



Formulation of Komba-Komba Leaf Extract Ointment (*Chromolaena odorata* L) for Wound Healing

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ABSTRACT

Wounds are physical injuries that can cause damage to skin tissue. The extract of komba-komba leaves (*Chromolaena odorata* L) contains flavonoids, saponins, and tannins, which are wound healers formulated as ointment preparations. This study aims to determine how administering komba-komba leaf extract ointment affects wound healing. The maceration method obtained a thick extract of komba-komba leaves. Komba-komba leaf extract ointment was made in three formulas based on differences in extract concentration: FI = 5%, FII = 10% and FIII = 15%). The ointment preparations obtained were subjected to organoleptic tests (color, odor, and consistency) and physical tests, including homogeneity, pH, viscosity, spreadability, stability tests, and scratch wound healing activity tests. The results showed that the extract's concentration affected the ointment preparation's color, consistency, and physical properties. The effectiveness test results for healing scratches showed that the ointment preparation with an extract concentration of 15% provided an effective healing speed.

Keywords: *Chromolaena odorata*; Formulation; Ointment; Wounds

INTRODUCTION

A wound is a condition in which body tissue is injured or damaged. Sharp objects, chemicals, animal bites, electric shocks, etc can cause this damage.¹ In general, wounds can be divided into two types: unintentional wounds and intentional wounds. Unintentional wounds usually occur in someone who has an accident, while intentional wounds typically occur in someone who undergoes surgery for a specific purpose. Types of wounds are divided into open wounds and closed wounds.² The human body automatically responds when a part of it is injured. This response involves cell regeneration and wound healing to restore the structure and function of damaged body tissue.³ Wound

healing in body tissue consists of three phases, namely the inflammatory phase, the proliferation phase, and the remodeling phase. In the wound healing process, several components play an important role such as collagen, angiogenesis or the formation of new blood vessels, and granulation.⁴

Research conducted in America states that the prevalence of wound patients is 350 per 1000. The etiology of wounds in patients varies with the data obtained, namely surgical wounds 113.3 million cases, trauma wounds 1.6 million cases, abrasions 20.4 million cases, burns 10 million cases, and decubitus ulcers 8.5 million cases.⁵ Based on Risesdas data from the Ministry of Health of the Republic

of Indonesia, there was an increase in the prevalence of wounds in Indonesia from 8.2% in 2013 to 9.2% in 2018.⁶ The high prevalence of wounds in Indonesia requires drugs for wound healing.

People generally use synthetic chemical drugs. One drug often used to minimize the impact of infection due to bacterial contamination is povidone iodine.⁷ Povidone iodine is also an external antiseptic with a microbicidal spectrum for the prevention or treatment of topical infections associated with surgery, cuts, and abrasions and for reducing mild mucosal irritation.⁸ However, the content of this synthetic drug can cause side effects during the wound-healing process.⁹ Long-term use of povidone-iodine has several side effects, such as inhibiting wound granulation, being more toxic when it enters the blood vessels, and causing irritation if the antiseptic in povidone-iodine is in high concentrations.¹⁰ The toxic properties of povidone-iodine towards fibroblasts will affect collagen formation and the formation of new tissue in wounds, thus inhibiting the wound closure process.¹¹

The community must be wiser in determining wound healing actions to minimize side effects for body health. Alternatives that the community can use to heal wounds are medicinal plants.¹² Medicinal plants are considered safer to use because they have relatively lower side effects when compared to synthetic chemical drugs. Komba-komba (*Chromolaena odorata*) is a medicinal plant that is used by the community as a wound medicine, to treat infections, headaches, and diarrhea, and as an astringent, antispasmodic, antihypertensive, anti-inflammatory, and diuretic. Komba-komba is a type of plant from the Compositae family that contains active compounds flavonoids, saponins, tannins, phytates, and cyanogenic glycosides that affect wound healing.¹³

Flavonoid compounds in komba-komba leaves have an antimicrobial effect that can inhibit the growth of microorganisms, one of which is bacteria,

by destroying the bacterial cell protein, and also functions to protect blood vessels.¹⁴ Saponin compounds have an antibacterial effect. Their working mechanism damages the cytoplasmic membrane, kills bacterial cells, and stimulates the formation of collagen to repair damaged body tissue.¹⁵ Tannin, flavonoid, and saponin compounds work together to function as antimicrobials and stimulate the growth of new cells in damaged body tissue.¹⁶ To optimize the benefits of the content of komba-komba leaf compounds in treating wounds, it is necessary to formulate it into a pharmaceutical preparation in the form of an ointment. The ointment preparation was chosen because it is a consistent preparation suitable for skin therapy caused by bacteria. The ointment is a semi-solid preparation that is easy to apply and contains various chemicals and drugs, which are generally used topically on parts of the body that are experiencing disorders, such as wounds, aches, and itching.

