbid
Positive Control (Medi-Klin)	Clear
Negative Control (DMSO 10%)	Turbid

Based on the research that has been done, the results of the liquid dilution test show that it starts to look clear at a concentration of 2.5% which shows the MIC value of cucumber peels extract against *Staphylococcus epidermidis* bacteria. The solution looks turbid at concentrations of 0.625% and 1.25%. According to research (Anjani et al., 2023) states that cucumber peels extract has MIC against *Escherichia coli, Streptococcus mutans* and *Pseudomonas aeruginosa* bacteria at concentrations of 1.87, 3.75 and 7.5 mg/ml. Due to the nature of gram-positive bacteria that have osmotic pressure 3-5 times greater than gram-negative bacteria, gram-negative bacteria are more susceptible to lysis. Lysis itself can cause the ability of bacteria to form colonies to disappear due to damage to the bacterial cell wall. Gram-positive bacterial cells consist of thick peptidoglycan which provides rigidity to maintain cell integrity (Suriaman, Permana, & Warman, 2016). Therefore, the concentration of cucumber peel extract needed to inhibit the growth of Escherichia coli bacteria is less than the concentration needed to inhibit bacteria from gram-positive bacteria.

The results of the liquid dilution test were then inoculated on solid agar media to determine the minimum bactericidal concentration (MBC) by the solid dilution method and the results shown in the figure and table.

Table 4. Liquid Dilution Test

Concentration	Total of Bacteria
5%	0
2,5%	64
1,25%	>300
0,625%	>300
Positive control	0
Negative control	>300

Based on the results of the antibacterial activity test of cucumber peel extract by solid dilution method, it can be concluded that the MBC of cucumber peels extract is 5% because no bacteria grow at that concentration. The solution was cultured on Mannitol Salt Agar media and incubated for 24 hours. The culture results showed pink and red colors. According to research (Abdilah & Kurniawan, 2022), pink and red bacterial colonies that grow on Mannitol Salt Agar are coagulase negative Staphylococcus group bacteria such as *Staphylococcus epidermidis*.

Formulation of Anti-Acne Cream Base

After obtaining the KHM of cucumber skin extract, acne cream preparations were made with a concentration of 2.5%; 3.5%; and 4.5% of the extract contained. Variations in extract concentration were carried out after obtaining the most optimal base formula. Cucumber skin extract cream was tested for antibacterial activity against *Staphylococcus epidermidis* bacteria by well diffusion agar method.

Evaluation Test of Cream Base

a. Organoleptic

This test is related to the comfort of the preparation when used because the cream is a topical preparation (Afianti & Murrukmihadi, 2015). The results of the organoleptical test of the cream base can be seen in the table below.

Table 5. Organoleptic Test of Cream Base

Formula	Color	Form	Odor
F1	White	Liquid	Typical chemical odor
F2	White	Liquid	Typical chemical odor
F3	White	Cream	Typical chemical odor
F4	White	Thick cream	Typical chemical odor

Based on the table, organoleptical results were obtained which were almost similar from the four formulas. It's just that there are differences in the consistency of the preparation which according to research (N. Sari, Samsul, & Narsa, 2021) is due to the concentration of stearic acid and TEA which have functions as emulgators in the preparation so that there is an increase in viscosity in the formula.

b. pH

The pH test is carried out to observe whether the pH of the preparation can be used safely without irritating the skin (N. Sari et al., 2021). A good cream preparation has a pH close to the pH of the skin, which is in the range of 4.5-6.5 (Lumentut et al., 2020). The results of the evaluation of the pH test of the cream base can be seen in the table below.

Table 6. pH Tests of Cream Base

Formula	pH			
	Replication 1	Replication 2	Replication 3	Average
F1	6,45	6,43	6,44	6,44
F2	6,33	6,24	6,25	6,27
F3	6,26	6,28	6,28	6,27
F4	6.16	6,17	6,18	6,17

It can be seen from the table that each concentration decreased in pH because each concentration contains different stearic acid. This is in line with research (Saryanti, D., Setiawan, I., and Safitri, 2019) which states that the higher the concentration of stearic acid contained, the more acidic the pH of a preparation due to the content of more acidic groups in stearic acid in the preparation. With this, irritation when the preparation is used can be minimized because the pH of the preparation is still in the skin pH range.

c. Homogeneity

The parameters of this test are that there are no more particles that have not been dissolved when the preparation is spread on the object glass (Budianor et al., 2022). The results of the homogeneity test evaluation of the cucumber skin extract cream base can be seen in the table below.

Table 7. Homoneity Test

Formula	Result
F1	Homogeneous
F2	Homogeneous
F3	Homogeneous
F4	Homogeneous

From the table above, it can be concluded that the four formulas are homogeneous with the absence of coarse particles that have not been dissolved in the preparation. There are only air bubbles which are supported by research (Chandra & Fitria, 2019) caused by the high speed of stirring and the length of time stirring during the preparation process.

d. Spreadability

The spreadability test is carried out to ensure that the preparation is easy to spread on the skin surface when applied (Chandra & Fitria, 2019). Optimal spreadability will make it easier for the preparation to spread when applied without requiring great pressure (Elcistia & Zulkarnain, 2018). The results of the evaluation of the spreadability of the cucumber skin extract cream base can be seen in the table below.

