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Antibacterial Activity Test of Anti-Acne Gel Preparations Containing Ethanol Extracts of Bidara Arab Leaf (*Ziziphus spina-christi* (L.) Desf) Againts *Propionibacterium acnes*

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Abstract

Bidara arab leaf (Ziziphus spina-christi (L.) Desf) is one of the plants that have the potential as an anti-acne. The content of secondary metabolites contained in bidara arab leaves include alkaloids, polyphenols, flavonoids, saponins, and tannins. These secondary metabolites can inhibit the growth of acne causing bacteria, namely Propionibacterium acnes. The purpose of this study was to create a good gel dosage form of the ethanol extract of bidara arab leaves and to test the antibacterial activity of the gel formulation against Propionibacterium acne. This research method was carried out experimentally on a laboratory scale, namely ethanol extract of bidara arab leaves made in the form of anti-acne gel preparations with several concentration, including F1(1%), F2 (3%), and F3 (5%). Then proceed with the evaluation of the preparation with organoleptic test, homogenity test, pH test, adhesion test, and dispersion test. Anti-acne gel preparations had antibacterial activity based on a concentration of 1% of 12.46 mm (strong), 3% of 13.66 mm (strong), and 5% of 14.71 mm (strong), negative control had no inhibition zone and positive control 20.92 mm (very strong). strong) So, it can be included that the formulation of anti-acne gel preparations able to inhibit the growth of Propionibacterium acnes.

Abstrak

Daun bidara arab (Ziziphus spina-christi (L.) Desf) merupakan salah satu tumbuhan yang berpotensi sebagai anti jerawat. Kandungan metabolit sekunder yang terdapat di dalam daun bidara arab diantaranya alkaloid, polifenol, flavonoid, saponin dan tanin. Metabolit sekunder tersebut dapat menghambat pertumbuhan bakteri salah satunya bakteri penyebab jerawat yaitu Propionibacterium acnes. Penelitian ini bertujuan untuk memformulasi ekstrak etanol daun bidara arab dalam bentuk sediaan gel yang baik dan mengetahui aktivitas antibakteri sediaan gel terhadap Propionibacterium acnes. Metode penelitian ini dilakukan secara eksperimental laboratorium, yakni ekstrak etanol daun bidara arab dibuat dalam bentuk sediaan gel anti jerawat dengan beberapa konsentrasi, diantaranya F1 (1%), F2 (3%), dan F3 (5%). Kemudian dilanjutkan dengan evaluasi sediaan melalui uji organoleptik, uji homogenitas, uji pH, uji daya lekat, dan uji daya sebar. Sediaan gel anti jerawat memiliki aktivitas antibakteri masing-masing pada konsentrasi 1% sebesar 12,46 mm (kuat), 3% sebesar 13,66 mm (kuat), dan 5% sebesar 14,71 mm (kuat). Dengan demikian dapat disimpulkan bahwa formulasi sediaan gel anti jerawat mampu menghambat pertumbuhan Propionibacterium acnes.

Keywords: *Bidara Leaf Ethanol Extract (Ziziphus spina-christi (L.) Desf.) Antibacterial, Anti-acne Gel.*

Kata kunci: *Ekstrak Etanol Daun Bidara Arab (Ziziphus spina-christri (L.) Desf.), Antibakteri, Gel Antijerawat*

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INTRODUCTION

The skin is the most external part of the body covering the human body. It represents 15% of the total bodyweight. On the outer surface of the skin, there are pores (cavities) through which perspiration flows. The skin has many functions, including protecting the body, as a means of sensation or

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communication, and as a means of temperature control. The desire of most humans, especially women, to have white, healthy, clean, and well-cared-for face skin. However, the treatment does not focus on the type of skin, causing new problems such as acne, dry skin, and others [1].

Acne is a skin condition that is experienced by most people, from teens to adults. Areas of pimples include the face, shoulders, chest, back, neck, and arms. It is believed that around the world, almost everyone has experienced acne so that acne is often seen a skin complaint that arises physiologically. In Indonesia, about 95-100% of men and 83-85% of women aged 16-17 have acne. Causes of acne include genetic factors, androgenic hormones, estrogenic hormones, progesterone hormones, food, psychology, seasons, bacterial infections, cosmetics, over-exposure to sunlight, and the other chemical. The factor involved in the onset of acne is *Propionibacterium acnes* [2].