METHODS

Equipment and materials

The tools used in this study were a mortar and pestle (Rofa), blender (Sanex), measuring cup (Pyrex), funnel (Pyrex), Erlenmeyer flask (Pyrex), jar (DLX Glass), stirring rod (Putra Masagus), evaporator (Buchi), and ointment pot (Em Cosmetics).

The materials used in this study were komba-komba (*Chromolaena odorata*) leaves from the mini herbal garden of PT. Palapa Muda Perkasa, Stearic Acid (Wilmar), Cera Alba (Palapa Muda Perkasa), Vaseline alba (Master Sun Chemical), Triethanolamine (Master Sun Chemical), Propylene Glycol (Echemi), Methyl Parabens (Raja Kimia), Aquadest (Putra Masagus), and 70% ethanol (Putra Masagus).

Plant determination

Plants to be studied before being collected and used as samples are first determined. Determination is carried out to know the truth of the plants to be studied, avoiding errors in collecting materials and avoiding the possibility of mixing the

plants to be studied with other plants. Determination of the Komba-komba plant (*Chromolaena odorata*) was carried out at the Pharmacy Laboratory of STIKes Widya Dharma Husada Tangerang.

Preparation of Komba-komba leaves

The procedure for making komba leaf extract begins with the leaves being washed repeatedly in running water, then aired without being exposed to sunlight, after which the komba-komba leaves are stored at a cool temperature in a clean, airtight container so that komba-komba leaves are obtained that are ready to be extracted.

Making komba-komba leaf extract

Maceration is done by putting 1000 grams of komba-komba leaves in a vessel, then adding 1000 mL of 70% ethanol and leaving it for 3x24 hours at room temperature while stirring repeatedly. Every 1x24 hours, the solvent is replaced. The resulting extract is filtered with filter paper. Furthermore, the filtrate is evaporated with a rotary evaporator at <60°C. Then, it is placed in a water bath until a thick extract of komba-komba leaves is obtained.¹⁷

Phytochemical test of komba-komba leaf extract

Phytochemical tests of Komba-komba leaf extract include alkaloid, saponin, tannin, triterpenoid/steroid, and flavonoid tests. The test methods used are alkaloid test using Mayer's reagent, saponin test using foam test, tannin test using FeCl₃, triterpenoid/steroid test using Liberman-Burchard reagent, and flavonoid test using Magnesium powder.

Formulation of komba-komba leaf extract ointment

The komba-komba leaf extract ointment was made using the melting method. Propylene glycol, cera alba, vaseline alba, stearic acid, distilled water, and triethylamine were heated until a thick mass was formed. Then methylparaben

was added and stirred until homogeneous and cooled. The homogeneous base was added with komba-komba leaf extract. The formulation of the komba-komba leaf extract ointment preparation was then evaluated for its characteristics:

Table 1. Formulation of komba-komba leaf extract ointment

Material (gram)	Formula		
	F1	F2	F3
Komba-komba leaf extract	0.5	1	2
Asam Stearad	1.5	1.5	1.5
Cera Alba	0.2	0.2	0.2
Vaseline alba	0.8	0.8	0.8
Trietanolamin	0.15	0.15	0.15
Propilen Glikol	0.8	0.8	0.8
Metil Parabens	0.5	0.5	0.5
Aquadest	56.55	52.05	42.05

Physical evaluation of komba-komba leaf extract ointment

To produce komba-komba leaf extract ointment that meets national standards, it is necessary to conduct tests on traditional medicines' safety and quality requirements according to BPOM Regulation No. 32 of 2019, including organoleptic, pH, homogeneity, spreadability and viscosity tests.¹⁸ Effectiveness test of komba-komba (*Chromolaena odorata*) leaf extract ointment on scratches.

Organoleptic test

The organoleptic evaluation was carried out by visual observation of the komba-komba leaf extract ointment preparation obtained through color, odor, and shape.^{19,20}

pH test

pH evaluation of komba-komba leaf extract ointment preparation using a pH meter instrument.