Based on this table, the greatest spreadability is in cream f3 which is still within the range of cream preparation requirements. According to research by Novia, Opod, Yamlean, & Mansauda (2024) this is due to the increase in the concentration of stearic acid and TEA in each formula because stearic acid is a fatty acid that can increase the viscosity of the preparation which causes the smaller the spreadability of the preparation. Based on the results of the study F1, F2, and F3 are included in the category of creams that are very easy to spread and F4 is included in the category of creams that spread easily. The most optimal formula is F3 which meets the requirements for the spreadability of cream preparations, namely 5-7 cm (Budianor, Malahayati, & Saputri, 2022).

Table 8. Spreadability Test

Weight (gram)	**F1(cm)**	**F2(cm)**	**F3(cm)**	**F4(cm)**
50	7,90	7,52	6,75	4,60
100	7,94	7,66	6,87	4,74
150	8,06	7,81	7,04	4,87

e. Adhesion

The adhesion test is carried out to determine how long the preparation can adhere to the skin so that the active substance can penetrate the skin and the desired therapeutic effect can be achieved (Saryanti, D., Setiawan, I., and Safitri, 2019). The results of the evaluation of the adhesion of cream base can be seen in the table below.

Table 9. Adhesion Test

Formula	Time (s)
F1	3,4
F2	3,4
F3	6,7
F4	9,8

Based on table 4.5.5. The four formulas have adhesion in the range of 3.4 seconds-9.8 seconds. It can be concluded that F1 and F2 do not meet the requirements and F3 and F4 have met the requirements for the adhesion of cream which is more than 4 seconds (Utari et al., 2018). This is influenced by the consistency of the preparation. The more concentrated the preparation, the greater the adhesion value but the smaller the dispersion. The density of the preparation is influenced by the concentration of stearic acid and TEA in the formula (Novia et al., 2024).

f. Emulsion type

The emulsion type test is carried out to ensure that the preparation that has been made is an oil-in-water (o/w) carried out by the dilution method. The results of the evaluation of the emulsion type test can be seen in the table below.

Table 10. Emulsion Type Test

Formula	Result
F1	Dissolved
F2	Dissolved
F3	Dissolved
F4	Dissolved

Based on the table above, the results show that all preparations are soluble in distilled water. So it can be concluded that the four preparations are oil-in-water (o/w) emulsion type. This is because the external phase which is water can dissolve by itself, namely water (Utari et al., 2018).

Antibacterial Activity Test of Cucumber Peels Extract Cream.

Antibacterial activity test of cucumber peel extract cream preparation against *Staphylococcus epidermidis* was conducted through agar diffusion method using Nutrient Agar. The cucumber peel extract was formulated in concentrations of 2.5%; 3.5%; and 4.5% in the preparation. The results of the antibacterial activity test are shown from the clear zone formed around the well which indicates that the preparation can diffuse into the well so that the bacterial growth activity is inhibited in the area that has been impregnated by the preparation (Bassy, Tunny, & Sahari, 2023). The observation results of the antibacterial activity test of cucumber skin extract preparations against *Staphylococcus epidermidis* can be seen in the table below.

Table 11. Antibacterial Activity

Formula	Diameter (mm)	Category
Negative control	0 mm	Weak
F1	33,00 mm	Very strong
F2	50,56 mm	Very strong
F3	52,70 mm	Very strong
Positive control	28,61 mm	Very strong

Based on the table and figure above, the negative control that does not contain extracts does not have antibacterial activity because there is no clear zone formed so it can be concluded that the cream base does not have antibacterial activity. While in positive control, a clear zone of 24.61 mm is formed, which can be concluded that the positive control of mediclin 1.2% gel also has very strong antibacterial activity. The three concentrations of the preparation have a very strong inhibition zone in the range of 33.00 mm to 52.70 mm. From the results of the inhibition zone produced, it can

be concluded that the cucumber peels extract cream preparation has very strong antibacterial activity against *Staphylococcus epidermidis*. After evaluating the preparation and testing antibacterial activity against *Staphylococcus epidermidis*, it can be concluded that the most optimal preparation is formula 3 with a combination of 10% stearic acid and 3% TEA in the formula. Formula 3 fulfills all the requirements of the preparation evaluation test and still has very strong antibacterial activity against *Staphylococcus epidermidis*.

CONCLUSION

Cucumber peels extract (*Cucumis sativus* L.) contains secondary metabolites of steroids, alkaloids, phenols, flavonoids, and saponins. Cucumber peels extract (*Cucumis sativus* L.) has antibacterial activity against Staphylococcus epidermidis with a KHM value of 2.5% and a KBM value of 5%. The most optimal formula is F3 with a combination of 10% stearic acid, 3% TEA, and 4,5% extract and meets all the requirements of the cream evaluation test. The three formulations have very strong antibacterial activity against Staphylococcus epidermidis.

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CONFLICT OF INTEREST

We declare that we don't have any conflict of interest.

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