



DATED THIS 26th DAY OF AUGUST, 2023

BETWEEN

**MAHSA UNIVERSITY, MALAYSIA
DU044 (B)**

AND

**INSTITUT ILMU KESEHATAN
BHAKTI WIYATA KEDIRI, INDONESIA
20541673**

MEMORANDUM OF UNDERSTANDING

This **MEMORANDUM OF UNDERSTANDING** is made on the 26th day of August, 2023

BETWEEN

MAHSA UNIVERSITY, MALAYSIA (Ministry of Higher Education Registration Certificate No. DU044 (B)), of which Malaysian Allied Health Sciences Academy Sdn Bhd (Company Registration No. 200401016011 / 654514-M) is the registered owner; and having its business address at Jalan SP 2, Bandar Saujana Putra, 42610 Jenjarom, Selangor Darul Ehsan, Malaysia (hereinafter referred to as the **"MU"**) of the one part;

AND

INSTITUT ILMU KESEHATAN BHAKTI WIYATA KEDIRI, INDONESIA (Nomor Pokok Sekolah Nasional: 20541673) and having its business address at Jl. KH Wachid Hasyim No.65, Bandar Lor, Kec. Mojoroto, Kota Kediri, Indonesia (hereinafter referred to as **"IIKBWK"**) of the other part;

whom hereinafter MU and IIKBWK are collectively referred to as **"Parties"** and individually as a **"Party"**; and this Memorandum of Understanding is referred to as this **"Memorandum"**.

WHEREAS -

- A. MU is a private higher educational institution established under Private Higher Education Institution Act 1996 which offers various study programmes in the fields of Medicine, Dentistry, Pharmacy, Health Sciences, Nursing, Business, Finance, Hospitality Management, Information Technology, and Engineering at the Foundation, Diploma, Degree, Masters, and Doctoral levels. MU is also a member of the MAHSA Group of Companies.
- B. IIKBWK is a private higher educational institution established with approval from Minister of Education and Culture, Research and Technology Republic of Indonesia that offers various study programmes in the fields of Nursing, Midwifery, Nutrition, Psychology, Traditional Chinese Medicine and Physiotherapy at the Professional Certificate, Diploma and Degree Level.
- C. Parties recognise their mutual interests and are desirous to collaborate with each other in an effort to pursue the objectives and benefits of their collaboration, which are more particularly described in Clause 2 below (**"Proposed Collaboration"**).
- D. Pursuant thereto, the Parties have agreed to enter into this Memorandum to record their respective commitments; and establish the basis for implementing new collaboration in the areas and manner as stated herein.
- E. The Parties hereby agree for the purposes of, and upon the terms and conditions set out in this Memorandum, to observe good faith towards one another in all matters affecting their dealings hereunder and interests herein.

NOW IT IS HEREBY AGREED as follows:

1. The Memorandum

- 1.1 The Proposed Collaboration of this Memorandum is as stated in Clause 2 herein.
- 1.2 Each Party represents to the other that this Memorandum does not constitute an obligation binding on either Party, with the exception of Clauses 3, 4, 6 and 14 herein.
- 1.3 Upon execution of this Memorandum, each Party agrees to provide to the other Party such information, confirmations and documents to enable the other Party, its representatives, advisers, consultants and agents, to evaluate and consider the manner of implementation of the Proposed Collaboration.
- 1.4 For the avoidance of doubt and without limiting the above in any way, this Memorandum creates no rights in favour of either Party.

2. Proposed Collaboration

- 2.1 The objective of this Memorandum is for Parties to develop co-operation and promote mutual agreement and excellence in potential projects, future co-operation, and knowledge exchange between the Parties.
- 2.2 In furtherance of this objective, the Parties agree to develop the following activities in collaboration in areas of mutual interests:
 - 2.2.1 to identify opportunities to collaborate in curriculum and practical development;
 - 2.2.2 to facilitate improvement and development of education and training in the health sector;
 - 2.2.3 to identify opportunities for academic implementation in the fields of Nursing/ Midwifery/ Pharmacy, or other related health fields;
 - 2.2.4 to facilitate exchange of students, administrative staff, academic activities, and information;
 - 2.2.5 to identify opportunities for collaboration in the field of research, joint activities, international activities, publications, seminars, academic activities, and implementation of educational programs;
 - 2.2.6 to facilitate the registration of degree programs and non-degree certificate programs and undergraduate short-term academic programs; and
 - 2.2.7 to identify opportunities of awarding of Bachelor's degree in Nursing / Midwifery / Pharmacy or other related allied health courses by MU to

the IIKBWK's students who successfully obtained a diploma / degree and to further their studies at MU in bachelor degree.