Spreadability test

The spreadability test of komba-komba leaf extract ointment was carried out by weighing 0.5 grams of ointment placed on

a round glass with another glass placed on top and left for 1 minute. Then, 100 grams of load were added and left for 1 minute, and the constant diameter was measured.^{21,20}

Viscosity measurement

This test uses a Brookfield viscometer by placing the ointment preparation in a large-mouthed container and then inserting a suitable spindle into the ointment until it is immersed.²²

Stability test

The stability test was conducted using the freeze-thaw cycle method for 12 days or 6 cycles. Each cycle consisted of 2 days, with the treatment of the ointment preparation being placed in a refrigerator at a temperature of 5°C for 24 hours and then placed at a temperature of 40°C for 24 hours, and the changes were observed.²¹

Effectiveness of komba-komba leaf extract ointment.

The effectiveness of kombu leaf extract ointment was tested on scratches. Volunteers with three parts of scratches with a length of 1 cm were given kombu leaf extract ointment with different formulations. Then, the wounds were observed and measured every day. This test met the requirements of the code of ethics (532/KEPK/FKM-UNEJ/VII/2024).

RESULTS AND DISCUSSION

The results of plant determination carried out at the Pharmacy Laboratory of STIKes Widya Dharma Husada Tangerang showed that the sample used was indeed a komba-komba leaf plant with the scientific name (*Chromolaena odorata*) from the *Acanthaceae* family. This study was conducted to determine the concentration of komba-komba leaf extract ointment formulation. The ointment base was water-soluble, and a physical evaluation with test parameters was conducted. The physical assessments carried out were organoleptic, pH testing, homogeneity testing, viscosity testing, spreadability testing, and stability testing. The results of organoleptic testing

of komba-komba leaf extract ointment can be seen in the table below:

Table 2. Organoleptic test results of komba-komba leaf extract ointment

Formula	Type of Examination		
	Color	Odor	Dosage Form
F1	cream green	specific komba-komba leaves	semi solid
F2	dark green	specific komba-komba leaves	semi solid
F3	dark green	specific komba-komba leaves	semi solid

The results of organoleptic testing of komba-komba leaf extract ointment (*Chromolaena odorata*) obtained formula one was pale green, formula 2 was dark green, and formula 3 was dark green. The homogeneity testing aims to determine whether the ointment is made homogeneous or evenly mixed between the active substance and the ointment base. The ointment must be homogeneous and is determined by applying it to a piece of glass or other suitable transparent material; it must show a homogeneous composition.

Table 3. Homogeneity test results

Formula	Homogeneity
I	Homogeneous and particle-free
II	Homogeneous and particle-free
III	Homogeneous and particle-free

The homogeneity test results of the komba-komba leaf extract ointment obtained a homogeneous ointment. Each component contained in the ointment is suitable and mixed evenly with the komba-komba leaf extract. In addition, there are no lumps or coarse grains in the ointment preparation. This means the komba-komba leaf extract can be used to prepare ointment.

The pH test of the komba-komba leaf extract ointment aims to see the acidity or alkalinity of a preparation; the more acidic a preparation is, the more it can irritate, and the more alkaline a preparation is, the more scaly it will be. The pH value of human skin is around 4.5 - 6.5.²³ The results of organoleptic testing of komba-komba leaf extract ointment showed that the ointment in formula I produced a creamy green ointment due to the lack of komba-komba leaf extract, and formulas II and III produced dark green ointments. The color difference is due to the amount of komba-komba leaf extract used. Formulas I, II, and III have a distinctive komba-komba leaf odor. The ointment formula preparation produced is semi-solid.

Tabel 3. pH test results

Formulation	pH
I	6.4
II	6.3
III	5.8

The pH test results carried out on the komba-komba leaf extract ointment preparation obtained almost the same pH value in each formulation. The pH measurement was carried out using a pH meter by looking at the monitor results on the pH meter. The komba-komba-komba extract ointment formulation (*chromolaena odorata*) had almost the same pH. Formula I had a pH of 6.4, formula II had a pH of 6.3, and formula III was 5.8. Based on these results, the komba-komba leaf extract ointment formulation was based on the pH of human skin.

Observation of the ointment's spreadability to see the distribution of the ointment preparation made, the distribution is said to be good if the more significant the distribution.²⁴

Table 4. Spreadability test results

Formula	spreadability (cm)
I	5.3
II	5.3
III	5.7

The results of the spreadability test were obtained in formula I of 5.3 cm, formula II of 5.3, and formula III of 5.7 cm. These results meet the requirements for good spreadability. Good ointment spreadability is between 5-7 cm.²⁵ The concentration of komba-komba leaf extract can influence the spreadability of the ointment; the more extract is used, the greater the spreadability. The spreadability of the ointment can also be influenced by the ointment base, namely propylene glycol, which can increase the spreadability of the ointment.²⁶ Spreading power is related to viscosity; the smaller the preparation's spreading power, the greater its viscosity.²⁷

Viscosity testing is done using a viscometer. The results of the viscosity test can be seen in the table below:

Table 5. Viscosity test results

Formula	Viscosity (cP)
I	8300
II	8500
III	9500

Viscosity aims to see the thickness of an ointment preparation.²² The formula of the komba-komba leaf extract ointment preparation with a combination of polyethylene glycol ointment base can affect the viscosity of the preparation because the two forms of substances are different. Viscosity is closely related to the spreading power and adhesion. The greater the viscosity of the ointment, the smaller the spreading power of the ointment and the longer the ointment's ability to adhere.²⁵ The viscosity value based on the quality requirements of skin preparations is 2000 - 50000 cps; this shows that all ointment preparations meet the viscosity requirements of good skin preparations.²²

Physical stability tests of komba-komba leaf extract ointment preparations were carried out to see the preparations' consistency in several concentrations.

Table 6. Ointment stability test

Formula	Cycle					
	1	2	3	4	5	6
Organoleptic test	F1. (cream green, characteristic odor, semi-solid) F2. (dark green, characteristic odor and semi-solid) F3 (dark green, characteristic odor and semi-solid)	F1. (cream green, characteristic odor, semi-solid) F2. (dark green, characteristic odor and semi-solid) F3 (dark green, characteristic odor and semi-solid)	F1. (cream green, characteristic odor, semi-solid) F2. (dark green, characteristic odor and semi-solid) F3 (dark green, characteristic odor and semi-solid)	F1. (cream green, characteristic odor, semi-solid) F2. (dark green, characteristic odor and semi-solid) F3 (dark green, characteristic odor and semi-solid)	F1. (cream green, characteristic odor, semi-solid) F2. (dark green, characteristic odor and semi-solid) F3 (dark green, characteristic odor and semi-solid)	F1. (cream green, characteristic odor, semi-solid) F2. (dark green, characteristic odor and semi-solid) F3 (dark green, characteristic odor and semi-solid)
pH	F1 (6.4) F2 (6.3) F3 (5.8)	F1 (6.2) F2 (6.0) F3 (5.8)	F1 (6.1) F2 (6.3) F3 (5.5)	F1 (6.3) F2 (6.6) F3 (5.8)	F1 (6.3) F2 (6.4) F3 (6.0)	F1 (6.4) F2 (6.3) F3 (5.8)
Homogeneity	homogeneous	homogeneous	homogeneous	homogeneous	homogeneous	homogeneous
Spreadability (cm)	F1 (5.3) F2 (5.3) F3 (5.7)	F1 (5.5) F2 (5.4) F3 (5.8)	F1 (5.6) F2 (5.6) F3 (5.8)	F1 (5.8) F2 (5.9) F3 (5.7)	F1 (5.8) F2 (5.8) F3 (5.9)	F1 (6.1) F2 (6.1) F3 (5.8)
Viscosity (cP)	8300 8500 9500	8190 8380 9320	8003 8298 9117	7932 8173 9031	7854 8153 8901	7791 8090 8870

The stability test was conducted using the freeze-thaw cycle method for 12 days or six cycles. In each cycle consisting of 2 days with the treatment of ointment preparations placed in a refrigerator temperature of 5°C for 24 hours and then placed at a temperature of 40°C for 24 hours, the changes were observed.²⁰

The stability analysis results of the komba-komba extract ointment showed that the three formulas made had good stability. The stability test of each cycle for the organoleptic results of the komba-komba leaf extract ointment preparation still had the same colour, namely, in F1, it was creamy green, had a distinctive odour and was half solid, and in F2 and F3, it was dark green, had a distinctive odour and was half solid. The homogeneity test results showed that F1, F2, and F3 were still homogeneous. The pH test of F1 (6.4), F2 (6.3), and F3 (5.8) showed that it was still in the good skin pH range. The spreadability test of F1 increased (6.1 cm), F2 (6.1 cm), and F3 (5.8 cm), still in the good spread

diameter range for the skin. The viscosity test of F1 decreased in each cycle (7791 cP), F2 (8090 cP), and F3 (8870 cP), still in the good viscosity range.

The effectiveness test of komba-komba leaf extract ointment (*Chromolaena odorata*) was carried out on scratch wounds.

The results of measuring the length of the scratch wound until it closes entirely in formula 1, formula II, and formula III. Data on changes in the average size of the wound in each group can be seen in Table 6 below:

Table 6. Average wound length of each formula

Day	Length of wound (cm)		
	F1	F2	F3
1	1	1	1
2	0.98	0.94	0.88
3	0.73	0.68	0.41
4	0.54	0.47	0.36
5	0.47	0.32	0.13
6	0.32	0.18	0

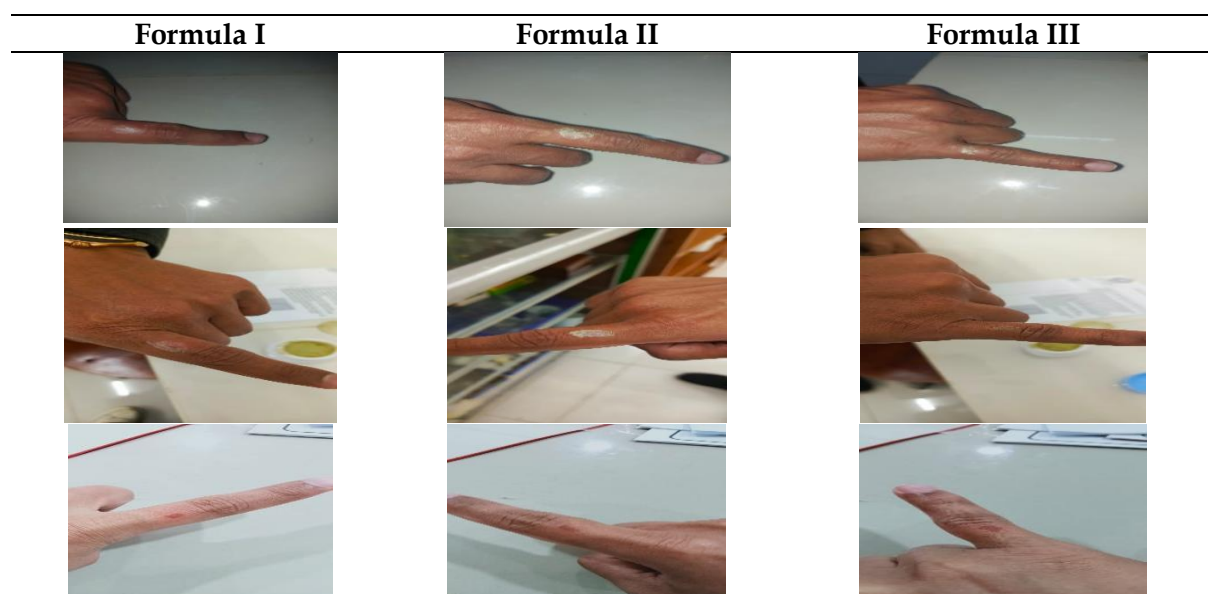


Figure 1. Microscopic image of a scratch wound

On the 2nd day, some scratch wounds had closed but had not closed completely. In F1 and F2, the wounds experienced a reduction in length. However, until the sixth day, the scratch wounds given with F1 and F2 had not closed completely. In F3, the wound continued to experience a reduction in length until it closed entirely on the 6th day of the third wound in the fifth. The wound closing process after the wound experienced the process of scab release. This indicates new cell growth has occurred by bringing the wound's edges closer together. The scab release process is where the tissue underneath is dry, and the edges of the wound begin to pull toward the center.

Healing of cuts with komba-komba leaf extract ointment also occurs due to flavonoid compounds in the extract, which function as antibacterials. In addition, flavonoid and polyphenol compounds are phenol compounds with antiseptic activity. The mechanism of these compounds damages the permeability of bacterial cell walls, microsomes, and liposomes due to the interaction between flavonoids and bacterial DNA, releasing transduction energy to the bacterial cytoplasmic membrane and inhibiting bacterial motility.²⁸ Flavonoid content kills or inhibits the growth of microorganisms in living tissue, such as the skin surface and mucous membranes. It can also reduce

inflammation by inhibiting cyclooxygenase and lipoxygenase.

CONCLUSION

Komba-komba leaf extract can be formulated as an ointment preparation with various concentrations. The results of the phytochemical test analysis showed that komba-komba leaf extract contains secondary metabolites. The best formulation in the effectiveness test of komba-komba leaves tested on scratches was F3.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors declare that the work presented in this article is original and that they will bear any liability for claims related to the content of this article.

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