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Formulation and Activity Test of Itchy Leaf Extract Anti-Acne Gel (*Laportea aestuans*) Against *Propionibacterium acne* Bacteria

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ABSTRACT

Laportea aestuans (commonly known as "daun gatal") contains various secondary metabolites with potential antibacterial activity. This study aimed to formulate an ethanol extract of *Laportea aestuans* leaves into a gel dosage form and to evaluate its antibacterial effectiveness against *Propionibacterium acnes*, the primary bacterium responsible for acne. An experimental design was employed by preparing gel formulations containing extract concentrations of 5%, 10%, and 15%. The antibacterial activity was evaluated using the diffusion method, while the physical quality of the gel was evaluated through organoleptic observations, homogeneity, pH, spreadability, and adhesion tests. The results showed that all gel formulations demonstrated good physical quality. The antibacterial assay showed inhibition zone diameters of 13.7 mm, 14.8 mm, and 16.7 mm for the 5%, 10%, and 15% formulations, respectively, which were classified as strong inhibition. Therefore, it can be concluded that the anti-acne gel containing ethanol extract of *Laportea aestuans* leaves effectively inhibits the growth of *Propionibacterium acnes*.

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INTRODUCTION

Indonesia's biodiversity is remarkably high, despite covering only 1.3% of the Earth's total land area, and Papua ranks first in terms of relative richness and endemism of plant species (Setiawan, 2022). Java, on the other hand, boasts the highest flora diversity, as it has been extensively explored. Habitat-wise, medicinal plants are distributed primarily in cultivated areas, with the majority found within forest areas: approximately 42% are found in lowland tropical rainforests, 18% in seasonal forests, 4% in coastal forests, and 3% in mangrove forests (Kusmana & Hikmat, 2015). Research into the discovery of plant-based herbal medicines has increased in recent decades, given the lengthy process of developing commercial therapeutic agents from synthetic compounds (Setiawan, 2022).

Based on previous research, itchy leaves are known to contain various secondary metabolites with potential analgesic, anti-inflammatory, and anticoagulant properties, as well as antibacterial, cytotoxic, and antioxidant activity. Furthermore, pharmaceutical applications of itchy leaves have also been developed in gel and powder forms. (Simaremare et al., 2019) Research conducted by (Pertiwi & Fernanda, 2019) reported that the itchy leaf herb contains flavonoids, alkaloids, terpenoids, saponins, and glycosides. Antibacterial activity tests against *Staphylococcus aureus* and *Escherichia coli* showed positive results, indicating the ability of itchy leaf extract to inhibit the growth of both bacteria.

Acne is a common skin condition and generally resolves spontaneously without specific treatment (Hanip et al., 2021). Factors contributing to acne include increased sebum production, follicular hyperkeratinization, the growth of acne-causing bacterial colonies, and inflammation. This inflammatory reaction is generally triggered by the presence of several types of bacteria, including *Staphylococcus epidermidis*, *Propionibacterium acnes*, and *Staphylococcus aureus*. Therefore, acne therapy can be performed by reducing the bacterial population through the use of antibacterial compounds (Nurrosyidah et al., 2019).

Acne treatment is generally carried out with antibiotics, such as chloramphenicol, clindamycin, erythromycin, or tetracycline. However, long-term antibiotic use has the potential to develop bacterial resistance and cause side effects such as skin irritation. Most anti-acne preparations on the market contain synthetic antibiotics, such as clindamycin and erythromycin, which work by binding to cell receptors or inhibiting enzyme activity. Long-term use of synthetic antibiotics can cause undesirable effects, including irritation, resistance, organ damage, and immunohypersensitivity reactions. Therefore, alternative acne treatments based on natural ingredients are needed, which are considered safer for the skin than the use of synthetic chemical compounds. (Nurrosyidah et al., 2019).