- 2.3 The development and implementation of specific activities developed under this Memorandum will be subjected to the respective formal written agreement negotiated and entered into separately, which will include but not limited to the financial arrangements, confidentiality, ownership and use of intellectual property, publication of articles or other work and other relevant matters.
- 2.4 The implementation of the Proposed Collaboration hereof shall depend upon the availability of resources and financial support of the Parties.
- 2.5 The Parties acknowledge the need to promote the programmes and activities pursuant to this Memorandum and hereby agree to use promotional materials which shall be approved by Parties.
- 2.6 The Parties agree that their respective employees and students who are engaged in the programmes and activities under this Memorandum shall carry out the programmes and activities in accordance with the applicable laws and regulations.
- 2.7 The Parties hereby agree that as to ensure on the success of the Proposed Collaboration, the roles and obligations of the Parties shall be more properly described and attached as an addendum to this Memorandum under **Annexure A** (hereinafter collectively referred to as "**Roles and Obligations of Parties**"), if applicable.

3. Confidentiality

3.1 Confidential Information

- 3.1.1 "**Confidential Information**" shall mean information (whether transmitted orally, in writing, electronically or in other form) relating to a Party's business, property and assets that is non-public or proprietary, and/or information which by their nature, or by the circumstances of their disclosure are or could reasonably be expected to be regarded as confidential to a Party or to any third party with whose consent or approval such information is used.
- 3.1.2 In no event shall any information constitute as Confidential Information hereunder –
 - 3.1.2.1 which was in the public domain prior to the date of this Memorandum;
 - 3.1.2.2 which becomes a part of the public domain following the date of this Memorandum not in any way caused by any act or omission of the Party receiving the information in breach of this Memorandum, or which becomes publicly available

other than as a result of a violation of any known confidentiality agreements; or

- 3.1.2.3 was within the possession of the Party receiving the information on a non-confidential basis from a source that is not bound, directly or indirectly, by a confidentiality agreement with the Party disclosing the information, prior to its being furnished.

3.2 Disclosure of Confidential Information

- 3.2.1 The Parties agree that the Confidential Information will be provided only to those of its officers, employees or advisers on a need -to- know basis (hereinafter referred to as “**Representatives**”) for purposes of this Memorandum and shall procure their respective Representatives’ compliance to Clause 3 herein.

- 3.2.2 The Confidential Information will be kept strictly confidential and each Party and its Representatives will not, directly or indirectly, at any time now or hereafter without the prior written consent of the other Party, disclose distribute, disseminate or supply to any person or authority (except as required by law in which event the Party disclosing or divulging Confidential Information must first notify the other Party in writing with details and evidence of the legal requirement) in any place and in whatever manner.

3.3 Use of Confidential Information

The Parties agree that the Confidential Information will be used only for the purposes of this Memorandum.

3.4 Return of Confidential Information

Immediately upon request by a Party all Confidential Information in whatever form will be returned to the Party that provided such Confidential Information and all documents and any data containing the Confidential Information will be destroyed (subject, however, to the inability to destroy data contained in routine computer backup systems).

3.5 Term of Confidentiality

The obligations under Clause 3 shall be binding upon Parties and cease to have any force and effect after five (5) years from the date of termination or expiry of this Memorandum. The confidentiality obligation for trade secrets shall survive the termination of this Memorandum.

4. Personal Data Protection

- 4.1 Both Parties hereby agree and undertake to each other:

- 4.1.1 that any personal data collected by the other Party including but not limited to the personal data of either Party's employees, students and clients (hereafter be referred to as "**Personal Data**"), such Personal Data must not be used for any other purposes other than for the purposes of this Memorandum;
 - 4.1.2 not to transfer any Personal Data to any third-party without the consent from the owner of the Personal Data;
 - 4.1.3 to take responsible measures to ensure that the Personal Data will be kept confidential, including not to sub-license, distribute, disclose, transfer or declare a trust of its rights in any of the Personal Data, in whole or in part, to any third party, without the express written consent of the other Party and any attempt to assign, transfer, sub-license or declare a trust of its rights without such consent shall render such assignment, transfer or sub-license, or declaration void and shall be construed as a breach of this Memorandum; and
 - 4.1.4 to comply with all rules, guidelines or regulations imposed by both Parties relating to personal data and also all applicable data protection laws in Malaysia under the Personal Data Protection Act 2010.
- 4.2 The obligation under this Clause 4 shall survive and shall be enforceable beyond the termination or expiry of this Memorandum.