P. acnes is the main microorganism present in the infra-infundibulum and these bacteria can reach the surface of the skin through the flow of sebum. Increasing the amount of triglycerides in sebum will increase the amount of *P. acnes*, because triglycerides in sebum are nutrients for *P. acnes*. *P. acnes* is thought to play an important role in causing inflammation in acne vulgaris by producing chemotactic factors and lipase enzymes which will convert triglycerides into free fatty acids, as well as stimulate activation of the classical and alternative complement pathways [3].

Acne treatment occurs by reducing sebum production, reducing skin inflammation, repairing follicular abnormalities and reducing the number of *P. acnes* colonies or their metabolic product. Administration of an antibacterial substance such as erythromycin, tetracycline, and clindamycin may reduce the *P. acnes* bacterial population. Overuse of an antibiotic can increase bacterial resistance to a specific antibiotic [3].

The use of both oral and topical antibiotics in an attempt to heal acne is still widely used. However, the incidence of antibiotic resistance is rising with many countries reporting over 50% bacterial strains of *P. acnes* against topical macrolesions, making it less effective. As a result, research to find alternative antibacterial agents to inhibit the spread of *P. acnes* infection must be developed. The choice of natural ingredients as antibacterial in the treatment of acne can be developed because apart from being relatively safer, the risks are also possible to be very small when

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compared to drugs made from chemicals [4].

One of the dosage forms used to treat infected sores is a gel-based dosage form. Gel preparations are better used for acne treatment because gel with polar solvents is easier to clean from the surface of the facial skin after use and do not contain oil which can increase the severity of acne. The benefits of topical gel preparations include increased activity and usability, the ability to deliver active substance or medicinal ingredients properly [5].

One of the plants with anti-acne potential is the bidara arab plant. The bidara arab leaf *(Ziziphus spina-christi* (L.) Desf.) is one of the plants of South Sulawesi, particularly at Luwu Regency and is a very rare plant at South Sulawesi. Bidara arab leaves are often used in religious medicine like ruqyah. It contains chemical compounds including alkaloids, polyphenols, flavonoids, saponins, and tannins. These secondary metabolites can stop the growth of bacteria, including the bacteria that cause acne, *P. acnes* [4].

According to previous studies, the ethanol extract of bidara Arab leaves (*Ziziphus spina-christi* (L.) Desf.) had antibacterial actitivy in inhibiting the growth of *P. acnes* as indicated by the presence of an inhibition zone, namely at a concentration of 2.5% (12.05 mm), 5% (12.29 mm), 10% (14.07 mm), 20% (12.72 mm), and 40% (11.57 mm). The concentration of the ethanol extract of bidara arab leaves which had good antibacterial activity is at a concentration of 10% (14.07 mm) for *P. acnes* with the diameter of the inhibition zone which is characterized by the formation of the largest clear zone [6].

Based on the description above, further research was carried out by making an anti-acne gel formulation containing bidara arab extract at a concentration of 1%, 3%, and 5% and then testing its antibacterial activity against *P. acnes.*

METHODOLOGY

Instruments and Materials

The instruments used were analytical balance (*Metler Toledo*®), beaker (*Pyrex*®), blenders, Brookfield viscometer, dropping pipette, Erlenmeyer (*Pyrex*®), maceration container, measuring cup (*Pyrex*®), mortar and pestle, micropipette, oven (*Elektrolux*®), petri dish, pH meter (*Lutron*®), reservoir, rotary evaporator (*IKA*®), scale pipette, sieves, spatula, test tube,watch glass, and waterbath.

The materials used in this study were aquadest, bidara arab leaf extract (*Ziziphus spina-christi* (L.) Desf.), 96% ethanol, HPMC, methyl paraben, Nutrient Agar (NA)

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medium, *P. acnes* bacteria, and propylene glycol.

Preparation of Bidara Arab Leaf Extract.

Simplicia bidara dried leaf material was weighed at 500 grams before being added to the maceration container. 96% ethanol solvent was added until completely submerged. Left it for 3-5 days, stirring occasionally. After the first extraction, the dregs were macerated with a fresh solvent. To create a thick extract, the extracted was concentrated using a rotary evaporator [7].

Phytochemical Screening

Phytochemical screening methods can be seen in the **Table 1.**

Table 1. Phytochemical Screening Methods [8]

Secondary Metabolites	Procedures	Positive Result
Flavonoid	Extract was mixed with distilled water, then heated and filtered. The filtrate was combined with Mg, 2N HCl, and amyl alcohol.	Colors like red, yellow, and orange
Alkaloid	Distilled water and 2N HCl were added, then heated and filtered. Mayer and Dragendroff reagents were added and vigorously shaken	Orange-yellow precipitate
Polyphenol	Extract was mixed with distilled water, then heated and filtered. After collecting the filtrate, $FeCl_3$ was added.	Phenolics: green, blue, greenish, red-purple. Polyphenols: brown precipitate
Tannin	Extract was mixed with distilled water, then heated for 15 minutes and shaken.	White precipitate
Saponin	The extract was mixed with 10 mL of hot water for 10 minutes before being filtered. The filtrate was shaken vertically at a constant pace for 10 seconds and then left for 10 minutes.	1 cm high foam

Making Gel Preparations

The formulation of bidara arab leaf extract gel is shown in the **Table 2.** First of all, weigh all the ingredients, then heat the aquadest over a bunsen or tripod to 80°C. After that, add the HPMC and mix until dissolved. In the mortar, slowly ground the methylparaben with the propylene glycol, then stir until dissolved. After that, mash it with HPMC in a mortar and pestle until homogeneous, then add the dissolved and filtered bidara arab leaf extract. Give each one the amount needed. Then, steadily grind until homogeneous till an anti-acne gel preparation was made from the bidara arab leaves [5].

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Gel Preparation Evaluation

a. Organoleptic Test

Gel preparation were done directly by observing the texture, color, and fragrance [5].

b. Homogeneity Test

A glass item containing 0.5 grams of gel was used for the homogeneity test. Then it's rubbed into the glass object. If no coarse granules are seen, the gel is homogenous [4].

c. Spreadability Test

The spreadability test was performed to determine the ability of the preparation to spread when applied to the skin surface. The gel preparation weighed up to 0.5 g. Then set it in the center of the glass plate. It then receives a weight of 150 g, starts the stopwatch, and waits for 1 minute. The diameter of the gel distribution was then measured, and the average diameter was computed[4].

d. Viscosity Test

Viscosity was measured with a Brookfield spindle viscometer No. 4 at 60 rpm. Then it was placed in a glass beaker with 100 g of gel. After that, record the test data using the conditions 500-10.000 mPa.s [9].

e. Adhesion Test

The gel adhesion test was carried out by weighing 0.25 g of gel preparation and laying it on a glass object. Give a 1 kg load, then set the stopwatch for 5 minutes. Replace it with a new load and set the timer for more than one second. After that, record the gel preparation's release time [9].

f. pH Test

The pH is measured with a pH meter, which is calibrated first with a standard neutral pH buffer solution and an acidic pH buffer solution until the tool displays the pH value. The elctrodes were then rinsed with distilled water and dried with tissue paper. Furthermore, the electrode is immersed in the gel base until the tool demonstrates a consistent pH. Human facial skin has a pH that ranges from 4.5 to 6.5 [5].

Table 2. Bidara Arab Leaf Gel Formula

Ingredients	Function	Concentration/Quantity				
		F1	F2	F3	K (-)	K (+)
Bidara arab leaf extract	Active substance	1%	3%	5%	-	Acne Spot Gel
HPMC	Gel base	2 g	2 g	2 g	2 g	
Methyl paraben	Preservative	0.2 g	0.2 g	0.2 g	0.2 g	
Propylene glycol	Humectant	15 mL	15 mL	15 mL	15 mL	
Aquadest	Solvent	ad 100 mL				

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Bidara Arab Leaf Extract Gel Preparation's Antibacterial Activity Test

a. Tool Sterilization

The antibacterial activity test tools were rinsed, dried, and sterilized in an autoclave at 121° for 60 minutes [6].

b. Nutrient Agar (NA) Media Preparation

Weighed up to 2 g of NA, then place it in the Erlenmeyer flask and dissolve it in 100 mL of distilled water. After that, heat it over the bunsen or 3 legs and stir it until it melts. The heated NA was sterilized in an autoclave for 15 minutes at 121°C [10].

c. P. acnes Pure Suspension Preparation

Prepare a sterike test tube and draw 3 mL of 0.9 NaCl liquid with a syringe. After that, put it in a test tube and streak the bacteria with a streak plate (scratch), then mix it until liquid turns hazy according to the McFarland turbidity standard [11].

d. Antibacterial Activity Testing

Antibacterial test using a well, first prepare a petri dish, then put the sterilized NA into a brown bottle as much as 5 mL, then put it in a petri dish as the basis for keeping the backup, once the NA had hardened, 3 holes were drilled in each petri dish. Then, using a syringe, mix 10 mL of NA with 0.3 mL of suspension in the calibrated brown bottle. Pour it into the petri dish, wait for it to solidify, then remove the reservoir. The anti-acne gel formulation was then placed in the wells at concentrations of 1%, 3%, 5%, negative control, and positive control. Afterward, incubated for 1x24 hours at 37°C [11].

RESULT AND DISCUSSION

Phytochemical Screening Results

Prior to formulation and testing, a phytochemical screening was performed, and the results shown in **Table 3.** Based on available references, phytochemical screening was performed to confirm the content of secondary metabolites in a plant. The pharmacological activity of a plant employed as an active ingredient can be estimated by its composition.

Table 3. Phytochemical screening outcomes

Secondary Metabolite	Result
Flavonoids	Yellow-orange (+)
Alkaloids	Yellow (+)
Phenols	Blackish blue (+)
Saponins	Foamy (+)
Tannins	White precipitate (+)

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The secondary metabolites included in the extract of bidara arab have the capacity as an antibacterial based on their distinct mechanisms. Alkaloids work as an antibacterial agent by interfering with the constituent components of peptidoglycan in bacterial cells, causing the cell wall layer to fall and causing cell death. Phenolic chemicals, on the other hand, have the ability to destroy microbes by denaturing cell proteins. A disruption in the permeability of the cell wall and cytoplasmic membrane can result in an imbalance of macromolecules and ions in the cell, resulting in lysis [12].

Flavonoid's antimicrobial mechanisms can be classified into three categories: inhibiting nucleic acid production, hindering cell membrane function, and inhibiting energy metabolism whereas saponins can cause protein and enzyme leakage from within the cell. Tannins can react with cell membranes, inactivate enzymes, and inhibit genetic material processes[12].

Bidara Arab Leaf Extract Gel Preparation and Evaluation

The creation of gel preparations follows the completion of the full extraction procedure up to the phytochemical screening. This gel preparation mixture contains both active and non-active components. The active ingredient is an anti-acne bidara arab leaf extract. HPMC was used as the gel base since it is gelling agent that can generate gels at low concentrations. HPMC is used as a gelling agent at a concentration of 2-10%. HPMC is a hydrophilic gel basis. The benefits of hydrophilic gel include its good skin dispersion, a cooling effect induced by slow evaporation of water on the skin, the fact that it does not clog skin pores, is readily rinsed off with water, and its ability to absorb moisture [13].

Methyl paraben was chosen as an antibacterial preservative because it is widely utilized in cosmetics, food goods, and medical formulations. Methyl parabens can be used alone or in combination with other parabens or antimicrobial agents. It is the most often used antimicrobial preservative in cosmetics. A methyl paraben content of 0.02-0.3% results in a mixture of preservatives with significant antibacterial action [14].

Humectant also aid in limiting water loss from within the gel, making it more stable. Propylene glycol was utilized as a humectant. The humectant propylene glycol concentration in topical applications is 15% [15].

Furthermore, organoleptic testing, homogeneity test, pH measurements, spreadability tests, viscosity measurements, and adhesion tests are performed on the gel formulation.

a. Organoleptic Test

Organoleptic testing was performed to examine the physical appearance visually, including shape, color, and

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smell. **Table 4** displays the findings of the observations.

b. Homogeneity Test

The homogeneity test is the mixing of materials in a gel mixture that demonstrates the preparation's homogeneous composition. **Table 5** shows the outcomes of the observations.

The gel that was created complies with the homogeneity standards; it is devoid of clumping particles and has no discernible coarse grains.

c. Spreadability Test

The spreadability test is heavily influenced by viscosity; the higher the viscosity, the smaller the spreadability diameter and vice versa. **Table 6** shows the results of the scatter power experiment.

The spreadability test determines the ability of the gel to flow or release from the tube. The higher the concentration of the extract, the lower the gel's spreading power, because the thicker the consistency, the lower the spreading power created.

d. Viscosity Test

According the **Table 7**, the four formulations still meet the good viscosity parameter requirements for gel preparations.

e. Adhesion Test

The adhesion test looks for gel that is released in under 4 seconds. According to the **Table 8** findings all gel formulation met the standards for good adherence.

f. pH Test

The pH measurement is used to determine whether the pH of the preparation matches the pH of the skin, which ranges from 4.5 to 6.5. **Table 9** shows the outcomes of the observation.

Table 4. Organoleptic Observations

Gel Formula	Texture	Color	Odor
F1	Semi solid	Pale yellow	Unique extract odor
F2	Semi solid	Rusty yellow	Unique extract odor
F3	Semi solid	Rusty yellow	Unique extract odor
K (-)	Semi solid	Transparent/clear	Base ingredient odor

Table 5. Homogeneity Test Results

Gel Formulation	Result
F1	Homogeneous
F2	Homogeneous
F3	Homogeneous
K (-)	Homogeneous

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Table 6. Spreadability Test Results

Gel Formulation	Spreadability	Ranges
F1	6.5 cm	5-7 cm
F2	5.5 cm	
F3	5.2 cm	
K (-)	5.5 cm	

Table 7. Viscosity Test Results

Gel Formulation	Viscosity	Ranges
F1	540 mPa.s	500-10.000 mPa.s
F2	569 mPa.s	
F3	620 mPa.s	
K (-)	530 mPa.s	

Table 8. Adhesion Test Results

Gel Formulation	Results	Ranges
F1	6.04/s	>4/s
F2	7.49/s	
F3	8.38/s	
K (-)	5.54/s	

Table 9. pH Test Results

Gel Formulation	pH	Ranges
F1	5.8	4.5 to 6.5
F2	5.7	
F3	5.5	
K (-)	6.3	

Antibacterial Activity Test

The antibacterial efficacy of bidara arab leaf extract (*Ziziphus spina-christi* (L.) Desf.) gel preparation against the growth of *Propionibacterium acnes* was tested utilizing the agar diffusion method with the well technique. The well method was used for this test because it is simpler to determine the area of the inhibition zone generated since bacteria migrate not only on the upper surface of the nutrient agar but also down to the bottom[16]. **Table 10** shows how the inhibition zone forms.

Table 10. Antibacterial Activity Test Results

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Gel Formulation	Inhibition Zone Diameter (mm)			Average (mm)	Category
	R1	R2	R3		
F1	12.73	14	14.6	12.46	Strong
F2	12.8	13.53	14.93	13.66	Strong
F3	11.86	13.46	14.6	14.71	Strong
K (-)	0	0	0	0	No inhibition zone
K (+)	20.1	20.16	22.5	20.92	Very Strong

According to the table, the wider the diameter of the inhibitory zone produced around the wells, the higher the gel concentration of the bidara arab leaf extract supplied. Formula 3 (5% extract) had the highest average inhibitory zone on *P. acnes* among the three formulations including bidara arab leaf extract.

In comparison to the formulation of bidara arab leaf gel, Acne Spot Gel operates as an antibacterial for acne skin. The Acne Spot Gel contains pegagan extract, which has antibacterial activity against both Gram-positive and Gram-negative microorganisms[17].

CONCLUSION

Based on the findings of the research, it is possible to conclude that the ethanol extract of bidara arab leaves can be made into a gel preparation with antibacterial activity that can suppress the growth of *Propionibacterium acnes*. F3 is the gel formulation with the best antibacterial, with an average inhibition zone diameter of 14.71 mm.

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