In Bandung City, it was reported that 12.9% of acne cases showed resistance to tetracycline, 45.2% to erythromycin, and 61.3% to clindamycin antibiotics. Cases of antibiotic resistance were also reported in several other countries, such as France, Mexico, and Korea (Madelina & Sulistiyaningsih, 2018). Most current anti-acne drugs have shown decreased effectiveness due to

bacterial resistance, and in some cases, patients experienced relapses after therapy (Piramitha et al., 2017). Therefore, the use of natural ingredients as an alternative acne therapy is a potential and safer approach to be developed.

One pharmaceutical preparation widely used in the treatment of infected wounds is a topical gel. Gels have a consistency suitable for treating various skin conditions caused by bacteria. Gels are commonly used for acute and chronic skin conditions because they penetrate the skin's layers to produce the desired therapeutic effect. Furthermore, gels are preferred by users because they are easy to apply, practical, provide a cooling sensation, aid in skin repair, maintain moisture, and have an emollient effect that can deliver active ingredients to the skin for specific topical and systemic effects. (Sawiji & Sukmadiani, 2021)

Based on various previous studies on the widespread distribution of the itchy leaf plant in Papua and its health benefits associated with its secondary metabolite content, this plant has great potential for development as a traditional medicine. Therefore, research is needed to formulate and test the activity of an anti-acne gel containing an extract of the itchy leaf (*Laportea aestuans*) from Jayapura Regency, Papua, against Propionibacterium acnes.

THEORETICAL REVIEW

The itchy leaf (*Laportea aestuans* L.) is a shrub belonging to the Urticaceae family. This family is widely distributed throughout the world, including Indonesia. In Indonesia, plants from the Urticaceae family have been traditionally used as medicine to treat various health problems, such as ulcers, boils, dysentery, urinary tract infections, itching, muscle pain, as an acid neutralizer, anti-inflammatory, and stress reliever (Subaryanti et al., 2022). The itchy leaf is known as a native Papuan herbal plant that has been used traditionally by local communities as a pain reliever. This plant is widespread in Papua, from coastal areas to mountainous regions (Simaremare et al., 2019).

METHODOLOGY

Tool

The tools that will be used are Autoclave, Petri dish, Incubator, Caliper, Laminar Air Flow, Lumpang and pestle (OneMad), Oven, pH meter, Water cooler, Rotary evaporator, Glass tool set, Analytical scale (Ohaus), Maceration Container

Material

The materials used in the study were aluminum foil, *ampicilin oxoid ampicilin paper disk, acetic acid anhydride, carbopol 940 2%, DMSO, 70% ethanol, 96% ethanol, FeCl3,* gloves, *concentrated HCl, concentrated H2SO4, gauze, white cotton 100 gr, chloroform, methyl paraben,* Merck Nutrient Agar, *paper disk blank* Oxoids, Dragendorf reagents, Burchard's Liebermen reagents, Mayer reagents, Wagner reagents, plastic wrap, propylene glycol 10%, *Propionibacterium acnes bacteria*, triethanolamine, gel tubes 25 gr.

Extraction Testing

Laportea aestuans is obtained from the Jayapura Regency area and then processed into simplicia through a drying process. Extraction is carried out using the maceration method. A total of 1 kg of itchy leaf simplicia powder is put in a glass container and soaked using a 70% ethanol solvent. The maceration process is carried out for three days with stirring every 24 hours. After the soaking process is complete, remaceration is carried out to ensure that the extraction of active compounds takes place optimally. The macerated filtrate is then evaporated using a rotary evaporator until a thick extract of itchy leaves is obtained(Risna, 2023).

Screening Phytochemistry

Alkaloid Test

The alkaloid qualitative test was carried out by adding Dragendorff, Mayer, and Wagner reagents to the ethanol extract of the itch leaves. The presence of alkaloid compounds is indicated by the formation of white deposits in the Mayer reagent, red deposits in the Dragendorff reactant, and brown deposits in the Wagner reagent

Flavonoid Test

Extract is added chloroform: aquadest (1:1), stirred and left until 2 layers (chloroform and water) are formed. The chloroform layer at the bottom is used for testing triterpenoid compounds and steroids. A portion of the water layer is taken and transferred into a test tube and added with magnesium powder and a few drops of concentrated HCl. The formation of orange to red color indicates the presence of flavonoid compounds.

Tannin Compound Examination

Addition of 1% FeCl3 reactant, into a test tube containing a layer of water. The dark blue or greenish-black color that forms indicates the presence of tannin compounds. The water layer in the test tube is shaken vigorously, the formation of foam that does not disappear with the addition of some concentrated HCl indicates the presence of saponins.

Triterpenoid and Steroid Testing

The chloroform layer separated in the flavonoid test was dripped into the drip plate, then added the Liebermann–Burchard reagent consisting of three drops of acetate anhydride and one drop of concentrated sulfuric acid. The formation of red or purple color indicates the presence of triterpenoid compounds, while green color indicates the presence of steroid compounds.

Saponin Testing

A total of 1 mg of the extract was added to 10 mL of distilled water, then shaken for 30 minutes until foam formed. The solution was then left upright for 30 minutes. The presence of stable foam indicates the possible presence of saponins. For confirmation, three drops of acid solution were added to the

solution; if the foam remains stable after the addition of acid, it is certain that the extract contains saponins.

Formula Design

Table 1. Anti-Acne Gel Formula

Material	**Use**	**Sum**				
		K(-)	**F1**	**F2**	**F3**	**K(+)**
Itchy Leaf Extract	Active Substances	-	5%	10%	15%	Come to Mediklin
Carbopol 940	Basis Gel	2%	2%	2%	2%	
Propylene Glycol	Humectant	10%	10%	10%	10%	
Methyl Paraben	Preservatives	0.1%	0.1%	0.1%	0.1%	
Trietanolamine	Penstabil pH	2%	2%	2%	2%	
Aquadest	Solvent	At 20 g	At 20 g	At 20 g	At 20 g	

Remarks : (K-) Negative control (gel formula without itch leaf extract), (F1) itch leaf extract concentration 5%, (F2) Gel with itch leaf extract concentration 10%, (F3) Gel with 15% itch leaf extract concentration , K(+) : Medi-klin® gel

Anti-Acne Gel Manufacturing

All additives are weighed according to the formula listed in Table 1. Carbopol 940 was developed using hot aquadest 20 times its weight. Next, triethanolamine and propylene glycol are added gradually while being eroded until a homogeneous gel base is formed. Methyl parabens that have been dissolved first are then added to the mixture. Once the gel base is perfectly formed, the ethanol extract of the itch leaves is added and stirred until homogeneous, then the preparation is put in a gel tube container.

Evaluation of the Physical Quality of Anti-Acne Gel Preparations

Organoleptic Test

Organoleptic testing is carried out by observing the gel preparation from the shape, smell and color of the preparation

Homogeneity Test

This examination is carried out by weighing 0.1 g of gel preparation, then applying it to the glass of a transparent object thinly and evenly, which must show a homogeneous particle size.

pH Test

pH checks are carried out using a pH meter. The number indicated by the pH meter is the pH value of the gel preparation.

Adhesive Strength Test

A total of 0.25 g of gel preparation is weighed, then placed on two glass objects that have been determined. Then, a weight of 1 kg is placed for 5 minutes on it. After that, install the object glass on the test device and then add a load of 80 g to the test device, then record the release time of the two object glasses.

Dispersion Test

A large amount of 0.5 g of gel preparation is carefully placed on graph paper coated with transparent glass, left for 15 seconds to calculate the area given by the preparation, then covered again with a certain weight (10 g, 20 g, 30 g, 40 g and 50 g) and left for 60 seconds. Then calculate the diameter of the spread given by the preparation. (Marina et al., 2024)

Antibacterial Activity Test

Sterilization Tools

All equipment used in testing antibacterial activity is first sterilized using an oven at 175°C or by autoclave at 121°C.

Creation of NA (Nutrient Agar) Media

The manufacture of NA media is carried out by dissolving 1.2 grams of NA powder into 60 mL of aqueducts, then heated and homogenized using *a magnetic stirrer*. Once homogeneous, the solution is sterilized by autoclave at 121°C for 15 minutes. The sterilized NA media is then aseptically poured into a petri dish in *the laminar air flow*, then left for a few minutes until it hardens

Rejuvenation of Pure Cultures of Bacteria

A total of one pure culture of *Streptococcus mutans* was taken using sterilized ose wire, then inoculated aseptically by scratching on an inclined medium. Furthermore, the media is incubated anaerobically at 37°C for 24 hours

Manufacture of Bacterial Suspension

The inoculated bacteria were then taken in one loop using a sterile loop wire, then suspended in a tube containing 5 mL of 0.9% physiological NaCl solution.

Antibacterial Activity Test Antibacterial Gel Anti-Acne Leaf Itch

The antibacterial activity test was carried out using the suction diffusion method. A petri dish is prepared, then 15 mL of Nutrient Agar (NA) is poured as a base layer and left to solidify. Next, the bacterial suspension mixture is poured into the NA medium and spread by *the spread plate* method. In each petri dish, three drainage holes are made as a place for sample application. An itchy leaf anti-acne gel with concentrations of 5%, 10%, and 15%, as well as positive control (Mediklin Gel) and negative control, respectively are inserted into the pre-made gout. The petri dish is then incubated for 24 hours at 37°C. After incubation, the diameter of the inhibited zone formed was measured using a caliper to determine the antibacterial activity (Nofriyanti et al., 2021)

RESULTS AND DISCUSSION

Itchy Leaf Extraction

Itch leaf extract is obtained through an extraction process using the maceration method. The maceration process is carried out by soaking simplicia of itchy leaves that have been crushed in 70% ethanol solvent as much as 2,500 mL for three days with occasional stirring. After the first process is completed, remaceration is carried out using the same amount of ethanol solvent and with a similar duration of time to obtain maximum extraction results. All the macerated and remacerated filtrates are collected, then evaporated until a thick extract is obtained. The extraction results showed a yield of 12.66% from 217.12 grams of itchy leaf simplicia. Based on the provisions of the Ministry of Health of the Republic of Indonesia (2010), a good yield has a value of more than 10%, so that the results obtained have met the criteria for good yield. The extraction data is presented in Table 1

Table 2. Extraction Results of Ethanol Extract of Itchy Leaves Maceration Method

Sample Name	Dry sample weight (g)	Weight of thick extract (g)	Percentage Return (%)
Itchy Leaves	217.12 grams	27.50 grams	12,66 %

The solvent used in the extraction process in this study is 70% ethanol, which is classified as a polar solvent. The selection of such solvents is based on the principle of *like dissolves like*, where polar compounds are more easily soluble in polar solvents, while nonpolar compounds tend to dissolve in nonpolar solvents. Thus, the use of 70% ethanol is considered optimal to dissolve polar compounds contained in itchy leaves. In addition, the widespread use of ethanol is due to its relatively non-toxic nature compared to solvents such as acetone and methanol, its economical cost, and its ability to be used in a variety of extraction methods. Ethanol is also considered safe to produce extracts that will be used in medicinal preparations and food. In addition, ethanol is a solvent that is easy to obtain, efficient, environmentally friendly, and has high extraction capabilities (Hakim & Saputri, 2020).

The maceration method is an extraction technique that involves soaking the material in a solvent that matches the characteristics of the active compound to be extracted. This method has the advantage of preventing damage to thermolabile compounds. The correct maceration time will result in optimal compound extraction, while too short a maceration time can result in incomplete extraction of the active compound into the solvent. (Yasacaxena et al., 2023)

Phytochemical Screening of Itchy Leaf Extract

Phytochemical screening is one of the qualitative tests carried out to determine the secondary metabolite compounds contained in ethanol extract of itchy leaves. The results of phytochemical screening as shown in table 2 show

that positive itch leaf extract contains alkaloid compounds, flavonoids, tannins, saponins and steroids.

Table 3. Phytochemical Screening Results of Secondary Metabolites of Ethanol Extract Itch Leaves

Compound	Reagents	Result	Conclusion
Alkaloid	Mayer	White deposits	Positive
	Dragendorf	Orange sediment	Positive
Flavonoid	Extract + Aquadest + Mg Powder + HCl p	Red	Positive
Tannins	Ekstrak + aquadest + FeCl3	Blackish green	Positive
Saponins	Extras + Aquadest + HCL P	Foam	Positive
Steroids	Extract + Chloroform + Liebermann Burchard Extracts	Green	Positive

The results of this study are in line with the findings of (Subaryanti et al., 2022), which stated that *daun gatal* herbs contain alkaloid compounds, tannins, flavonoids, saponins, steroids, and triterpenoids. Similar findings were also reported by (Kambu et al., 2024), which showed that the ethanol extract of *daun gatal* was positive for containing flavonoids, alkaloids, terpenoids, saponins, and tannins.

The identification of flavonoid compounds was carried out using ethanol leaf extract combined with distilled water, magnesium powder, concentrated hydrochloric acid, and amyl alcohol. This reaction produced an orange color derived from the formation of flavilium salts, which subsequently caused the solution to turn red.

The results of the identification of saponin compounds showed a positive reaction marked by the formation of stable foam. This is caused by the presence of polar and nonpolar groups in the saponin molecules that form micelles during the shaking process.

The alkaloid test gave positive results in the form of a red precipitate with Dragendorff's reagent and a brown precipitate with Wagner's reagent. Meanwhile, the results of glycoside identification showed a positive reaction marked by a color change to green after the addition of the Liebermann–Burchard reagent, which is caused by electron transition in the unsaturated groups (Kambu et al., 2024).

The identification test for terpenoid compounds also showed positive results with the formation of a brown ring due to an oxidation process that produces conjugated double bonds (Pertiwi & Fernanda, 2019).

These secondary metabolite compounds are known to have various biological activities, including antibacterial, antioxidant, anticancer, and anti-inflammatory properties (Simaremare et al., 2019).

Formulation and Evaluation of Itchy Leaf Extract Mouthwash Preparations

The formulation of itch leaf ethanol extract gel preparations is divided into 4 groups consisting of negative control (base), namely gels that do not contain itch leaf extract, F1, which is an anti-acne gel that contains 5% Itch leaf extract, F2 yairu anti-acne gel which contains 10% Itch leaf extract, and F3, which is an anti-acne gel that contains 15% Itch leaf extract. The formulation of the preparation consists of active ingredients and additives. The active ingredients are in the form of itchy leaf extract and additional ingredients consisting of a Karbopol 940 base in combination of Triethanolamine and propylene glycol. The results of the formulation of the itchy leaf ethanol extract gel preparation are shown in figure 1.

Figure 1. Itchy Leaf Ethanol Extract Gel Preparation

Physical quality testing of the itchy leaf ethanol extract gel preparation to ensure that the resulting preparation meets the quality requirements of a good gel preparation. This test includes organoleptic test parameters to see the physical activity of the preparation by observing the shape, color and smell of the preparation that has been made. In addition, homogeneity, pH, dispersability and adhesion are tested. The results of the preparation evaluation can be seen in table 4.

Table 4. Results of Evaluation of Itchy Leaf Extract Gel Preparations

No.	Formula	Types of Observations	Observation Results
1.	K (-)	Shape	Semi-Compact
	F1		Semi-Compact
	F2		Semi-Compact
	F3		Semi-Compact
2.	K (-)	Color	Putih

	F1		Greenish Yellow
	F2		Brownish Green
	F3		Blackish Green
3.	K (-)	Construction	Typical Base
	F1		Green tea
	F2		Green tea
	F3		Green tea
4.	K (-)	Homogeneity Test	Homogeneous
	F1		Homogeneous
	F2		Homogeneous
	F3		Homogeneous
5.	K (-)	pH Test	4.7
	F1		4.8
	F2		4.8
	F3		4.6
6.	K (-)	Dispersion Test	5.9
	F1		5.9
	F2		5.4
	F3		5.6
7.	K (-)	Adhesive Strength Test	4.56
	F1		4.61
	F2		5.38
	F3		5.07

Description: (K-) : Negative control (gel formula without itch leaf extract, (FI) gel with itch leaf extract concentration 5%, (F2) Gel with itch leaf extract concentration 10%, (F3) Gel with 15% itch leaf extract concentration

Homogeneity is one of the important aspects because it affects the uniformity of the distribution of drugs in preparations. A gel is said to be homogeneous if it has a uniform color and does not contain particles or rough materials that can be physically felt. Based on the results of the homogeneity test

carried out on all formulas, it was obtained that each preparation showed a uniform color and no particles were found, so that the preparation of itchy leaf extract gel can be declared homogeneous (Febrianto & Alvyani, 2020)

pH testing is carried out to ensure that the resulting preparations have an acidity level that matches the pH of the skin, as this factor affects safety and comfort during use. If the pH of the preparation does not match the pH of the skin, it can cause irritation that causes discomfort. Generally, the pH of the skin ranges from 4.5 to 6.5. Based on the results of pH measurement on the itchy leaf extract gel preparation after the manufacturing process, the pH value of F1 was 4.8, F2 was 4.8 and F3 was 4.6. This value indicates that all three formulas have a pH close to the pH of the skin so that it can be declared safe to use (Setyawan et al., 2023)

The spreadability test aims to assess the ability of a preparation to spread on the surface of the skin when used. Gel preparations are categorized as good if they have a spread between 5–7 cm. Dispersability is an important characteristic of formulation because it affects the movement of the active ingredient to the target area in the right dosage and affects ease of use (Hikmah et al., 2023). Based on the results of the dispersion test presented in table 4, it can be seen that there is a difference in the dispersion diameter in each formula. The test was carried out three times of replication, then an average score was taken for each formula. The results showed that formula 1 had a dispersion of 5.9 cm, formula 2 of 5.4 cm, and formula 3 of 5.6 cm. Based on the dispersion value obtained, the itch leaf gel preparation met the criteria for good dispersion data.

Adhesion tests were performed to evaluate the ability of the gel preparation to maintain its adhesion to the surface of the skin, which reflects the effectiveness of the preparation in releasing the active substance as well as providing pharmacological effects. Based on the test standards of semi-solid preparations, preparations are said to have good adhesion if they show an adhesion time of more than 4 seconds. The longer the topical preparation is able to adhere to the skin, the greater the chance of the active substance being optimally absorbed. Based on the test results presented in Table 4, the entire gel formulation of itch leaf extract has met the criteria for adhesion parameters that are in accordance with the requirements of the gel preparation (Tjitrarukmana, 2022).

Antibacterial Activity Test Anti-Acne Gel Itchy Leaf Extract

The antibacterial activity test of the anti-acne gel of itchy leaf extract was carried out by the assay test method on formula 1, 2 and 3 gel preparations using positive control of Mediklin Gel and negative control of gel base. The results of the observation of the diameter of the inhibition zone of anti-acne gel preparations against *Propionibacterium acnes* are shown in table 5.

Table 5. Results of observation of the diameter of the inhibition zone of anti-acne gel preparations against *Propionibacterium acnes*

Formula Gel	Diameter of the barrier zone				Category
	Replication 1	Replication 2	Replication 3	Average	
F1	14.2	13.4	13.7	13,7	Strong
F2	14.3	15.3	14.8	14,8	Strong
F3	16.7	17.2	16.3	16,7	Strong
K (+)	18.6	17.9	18.2	18.2	Strong
K (-)	0	0	0	0	None

Description : (K-) : Negative control (gel formula without itch leaf extract), (, (FI) Gel with 5% itch leaf extract concentration, (F2) Gel with 10% itch leaf extract concentration, (F3) Gel with 15% itch leaf extract concentration, K (+) : Mediklin Gel

The results of the measurement of the diameter of the inhibition zone of ethanol extract of the itch leaf against *the bacteria Propionibacterium acnes* showed the presence of clear zones at concentrations of 5%, 10%, and 15%, respectively of 13.7 mm, 14.8 mm, and 16.7 mm, which are included in the strong category. These findings suggest that itchy leaf ethanol extract has antibacterial activity that is able to inhibit the growth of *P. acnes bacteria*. However, the inhibition of ethanol extract of itch leaves is still lower compared to the antibiotic Clindamycin phosphate (Mediklin Gel), which has an inhibition zone diameter of 18.2 mm and is also in the strong category. Clindamycin is known to work by inhibiting the formation of peptide bonds through reversible binding to the 50S ribosomal subunit, thereby inhibiting protein synthesis and bacterial growth. Meanwhile, the negative control in the form of a gel base did not indicate the presence of an inhibition zone. The results of testing the antibacterial activity of the itchy leaf ethanol extract gel also indicated that the ethanol solvent used in the extraction process was able to dissolve compounds that had the potential to be antibacterial. This is in line with the results of phytochemical analysis which showed that ethanol extract of itchy leaves contains secondary metabolite compounds such as alkaloids, flavonoids, tannins, saponins, and steroids that play a role in inhibiting the growth of bacteria (Kambu et al., 2024)

The mechanism of action of alkaloids as antibacterials is carried out by interfering with the process of forming peptidoglycan components in bacterial cells, so that the cell wall is not formed perfectly and causes the death of bacterial cells. While flavonoids have an antibacterial mechanism of action by damaging the lipid structure and DNA of bacteria through interaction with phospholipids on the cytoplasmic membrane. As a result, phospholipids lose their ability to maintain the integrity of the cytoplasmic membrane, resulting in the leakage of cellular components and the release of substances that play a role in metabolic processes, which ultimately leads to the death of bacterial cells (Ramadhani et al., 2024)

The mechanism of action of tannins as antibacterial is carried out by causing lysis in bacterial cells. Tannins interact with the polypeptides that make up the bacterial cell wall, thereby inhibiting the process of cell wall formation and causing the cell wall to become imperfect. In addition, tannins are also known to inhibit the activity of reverse transcriptase and DNA topoisomerase enzymes, which play an important role in the process of replication and formation of bacterial cells, resulting in the death of bacterial cells. Alkaloids have antibacterial activity with a mechanism that interferes with the components that make up peptidoglycan in bacterial cells, so that the formation of cell walls does not take place perfectly and leads to the death of bacterial cells. In addition, alkaloids also act as DNA interclaators and are able to inhibit the activity of the topoisomerase enzyme in bacterial cells, resulting in disruption of DNA replication and transcription processes (Niken et al., 2022). The mechanism of action of steroids as antibacterial is related to their ability to interact with the lipid membrane of bacterial cells, thereby disrupting the integrity of the membrane. The interaction of steroids with membrane phospholipids can increase permeability to lipophilic compounds, which leads to instability of membrane structures and leads to lysis and bacterial cell death (Risna, 2023)

CONCLUSIONS AND RECOMMENDATIONS

Itchy leaf ethanol extract has been successfully formulated into an anti-acne gel preparation that meets physical quality standards. The results of the antibacterial activity test showed that the gel with an extract concentration of 5%, 10%, and 15% produced a inhibition zone diameter of 13.7 mm, 14.8 mm, and 16.7 mm, respectively, which fell into the strong category. Thus, it can be concluded that anti-acne gels containing ethanol extract of itchy leaves are effective in inhibiting the growth of *Propionibacterium acnes bacteria*.

FURTHER STUDY

Based on these findings, further studies are recommended to optimize the formulation of the itchy leaf ethanol extract gel by evaluating its long-term stability, skin irritation potential, and effectiveness through in vivo or clinical trials. Future research may also explore the synergistic effects of combining the extract with other natural or synthetic anti-acne agents, as well as investigate the molecular mechanisms underlying its antibacterial activity against *Propionibacterium acnes*. Additionally, expanding the scope of testing to include other acne-causing microorganisms and assessing the gel's antioxidant or anti-inflammatory properties could provide a more comprehensive understanding of its therapeutic potential.

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