5. Duration and Termination

5.1 Duration

This Memorandum and all rights and obligations hereunder shall take effect from the date of this Memorandum hereof for a period of five (5) years. Each Party shall review the status of the Memorandum at least six (6) months before the end of the five-year period to determine whether it wishes to continue and, if so, whether any modifications are required. The period of validity of this Memorandum may only be extended by the mutual written consent of both Parties.

5.2 Termination

If a Party decides that for whatsoever reason, it wishes to withdraw from this Memorandum, it may so withdraw and terminate this Memorandum by giving the other Party three (3) months' notice in writing of its intention to withdraw, in which case the withdrawing Party shall thereupon cease to participate in the execution of the Proposed Collaboration and shall have no liability for the subsequent actions of the other Party.

5.3 Survival of Obligations

The termination of this Memorandum does not affect:

5.3.1 any obligation of that Party which accrued prior to termination and which remain unsatisfied; and

5.3.2 any provision of this Memorandum which is expressed as continuing in effect after termination.

6. Intellectual Property Rights

6.1 Neither Party shall use the other Party's logo or other trademarks or make public or make any reference to the other Party in any of the Party's proposal, advertising activities, marketing materials, brochures or similar documents without the prior written consent of the other Party.

6.2 The Parties hereby agree that to the extent permitted under any applicable laws and regulations, ownership of intellectual property rights of any proprietary information or data, computer system or database invented, developed, created or discovered solely and separately by either Party or obtained through the sole and separate effort of either Party, shall be solely owned by the Party concerned.

6.3 The Parties hereby agree that to the extent permitted under any applicable laws and regulations, ownership of intellectual property rights of any proprietary information, system or database invented, developed, created or discovered jointly by the Parties or obtained through the joint activity effort, shall be owned by the Parties jointly and subjected to the terms and conditions mutually agreed upon in a separate agreement pertaining to ownership of joint intellectual property rights.

6.4 Either Party may transfer or assign its title or interest in whole or in part, in the intellectual property rights covered by this Memorandum to the other Party whereby such transfer or assignment must be in writing and shall be effective only upon the written acceptance of the other Party.

7. Force majeure

Neither Party shall be liable to the other Party in respect of any delay in performing or failure to perform any of its obligations hereunder if such delay or failure results from acts or intervention of Government or Government agencies; fire, flood or explosion; Act of God; declared or undeclared war, or riots or civil commotion; strikes or other industrial disputes; local and / or global pandemic; or any cause outside its reasonable control.

8. Assignment

Neither Party will be entitled to assign all or any part of its rights and obligations hereunder without the prior written consent of the other Party, with the exception of an assignment to any other company in the group of companies to which the assigning Party belongs to. The aforesaid consent shall not be unreasonably withheld or delayed and, in any event, shall be given unless the other Party, acting reasonably and in good faith, objects to the identity and/or involvement of the proposed assignee as being contrary to its commercial and/or business interests.

9. Publicity

- 9.1 Neither Party shall for publicity purposes make use of the name, or of any trade name or trademark, of the other Party, or of any information obtained under or in connection with this Memorandum from the other Party, without the prior written consent of the other Party.
- 9.2 Neither Party shall issue any publicity or other announcement in relation to this Memorandum and the Proposed Collaboration (whether transmitted orally, in writing, electronically or in other form, including but not limited to press releases and/or announcements) without the prior written approval of the other Party of the form and content thereof, which approval shall not be unreasonably withheld or delayed.

10. Notice

- 10.1 Any notice or communication which a Party is required or authorised by this Memorandum to serve on the other Party, shall be sufficiently served if sent to the other Party at the address specified below:

- 10.1.1 by hand; or
10.1.2 by registered post or recorded delivery; or
10.1.3 by electronic mail confirmed by receipt of such communication.

(i) to MU

Address : MAHSA University,
Jalan SP2, Bandar Saujana Putra,
Jenjarum, 42610 Selangor, Malaysia

Contact : Prof. Zahrah Binti Saad
Person

Email : zahrah@mahsa.edu.my

Attention : Director, International Relations

(ii) to IIKBWK

Address : Jl. KH Wachid Hasyim No.65, Bandar Lor,
Kec. Mojoroto, Kota Kediri, Indonesia

Contact : Prof. Dr. apt. Muhamad Zainuddin
Person

Email : pkhm@iik.ac.id

Attention : Rector

- 10.2 Notices sent by registered post or recorded delivery shall be deemed to have been served three (3) days following the date of posting if local address and seven (10) days following the date of posting if oversea address. Notices sent by electronic mail where such is an established means of communication between the Parties shall be deemed to have been served on the day of transmission, if transmitted before 16:00 hours (in the receiving parties' transmission) on a working day but otherwise on the next working day. In all other cases, notices and other communications will be deemed to have been served on the day they were received which is deemed to be on the same day that it was sent out and / or instantaneously.

11. Entire Agreement and Non-Waiver

- 11.1 This Memorandum supersedes and invalidates all other commitments, representations and warranties relating to the subject matter hereof which may have been made by the Parties either orally or in writing prior to the date hereof, and which shall become null and void from the date this Memorandum is signed. Each Party warrants and represents to the other that it has not relied on any such commitment, representation, or warranty in entering into this Memorandum. Nothing in this clause shall limit or exclude any liability for fraud. Any amendment to this Memorandum (to be effective), must be in writing and signed by an authorised representative of each Party.
- 11.2 The failure of a Party to insist in any one or more instances upon the performance of any provisions of this Memorandum shall not be construed as a waiver or relinquishment of that Party's right to future performance of such provisions and the other Party's obligation in respect of such future performance shall continue in full force and effect.

12. Costs

Each Party shall be responsible for its own costs in connection with the negotiation and preparation of this Memorandum. The stamp duty levied by the relevant authority in connection with the stamping of this Memorandum shall be borne by MU.

13. Governing Law

- 13.1 The interpretation, construction and performance of this Memorandum, and any non-contractual obligations arising under it, shall be governed exclusively by Malaysian and Indonesian laws and the Parties expressly submit to the exclusive jurisdiction of the Asian International Arbitration Centre (AIAC).
- 13.2 Any reference to a statutory provision shall include that provision as from time to time modified or re-enacted whether before or after the date of this Memorandum so far as such modification or re-enactment applies or is capable of applying to any transactions entered into prior to this Memorandum and (so far as any liability thereunder may exist or can arise) shall include also any past statutory provision (as from time to time modified or re-enacted) which such provision has directly or indirectly replaced.

14. Liability and Indemnity

- 14.1 Parties shall accept liability to pay damages for actual losses and liabilities including costs arising as a direct result of breach of confidentiality (as per Clause 3 herein), infringements of Parties' intellectual property rights (as per Clause 6 herein) and any conduct in violation of the Personal Data Protection Act 2010 (as per Clause 4 herein).
- 14.2 This provision shall survive and continue for so long as it is necessary to give its full effect, notwithstanding any other provision in this Memorandum.

15. Others

- 15.1 The undersigned represent and warrant that they are authorised to and have full power to execute, be bound by, deliver and perform the terms and conditions of this Memorandum.
- 15.2 The parties agree that this Memorandum can be executed by electronic methods (whether by PDF scan, utilisation of an electronic signature platform or application) without the need for an exchange of physical hard copies and shall have the same effect, validity, enforceability, and admissibility as a physical signature to the fullest extent permitted by applicable laws. However, should there be a need to abide by the instructions of the Collector of the Inland Revenue Board of Malaysia upon submission of this Memorandum for stamping, Parties shall re-execute this Memorandum for the purpose of adhering to the Stamp Act 1949.

IN WITNESS WHEREOF the parties hereto have hereunto set their hands the day and year first abovewritten.

Seal affixed and / or
signed by for and on behalf of
**MAHSA UNIVERSITY,
MALAYSIA
(DU044(B)),**
in the presence of

Professor Zahrah Saad
Director
International Relations
MAHSA University
Level 10, Unity Building,
Jalan SP2, Bandar Saujana Putra,
42610 Jenjarom, Kuala Langat, Selangor.

Name: Prof. Zahrah Binti Saad
Designation: Director, International Relations

Prof. Dato' Dr. Ikram S. Ismail FASc
Vice Chancellor
Chancellery
MAHSA University
Level 10, Unity Building,
Jalan SP 2, Bandar Saujana Putra,
42610 Jenjarom, Kuala Langat, Selangor.

Name: Professor Dato' Dr. Ikram Shah bin Ismail
Designation: Vice Chancellor

Seal affixed and / or
signed by for and on behalf of
**INSTITUT ILMU KESEHATAN
BHAKTI WIYATA KEDIRI,
INDONESIA
(20541673)**
in the presence of,



Name: Prof. Dr. apt. Muhamad Zainuddin
Designation: Rector

Name:
Designation:

RESEARCH REPORTS
INTERNATIONAL RESEARCH COLLABORATION



BHAKTA
Institut Ilmu Kesehatan



**FORMULATION AND EVALUATION OF ANTIBACTERIAL
ACTIVITY OF EMULGEL PREPARATION CONTAINING
MUNTINGIA CALABURA L. LEAVES EXTRACT**

**Lia Agustina
Munifatul Lailiyah
Ninis Yuliati
Erfan Tri Prasongko
David Raditya Soehartono
Nurul Istiqomah
M Dayoob**

International Research Collaboration

**LEMBAGA PENELITIAN DAN PENGABDIAN MASYARAKAT
INSTITUT ILMU KESEHATAN BHAKTI WIYATA KEDIRI**

2025

APPROVAL SHEET

1. Research Title : Formulation And Evaluation Of Antibacterial Activity Of Emulgel Preparation Containing Muntingia Calabura L. Leaves Extract
2. Principal Investigator
 - a. Full Name : Lia Agustina
 - b. Sex : F
 - c. ID (NIDN) : 0415088602
 - d. Position : Head researcher
 - e. Faculty/Departmen: Institut Ilmu Kesehatan Bhakti Wiyata Kediri, Indonesia
 - f. Phone/Facs : -
 - g. Phone/Facs/E-mail : lia.agustina@iik.ac.id
3. Budget In Kind/Cash

Years	Institutional Funds (Institut Ilmu Kesehatan Bhakti Wiyata Kediri)	External Funds (MAHSA University and University of Miyazaki)
Years 1	IDR 40.000.000,00	IDR 60.000.000,00

Approved by,

Academic Director

Institut Ilmu kesehatan Bhakti Wiyata

Principal Investigator

MAHSA University



Ninis Yulianti, S.Si., M.Kes
NIK. 1996.0064

Prof. Dato' Dr. Ikram S. Ismail FASc
Vice Chancellor
Chancellery
MAHSA University
Level 10, Unity Building,
Jalan SP 2, Bandar Saujana Putra,
42610 Jenjarom, Kuala Langat, Selangor.

THE STATEMENT OF WILLINGNESS TO COLLABORATE IN INTERNATIONAL RESEARCH

The undersigned below,

Name : Lia Agustina

Position : Head researcher

Affiliation : Institut Ilmu Kesehatan Bhakti Wiyata Kediri, Indonesia

hereby declares that I am/we are willing to cooperate in International Collaborative Research with the title: **Formulation And Evaluation Of Antibacterial Activity Of Emulgel Preparation Containing Muntingia Calabura L. Leaves Extract**

The Principal Investigator of this International Collaborative Research is as stated below:

Name : M Dayoob

Study Program / Department : MAHSA University

INSTITUT ILMU KESEHATAN BHAKTI WIYATA

Thus, this Statement Letter is made with full awareness and responsibility without any element of coercion in its making so that it can be used properly.

Academic Director

Institut Ilmu kesehatan Bhakti
Wiyata



Ninis Yuliati, S.Si., M.Kes
NIK. 1996.0064

RESEARCH ACKNOWLEDGMENT

First and foremost, I would like to express my deepest gratitude to God Almighty for providing me with the strength, health, and patience to complete this research project.

I would like to extend my heartfelt appreciation to MAHSA University, UAE for their generous financial support, which made this research possible. The grant provided by the International research fund from the MAHSA University, UAE was instrumental in advancing our study on **Formulation And Evaluation Of Antibacterial Activity Of Emulgel Preparation Containing Muntingia Calabura L. Leaves Extract**

My sincere thanks also go to the esteemed institutions that have supported and collaborated in this research:

1. Institut Ilmu Kesehatan Bhakti Wiyata Kediri
2. MAHSA University

The collaborative efforts and resources provided by these institutions were crucial in the successful execution of this study. I am grateful for the guidance, facilities, and support extended by the faculty members and staff at each institution.

I would also like to acknowledge the invaluable assistance and encouragement from my supervisors, colleagues, and all the researchers involved in this project. Their expertise and insights were vital in navigating the complexities of the research.

Finally, I am indebted to my family and friends for their unwavering support and understanding throughout the duration of this research. Their love and encouragement have been a constant source of motivation.

Thank you.

ABSTRACT

Background and aims: Acne develops due to the obstruction of pilosebaceous follicles by accumulated sebum, keratinocytes, and microbial colonization. Certain secondary metabolites from plants possess anti-acne properties, including karsen (*Muntingia calabura* L.). This study aims to formulate and evaluate the anti-acne activity of an emulgel against *Propionibacterium acnes*. The ethanolic extract from *Muntingia calabura* L. leaves was used in the formulation. **Methods:** The extraction process was carried out using maceration. The ethanolic extract of karsen was utilized as the active ingredient in the emulgel formulation. The emulgel was evaluated based on its organoleptic properties, homogeneity, pH, emulsion type, spreadability, and adhesion. The antibacterial activity was assessed through an in vitro antibacterial assay.

Results: The extraction yield was 10.8%. The extract contained flavonoids, tannins, and saponins. The formulated emulgel had a semi-solid consistency, a brownish-green color, a distinct odor characteristic of *Muntingia calabura* L. leaves, and was homogeneous. It had a pH range of 4.87–5.40, an oil-in-water (O/W) emulsion type, a spreadability of 5.1–5.8 cm, and an adhesion time of 3.26–4.36 seconds. The formulation exhibited anti-acne activity against *Propionibacterium acnes*, with the highest inhibitory activity observed at a concentration of 12%. **Conclusion:** The ethanolic extract from *M. calabura* L. leaves can be successfully formulated into a stable emulgel. The formulated emulgel exhibits antibacterial activity against *Propionibacterium acnes*.

Keywords: Antiacne, antibacterial activity, emulgel, karsen.

LIST OF CONTENTS

RESEARCH REPORTS	i
ABSTRACT.....	4
LIST OF CONTENTS	5
CHAPTER 1 INTRODUCTION.....	6
CHAPTER 2: RESEARCH METHODS.....	6
CHAPTER 3: RESULTS AND DISCUSSION.....	19
CHAPTER 4: NEXT STAGE PLAN.....	33
CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS	34
REFERENCES	35

CHAPTER 1 INTRODUCTION

Skin is the largest organ composing the human body, located on the outermost layer and covering the entire body surface. Its outermost position causes the skin to be the first to receive stimuli such as touch, pain, and harmful external influences. These factors make the skin vulnerable to diseases. One of the skin diseases most commonly suffered by the public is acne (Kumesan et al., 2013).

Acne is a disease of the skin surface on the face, neck, chest, and back that appears when the oil glands in the skin become overly active, causing the skin pores to become clogged with excessive fat deposits. If these deposits mix with sweat, dust, and other dirt, they will form fatty deposits with black spots on top called comedones. If bacterial infection occurs in these comedones, inflammation develops, which is known as acne. Acne varies in size from small to large, is reddish in color, sometimes contains pus, and causes pain (Djajadisastra et al., 2009).

One of the bacteria that causes acne is *Propionibacterium acnes*. *P. acnes* is a gram-positive rod-shaped bacterium that plays a role in acne formation and is part of the normal flora of human skin. This bacterium contributes to the pathogenesis of acne by producing lipase that can break down free fatty acids from skin lipids. These fatty acids can cause tissue inflammation and contribute to acne formation (Sari et al., 2015).

Acne treatment is usually carried out using antibiotics and chemical substances such as sulfur, resorcinol, salicylic acid, benzoyl peroxide, azelaic acid, tetracycline, erythromycin, and clindamycin. However, these medications also have side effects such as antibiotic resistance and skin irritation. Therefore, it is necessary to search for antibacterial drugs derived from natural ingredients, which are known to be safer compared to chemical-based medicines (Kumesan et al., 2013). The demand for

traditional acne medicine is currently very popular among the public. One plant known to have antibacterial activity is the kersen leaf. Besides having antibacterial properties, kersen leaves also function as anti-inflammatory, antipyretic, and antioxidant agents because they contain flavonoids, steroids, alkaloids, tannins, glycerol, and saponins (Buhian et al., 2016). However, the antibacterial activity of kersen leaves is caused by the presence of tannins, flavonoids, and saponins (Zakaria et al., 2006).

According to research conducted by Charina et al., 2016, the 96% ethanol extract of kersen leaves has antibacterial activity. The antibacterial activity test results at a concentration of 0.5% showed inhibition zone diameters of 6.45 mm against *Escherichia coli* bacteria and 6.44 mm against *Staphylococcus aureus* bacteria. Kersen leaf ethanol extract also has antibacterial activity against *P. aeruginosa* with an inhibition zone of 20 mm, *S. typhimurium* 19 mm, and *B. subtilis* 17 mm (Buhian et al., 2016).

To facilitate its use as an anti-acne medication, kersen leaves are made into an extract and then formulated into an emulgel preparation. Emulgel is a dosage form of emulsion, either water in oil (w/o) or oil in water (o/w), prepared in gel form by adding a gelling agent. The advantage of the emulgel form is that the emulsion content can provide high penetration ability (Singla, 2012). Other advantages of emulgel preparations for topical use are that they are more stable, easy to spread, and not too oily (Haneefa et al., 2013).

An emulgel preparation consists of an emulsion and a gel. The emulsion system uses Tween 80 and Span 80 as emulsifying agents because Tween 80 is a water-soluble emulsifying agent capable of forming oil-in-water (M/A) emulsions. Span 80 is a nonionic emulsifying agent in which the lipophilic group is more dominant. Water-soluble emulsifying agents mixed with fat-soluble emulsifying agents are able to form and maintain emulsions more effectively compared to the use of a single emulsifying agent

(Kim, 2005). Tween 80 and Span 80 are nonionic emulsifiers that tend to have balanced hydrophilic and lipophilic properties (Syamsuni, 2007), while the gel system uses Carbopol 940 as the gelling agent. Carbopol 940 is a hydrophilic gel base that has greater stability, high viscosity of 40,000–60,000 Mpas, is non-irritating, and non-toxic, making it suitable as a gel base (Rowe et al., 2009).

Based on the background above, research will be conducted regarding “Formulation of Anti-Acne Emulgel from Ethanol Extract of Kersen Leaves (*Muntingia calabura* L.) and In Vitro Antibacterial Activity Test Against *Propionibacterium acnes* Bacteria.”

CHAPTER 2: RESEARCH METHODS

A. Research Design

The research design method used in this study is true experimental research. True experimental research is a study conducted by carrying out experimental activities aimed at determining the symptoms or effects that arise as a result of certain treatments or experiments (Notoatmodjo, 2010).

B. Research Location and Time

1. Research Location

This research was conducted in 4 laboratories: extract testing in the Traditional Medicine Laboratory, emulgel preparation in the Semi-Solid Laboratory, antibacterial testing in the Bacteriology Laboratory, and the Sterile Laboratory of IIK Bhakti Wiyata Kediri.

2. Research Time

The study was conducted from March to June 2025

C. Population, Sample, and Sampling Technique

1. Research Population

Population is the entire research object that has certain qualities and characteristics determined by the researcher to be studied and then conclusions are drawn (Notoatmodjo, 2012). The population in this study was anti-acne emulgel of ethanol extract of kersen leaves (*Muntingia calabura* L.).

2. Research Sample

A sample is part of the population taken in a certain way in which measurements are carried out (Notoatmodjo, 2012). The samples in this study were anti-acne emulgel of ethanol extract of kersen leaves (*Muntingia calabura* L.) with concentrations of 4%, 8%, and 12%.

3. Sampling Technique

The sampling technique used in this study was simple random sampling. The selection of this sampling technique was based on the principle that each member or unit of the population had the same opportunity to be selected as a sample (Notoatmodjo, 2012).

D. Research Variables

1. Independent Variable

The independent variable is a variable that influences or causes the emergence of the dependent variable. The independent variable in this study was the formulation of anti-acne emulgel preparations of ethanol extract of kersen leaves (*Muntingia calabura* L.) with various concentration variations, namely 4%, 8%, and 12%.

2. Dependent Variable

The dependent variable is a variable that is influenced or becomes the result of the existence of the independent variable. The dependent variables in this study were the inhibitory activity against bacteria in the anti-acne emulgel preparation of ethanol extract of kersen leaves, observation of the quality stability of the anti-acne emulgel preparation of ethanol extract of kersen leaves including organoleptic properties, homogeneity, pH, and emulsion type, as well as acceptability (spreadability and adhesiveness).

3. Controlled Variables

Conditions during the study, namely place, time, observation, room temperature, air humidity, and sterility.

F. Research Instruments

1. Research Equipment

The equipment used in this study included Erlenmeyer flask equipment (Pyrex), stirring rods, beakers (Pyrex), test tubes (Pyrex), measuring cylinders (Pyrex), droppers, test tube racks, analytical balance, incubator, autoclave, rotary evaporator, oven, forceps, caliper, magnetic stirrer, aluminum foil, petri dishes, inoculating loop, filter paper, knife, mortar and pestle, dish, stirring rod, fluorescent lamp, and pH meter.

2. Research Materials

The materials used in this study included kersen leaves, 96% ethanol, concentrated HCl, Mg powder, HCl solution, 1% FeCl₃, carbopol 940, triethanolamine (TEA), propylene glycol, tween 80, span 80, liquid paraffin, distilled water, *Propionibacterium acnes* bacteria, MHA medium (Mueller Hinton Agar), NB medium (Nutrient Broth), and Medi-Klin® gel (positive control).

G. Data Collection Procedures

1. Plant Determination

Cherry leaves (*Muntingia calabura* L.) that had been obtained were first determined. The purpose was to verify the correctness of the plant as the research object. Determination was carried out at UPT Materia Medica Batu.

2. Material Collection

Cherry leaves were obtained from UPT Materia Medica Batu.

3. Preparation of Cherry Leaf Simplisia

The preparation of cherry leaf simplisia was carried out at UPT Materia Medica Batu.

4. Preparation of Ethanol Extract of Cherry Leaves

The preparation of ethanol extract of cherry leaves was carried out at UPT Materia Medica Batu, by:

- a. Weighing 3 kg of cherry leaf powder.
- b. Wetting the powder with 2 L of 96% ethanol solvent.
- c. The powder that had been moistened with the solvent was placed into a jar, leveled, and additional 96% ethanol solvent was added until submerged (the solvent used was at least twice the weight or more). The added solvent amounted to 8 L. The jar was tightly closed for 24 hours and shaken on a digital shaker at a speed of 50 rpm.
- d. The extract was filtered using a cloth filter. The extract was collected in an Erlenmeyer flask.

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- e. The residue was placed back into the jar and solvent was added until submerged (at least 5 cm above the surface), in this case using 10 L.
 - f. Left overnight or for 24 hours on a shaker at 50 rpm.
 - g. Remaceration was carried out until the filtrate/extract became clearer, using 10 L of solvent.
 - h. All liquid extracts from the first to the last extraction were combined and evaporated using a large rotary evaporator. The evaporation process required 4 hours and 30 minutes.
 - i. The resulting extract was evaporated/heated on a water bath for 2 hours.

5. Ethanol-Free Test

The ethanol-free test of cherry leaf extract was carried out by ethanol esterification. The extract was added with acetic acid and concentrated sulfuric acid, then heated. The extract was declared ethanol-free if no ester odor was detected (Setyani et al., 2016).

6. Phytochemical Screening

a. Flavonoid Identification

A total of 1 ml of test extract solution was mixed with 3 ml of 70% ethanol, shaken, heated, and shaken again, then filtered. The obtained filtrate was then added with 0.1 g Mg powder and 5 drops of concentrated HCl. The formation of yellow, orange, or red color in the solution indicated a positive result for flavonoids (Setyowati, 2014).

b. Tannin Identification

A total of 1 ml of test extract solution was reacted with 1% FeCl₃ solution. The formation of dark blue or blackish-green color indicated a positive result for tannin compounds (Setyowati, 2014).

c. Saponin Identification

A total of 1 ml of test extract solution was placed into a test tube, then 10 ml of hot distilled water was added, cooled, and shaken vigorously for 10 seconds. A positive result was indicated by the formation of foam lasting no less than 10 minutes, with a height of 1 cm to 10 cm, and after the addition of 1 drop of 2N hydrochloric acid the foam did not disappear (Setyowati, 2014).

7. Thin Layer Chromatography Test

Testing using TLC employed GF 254 silica gel activated by heating in an oven at 100°C for 1 hour. The ethanol extract of cherry leaves was spotted onto the TLC plate. The mobile phase used was n-butanol: glacial acetic acid: water (4:1:5), which had been saturated using filter paper. The silica gel was placed into a chamber containing the mobile phase. The mobile phase was allowed to rise to the upper limit of the silica gel. The silica gel was dried, then observed under visible light (visual), UV light at 254 nm and 366 nm. The TLC plate was exposed to ammonia vapor, then observed again under visible light (visual), UV light at 254 nm and 366 nm, and then the R_f value was calculated. The comparator used was rutin.

8. Preparation of Anti-Acne Emulgel Formulation of Cherry Leaf Ethanol Extract with Various Concentrations and Negative Control

a. Preparing tools and materials.

b. Preparing the water phase by:

- 1) Weighing 0.45 g of tween 80 and placing it into a beaker glass.
- 2) Weighing cherry leaf ethanol extract (formulation I 4%, II 8%, and III 12%), placing it into a beaker glass and adding 10 ml of distilled water, stirring until dissolved, then adding it into the beaker glass containing tween 80 and stirring on a magnetic stirrer at 70°C until homogeneous.

c. Preparing the oil phase by:

- 1) Weighing 1.5 g of liquid paraffin and placing it into a beaker glass.
- 2) Weighing 0.3 g of span 80, placing it into a beaker glass on a magnetic stirrer at 70°C, stirring until homogeneous.

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- d. Mixing the oil phase into the water phase on a magnetic stirrer at 70°C and stirring until an emulsion formed.
 - e. Taking distilled water measuring 4.5 ml and placing it into a mortar.
 - f. Weighing 0.45 g of carbopol 940, sprinkling it into the mortar containing distilled water and waiting until it expanded.
 - g. Weighing 0.3 g of triethanolamine (TEA), placing it into the mortar and grinding until homogeneous.
 - h. Weighing 4.5 g of propylene glycol, placing it into the mortar and grinding until homogeneous.
 - i. Adding the emulsion into the mortar containing the gel and grinding until homogeneous.
 - j. Adding the remaining distilled water up to 30 g, stirring until homogeneous and an emulgel preparation was formed.
 - k. Placing the emulgel preparation into a container.

9. Testing of Anti-Acne Emulgel Preparation of Cherry Leaf Ethanol Extract

a. Stability testing, including:

1) Organoleptic Examination

Organoleptic analysis of emulgel included (Kumesan, 2014):

- a) