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Formulation of Lahuna Leave Extract (*Chromolaena odorata*) and Binahong Leave Extract (*Anredera cordifolia*) as Antiseptic Ointments

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Abstract. The incidence of antimicrobial resistance is increasing, so alternative compounds are needed that can be used as active ingredients to reduce pathogenic bacteria. Natural products extracted from the plants can be used as alternative strategies to reduce pathogenic bacteria, Lahuna leaves and binahong leaves have the potential as a source of active ingredients which, based on phytochemical tests, contain flavonoid, alkaloid, saponin, tannin and steroid. The main aim of the present work was the effectiveness of Ointment formulations of lahuna leaves and binahong leaves as antiseptic. Ointment preparations were made with 5 formulas based on organoleptic evaluation showing the five formulas in semi-solid form, color, and characteristic odor of extracts. homogeneous and can spread evenly. The pH test showed a value of 7.3 for formulas I, IV and V while formulas II, and VI were 7.5. This result corresponds to the quality of the preparation on the skin of 4.5-8. *In vitro*, test showed formulas I and III had inhibition against *Staphylococcus aureus* ATCC 25923.

Introduction

The incidence of antimicrobial resistance is increasing, so alternative compounds are needed that can be used as active ingredients to reduce pathogenic bacteria. The use of natural materials as a source of active compounds has been developing since time immemorial, and plays an important role in the development of modern medicine (Das and Satyaprakash *et al.*, 2018). Plants that have medicinal properties are caused by the content of complex compounds such as secondary metabolites (El-Gied *et al.*, 2015). Secondary metabolite compounds have been scientifically proven to have antibacterial properties that can inhibit the growth of microorganisms (Rudiana *et al.*, 2021). Flavonoids are polyphenolic compounds that can inhibit the growth of pathogenic microorganisms and antibiotic-resistant bacteria (Thebti *et al.*, 2023). In addition, other compounds that have antibacterial activity, namely alkaloids (Rahma *et al.*, 2023) tannins and saponins (Risna, 2023) Natural ingredients that are widely used by the community Balong village, Ujung Loe District, Bulukumba Regency, South Sulawesi, Indonesia, as

traditional medicines, namely lahuna (*Chromolaena odorata*) and binahong (*Anredera cordifolia*). The people of Bulukumba, traditionally use lahuna leaves as a wound medicine that can stop bleeding in wounds and accelerate wound healing. Meanwhile, binahong leaves are used as an itch remedy and accelerate wound healing and are used as facial skin care.

Lahuna is a plant that originates from tropical America and spreads in tropical areas of Asia, Austria and West Africa. Lahuna can form dense thickets and is invasive and is therefore considered a nuisance plant or weed. In lahuna leaves, pyrrolizidine alkaloids, flavonoids, phenolic acids and terpenoids were found (Noguchi and Kato, 2023). The ethanol extract of lahuna leaves formulated with betel leaves is used as a source of active ingredients in the manufacture of liquid soap which has very strong antibacterial activity against *E. coli* (Jumrah and Rosmaniar, 2023). and *S. aureus* (Jumrah *et al.*, 2023). Previous research stated that an ointment made from the extract of tacklen leaves (another name for lahuna) could heal burns in mice tested almost as well as standard medicine (Kanedi *et al.*, 2020).

Lahuna has extraordinary ethno pharmacological

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properties because it has antibacterial, anti-inflammatory, antioxidant and analgesic activities (Aziz *et al.*, 2020). *In vitro* study revealed that ethyl acetate extract lahuna leaf had antibacterial activity with an inhibitory power of 18.67 mm against *Pseudomonas aeruginosa* isolated from patient wounds (Alabi, 2020). In addition, lahuna leaves contain flavonoid compounds such as -4',5,7-trimethoxy flavanone, and 5-hydroxy-3,7,4'-trimethoxyflavone which have antibacterial activity against *E. coli*, *S. aureu*, *K. pneumoniae*, *A. fumigatus* and *C. Neoformans* (Omokhua-Uyi *et al.*, 2020)

Binahong plants are native to South America and are widespread through Australia, Africa, the United States, New Zealand and Asia. Binahong contains alkaloid, flavonoid, triterpenoid, steroid, phenolic acid, glycoside, tannin and saponin. And has functional properties such as antimicrobial, antioxidant, ant hyperlipidemia, anti-inflammatory, analgesic, ant obesity and antidiabetic. And the results of *in vivo* and *in vitro* tests using a mouse model did not show any signs of toxicity, so it is safe to use as medicine (Tedjakusuma and Lo, 2022). Binahong leaf extract gel 3% can help heal hard tissue after tooth extraction, this is initiated by the content of secondary metabolites which induce the release of growth factors which play a role in angiogenesis and bone regeneration (Hanafiah *et al.*, 2021) In addition, binahong has antibacterial activity against *Staphylococcus aureus*, antifungal activity *Candida albicans* (Alba *et al.*, 2020). Other studies have shown that the combination of binahong can repair cells thereby accelerating wound healing, this is due to the content of saponin secondary metabolites which can increase the expression of transforming growth factor-alpha (TGF- α) and transforming growth factor-beta (TGF- β) and the properties of saponin as antiseptic and contains other compounds such as apigenin and flavonoids (Nazliniwaty *et al.*, 2022) In addition, binahong leaf extract has an anti-inflammatory effect on colonic inflammation in mice (Utami *et al.*, 2023).

Based on research on lahuna leaves and binahong leaves, they show their potential to be used as a source of active ingredients that act as antiseptics. With the combination of active ingredients, lahuna leaves and binahong leaves can increase antiseptic activity. Antiseptics are one of the common components for effective treatment against pathogenic bacteria, especially those that are antibiotic resistant (Zharkova *et al.*, 2023) The active ingredients of lahuna leaves and binahong leaves are formulated in the form of an ointment for topical use. In the community, ointment preparations have been widely marketed, however, the active ingredients used are synthetic chemical compounds that can irritate the skin, besides that the massive use of antiseptic ointments increases the

incidence of antibiotic resistance. (Cahyadi *et al.*, 2019) So active ingredients from natural ingredients are needed to overcome the incidence of antibiotic resistance, namely by formulating lahuna leaves and binahong leaves in the development of antiseptic ointment preparations and as an alternative treatment in inhibiting pathogenic bacterial infections, especially those that are resistant to antibiotics.

Experimental

Material and Methods

The equipment used in this study included a blender (Miyako), basin, filter, object glass, standard glassware (Pyrex), rotary evaporator (IKA RV 10 digital), analytical balance (ADAM), magnetic stirrer, caliper, digital pH meter (Mediatech) and Petri dishes.

The materials used in this study included binahong leaves, lahuna leaves, 96% ethanol, anhydrous lanoline, Vaseline, distilled water, Wagner reagent, HCl, FeCl₃, libermann-burchard reagent, Muller Hinton Agar, paper disk, *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853.

Procedures

Sample Preparation

Lahuna leaves and binahong leaves taken in Balong village, Ujung Loe District, Bulukumba Regency, South Sulawesi, Indonesia. Lahuna leaves and binahong leaves were collected and cleaned using running water until the leaf samples were clean and free of dirt. The clean samples were drained and then cut into small pieces to facilitate the drying process. Drying was carried out at room temperature by aerating until the leaf samples were dry, the dried leaf samples were crushed using a blender to obtain powder. The sample powder was sieved to obtain simplicial powder. Simplicial powder is stored in a closed container.

Extraction

The process of extracting lahuna leaves and binahong leaves was carried out by maceration method 96% ethanol for 1 x 24 hours while stirring occasionally. Then the sample was filtered using filter paper. The first screening obtained filtrate and residue. The residue obtained is then macerated with the same treatment until a second filtrate is obtained. The maceration process is stopped if the filtrate obtained is clear. The collected filtrates were put together which were then concentrated using a rotary evaporator to obtain a thick extract. The concentrated extract was weighed and the yield was calculated.

Phytochemical Analysis

Steroid test using *a* libermann-burchard reagent, 10 mg of lahuna leaf extract and binahong leaf extracts dripped with libermann-burchard reagent until a positive bluish-green color is formed for steroids.

To test alkaloid compounds, 10 mg of lahuna and binahong leaf extracts were added with 10 ml of HCl and heated for 2 minutes while stirring continuously, then filtered. The filtrate was added with 5 ml of HCl and Wagner's reagent.

The Flavonoid test was carried out by adding 5 ml of ethanol and a few drops of FeCl₃ to each extract of lahuna and binahong leaves as much as 10 mg. A positive test is marked by a color change to blue, purple, green, red, to black. If up to 20 drops of FeCl₃ are added and there is no color change, then the flavonoid is negative.

Saponin test, lahuna leaf extract, and binahong leaf extract 0.5 g each added with 5 ml distilled water and shaken vigorously. A positive test is indicated by the formation of foam/foam.

And tannin test, lahuna leaf extract, and binahong leaf extract boiled each 0.5 in 20 ml of distilled water in a test tube. Filtered and added a few drops of 0.1% FeCl₃ until it changes color. Positive results are indicated by the formation of a brownish-green or blackish-blue color.

Preparation of Ointment Base

The ointment base is made by mixing anhydrous lanoline with Vaseline. Mixing uses a magnetic stirrer to mix homogeneously.

Preparation of Antiseptic Ointment

The ointment formulation of Lahuna leaf extract and binahong leaf extract is made by adding the ointment base little by little to each lahuna leaf extract and binahong leaf extract according to the formula design in Table 1.

Table 1. Formula for ointment of Lahuna leaf extract and Binahong leaf extract

Material	Formula (Gram)				
	I	II	III	IV	V
Lahuna extract	2	-	1.25	1	0.75
Binahong extract	-	2	0.75	1	1.25
Ointment Base	18	18	18	18	18

Evaluation of Ointment Preparations

Organoleptic test. Organoleptic tests are carried out to see the physical appearance such as shape, color and smell. Organoleptic assessments were carried out on day 1, day 7,

day 14, day 21 and day 30. Good quality ointment is in the form of a semi-solid dosage form, the ointment has a characteristic smell of the extract used and is colored like the extract.

Homogeneity test. The homogeneity test is observing the results of applying the ointment to a glass plate. Homogeneous ointment preparations are characterized by the absence of lumps in the basting results, an even structure and a uniform color from the starting point of application to the end point of application.

pH test. The pH test was carried out using a pH meter (which was calibrated with a pH buffer solution before each measurement), then the electrode which had been cleaned with distilled water was dipped into 1 g of ointment sample which had been diluted with 10 ml of distilled water then examined at room temperature, the pH value that appears on the pH meter scale is read and recorded.

Spread ability test. The spread ability test was carried out by installing a pair of glass plates, one of which was a glass slide. Ointment is placed on the surface of the glass plate as much as 0.1 g. The object glass plate is placed on top of the ointment symmetrically, with the addition of a load of 20, 30, 40 and 50 g placed on the object glass plate for 1 minute, then the diameter of the ointment is measured by using a caliper.

In vitro Test of Ointment Preparations

The Ointment formulation that has been made was tested for its antibacterial activity against *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853. Using the agar diffusion method with the paper disk technique. *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853 was inoculated into Muller Hinton Agar medium (MHA) and then incubated for 18 hours at 37 °C. And each Ointment formulation was smeared into a paper disk. The paper disk was placed on Muller Hinton Agar medium containing *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853, incubated at 37 °C for 24 hours, and observed. The clear zone formed was measured using a caliper.

Result and Discussion

Sample Preparation

Preparation of simplicia begins with collecting samples of lahuna and binahong leaves, which are then washed, chopped, dried, milled using a blender and sieved to obtain simplicia powder. Lahuna leaf and binahong leaf simplician powder is brownish green. Dried simplicia powder is stored in a closed plastic container.

Extraction

Lahuna leaf and binahong leaf simplicia were macerated using 96% ethanol. The use of 96% ethanol is intended to be able to extract the metabolite compound components contained in simplicia, besides that ethanol is not toxic so it is safe to use for pharmaceutical preparations (Sahumena *et al.*, 2023). Simplicia lahuna leaves and binahong leaves are each macerated in 500 g in 96% ethanol. The maceration results obtained each 3 liters of filtrate, which then evaporated the solvent using an evaporator to obtain a thick extract. The thick extract of lahuna leaves was 72.91 g with a yield value of 14.58% while the thick extract of binahong leaves was 53.17 g with a yield value of 10.63%.

Phytochemical Analysis

Phytochemical analysis of Lahuna leaf extract and binahong leaf extract is aimed at screening secondary metabolite compounds contained using various types of reagents such as Wagner, Libermann-Burchard (Kaempe *et al.*, 2023). The results of the analysis are shown in Table 2.

Table 2. Results of phytochemical analysis of lahuna leaf extract and binahong leaf extract

Group	Lahuna leaf extract	Binahong leaf extract
Flavonoid	+ Blackish	+ greenish
Alkaloid	+ Brownish green	-
Steroid	+ Bluish green	+ Bluish green
Saponin	-	+There are bubbles
tannin	+ Brownish green	+ Brownish green, there is sediment

Based on these tests, the compounds contained in lahuna leaf extract are flavonoid, alkaloid, steroid, and tannin. Meanwhile, binahong leaf extract contains flavonoid, steroid, saponin, and tannin. The content of potential secondary metabolites as antibacterial. The research Kappele, *et al* (2022), have used the ethanol extract of nutmeg leaves as a source of active compounds which have been shown to have inhibitory properties against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Other studies Salimi *et al.* (2019) stated that the pentacyclic lupenol triterpenoid compound in Moringa leaves has moderate antibacterial activity against *S. aureus* and *E. coli* (Salimi *et al.*, 2019). The use of natural ingredients as active ingredients in *Ointment* has been widely developed,

one of which is the use of Clove Leaf extract (*Syzygium aromaticum* L.) which exhibit antibacterial activity against *S. aureus* (Arni *et al.*, 2023), Kampo herbal ointments for skin wound healing (Traversaz *et al.*, 2023), and ointments formulation semprawang leaves (*Dilenia ochreatea*) for the treatment of scady (Yohandini *et al.*, 2023).

Preparation of Ointment Base

The ointment base is prepared by mixing anhydrous lanoline with vaseline to produce a yellowish semi-solid ointment base as shown in Figure 1.



Figure 1. Ointment base

Preparation of Ointment Preparations of Lahuna Leaf Extract and Binahong Leaf Extract

The ointment is formulated into 5 formulations with varying concentrations of lahuna and binahong extracts. Formula I added 100% lahuna extract in an ointment base, formula II added 100% binahong extract, formula III added lahuna extract and binahong extract with a ratio of 75%: 25%, Formula IV with a ratio of 50%: 50% and Formula V 25%: 75%. Variations in ointment preparation formulas can be seen in Figure 2.



Figure 2. Formula ointment

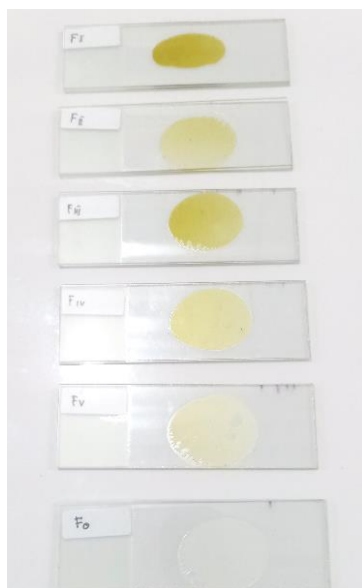
Evaluation and Characterization of Ointment Preparations

Organoleptic test. The organoleptic test is carried out with a descriptive assessment by assessing the physical appearance, namely shape or texture, color and smell. The assessment results are shown in table 3.

Table 3. Results of organoleptic assessment of ointment formulations

Evaluation	Ointment Base	Formula I	Formula II	Formula III	Formula IV	Formula V
Texture	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft
	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft
Days 1, 7, 14, 21 & 30	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft
	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft
	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft	Semi solid, soft
Color	Yellowish	Blackish green	Deep green	Blackish green	Dark green	Light green
	Yellowish	Blackish green	Deep green	Blackish green	Dark green	Light green
	Yellowish	Blackish green	Deep green	Blackish green	Dark green	Light green
Days 1, 7, 14, 21 & 30	Yellowish	Blackish green	Deep green	Blackish green	Dark green	Light green
	Yellowish	Blackish green	Deep green	Blackish green	Dark green	Light green
	Yellowish	Blackish green	Deep green	Blackish green	Dark green	Light green
Smell	Typical ointment base	Typical of lahuna extract	Typical of binahong extract	Typical of lahuna extract	A special blend of Lahuna Binahong extract	Typical of binahong extract
	Typical ointment base	Typical of lahuna extract	Typical of binahong extract	Typical of lahuna extract	A special blend of Lahuna Binahong extract	Typical of binahong extract
	Typical of ointment bases	Lahuna extract special	Typical binahong extract	Lahuna extract special	A special blend of Lahuna Binahong extract	Typical binahong extract
	Typical of ointment bases	Lahuna extract special	Typical binahong extract	Lahuna extract special	Typical blend of lahuna binahong extract	Typical binahong extract
	Typical of ointment bases	Lahuna extract special	Typical binahong extract	Lahuna extract special	Typical blend of lahuna binahong extract	Typical binahong extract
Days 1, 7, 14, 21 & 30	Typical of ointment bases	Lahuna extract special	Typical binahong extract	Lahuna extract special	Typical blend of lahuna binahong extract	Typical binahong extract
	Typical of ointment bases	Lahuna extract special	Typical binahong extract	Lahuna extract special	Typical blend of lahuna binahong extract	Typical binahong extract
	Typical of ointment bases	Lahuna extract special	Typical binahong extract	Lahuna extract special	Typical blend of lahuna binahong extract	Typical binahong extract
	Typical of ointment bases	Lahuna extract special	Typical binahong extract	Lahuna extract special	Typical blend of lahuna binahong extract	Typical binahong extract
	Typical of ointment bases	Lahuna extract special	Typical binahong extract	Lahuna extract special	Typical blend of lahuna binahong extract	Typical binahong extract

Homogeneity test. The homogeneity test of the ointment preparation was carried out by smearing the ointment preparation on the slide, homogeneous results were shown by the absence of lumps, coarse grains, flat structure and uniform color. As seen in Figure 3.

**Figure 3.** Homogeneity test results

pH test. The pH value of the ointment formulation was measured using a pH meter. The measurement results are shown in Table 4.

Table 4. pH value of ointment preparations

Formulas	pH value
Base	7.3
I	7.3
II	7.5
III	7.5
IV	7.3
V	7.3

Based on measurements of the pH value of the ointment preparation, it shows compliance with the Indonesian National Standard (SNI) 164399-1996 concerning the quality of preparations for the skin with a pH range of 4.5-8 (Rahmawati and Samodra, 2022). And the pH test results show that the pH of the ointment formulation of Lahuna leaf and binahong leaf extract is around 7.3-7.5.

Spreadability test. The ointment preparation was tested for spreadability by placing a 0.1 g ointment preparation on a glass surface and given a load of 20 g, 30g,

40 g and 50 g. The aim of the spreadability test is to see the ability of the ointment to spread on the skin when applied (Ambarwati, 2021). The results of the spreadability test are shown in Table 5.

Table 5. Spreadability test results

Formulas	Burden			
	20(g)	30(g)	40(g)	50(g)
I	2.5cm	2.5cm	3 cm	3.5cm
II	2.5cm	2.5cm	3cm	3cm
III	2.5cm	2.5cm	3 cm	3 cm
IV	2.5cm	2.5cm	3 cm	3cm
V	2.5cm	2.5cm	3cm	3cm

In vitro Test of Ointment Preparations

In vitro test of ointment preparations using *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853. *Staphylococcus aureus* and *Pseudomonas aeruginosa* are pathogenic bacteria that cause infectious diseases, especially on the skin, such as boils and acne. Testing of the ointment formulation against *Pseudomonas aeruginosa* ATCC 27853 did not give an inhibition zone. While testing the ointment against *Staphylococcus aureus* ATCC 25923, only formulas I and III showed inhibition zones, namely 8.18 mm and 8.93 mm.

The ointment formulation does not have inhibitory power against *Pseudomonas aeruginosa*, although in the research Lahuna leaf and binahong leaf extracts had antibacterial activity against *Pseudomonas aeruginosa*. This is due to the active ingredients contained in the extract not being completely distributed into the ointment formula so the active ingredients in the ointment are not strong enough to inhibit *Pseudomonas aeruginosa*. Besides that, *Staphylococcus aureus* and *Pseudomonas aeruginosa* have different cell wall structures. The cell membrane structure of the Gram-positive bacteria *Staphylococcus aureus* is composed of layers of peptidoglycan, teichoic acid and lipoproteins. Meanwhile, *Pseudomonas aeruginosa* is Gram-negative with complex cell walls. The outer membrane of Gram-negative bacteria contains phospholipids, lipopolysaccharides and lipoproteins in large quantities so that they can protect the lysis of peptidoglycan and protect cells from external environmental influences, including hypertonic environments (Alouw *et al.*, 2022). Therefore there are differences in the inhibitory power of the ointment formulation against *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

The results of the resistance measurement are shown in Table 5.

Table 6. *In vitro* test results for ointment preparations

Formulas	Test results	Test results
	Inhibitory Power against <i>Staphylococcus aureus</i> ATCC 25923 (mm)	Inhibitory Power against <i>Pseudomonas aeruginosa</i> ATCC 27853 (mm)
I	8.18	0.00
II	0.00	0.00
III	8.93	0.00
IV	0.00	0.00
V	0.00	0.00

Based on these tests, it shows that the ointment formulation that have a higher concentration of lahuna extract provide inhibition against *S. aureus*. According to research (Azizah and Samodra, 2023) which reveals that the content of bioactive components plays an important role in inhibiting the activity of microorganisms. Research by Alouw (2022) shows that the content of active compounds such as flavonoid, saponin and tannin from cherry leaf extract causes the growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa* bacteria to be inhibited, which is marked by the formation of a clear zone. Increasing the concentration of cherry leaf extract shows that the resulting inhibitory power is greater.

Conclusion

Based on the research results, it shows that lahuna leaf extract and binahong leaf extract can be formulated in the form of an ointment. With the evaluation results in the form of an organoleptic test, namely semi-solid form, color and distinctive odor of the extract. The homogeneity test shows that the ointment preparation is homogeneous, and can spread evenly. The pH test showed a value of 7.3 for formula I, IV and V while formula II and VI were 7.5 and safe for skin application. For *in vitro* tests, ointment formulations I and III have inhibitory power against *Staphylococcus aureus* ATCC 25923.

Suggestion, research related to antiseptic ointment formulations of Lahuna leaf extract and binahong leaf extract needs to be continued, especially irritation tests so that they are safe for use by the general public.

Conflict of Interest

The authors declare that there is no conflict of interest.

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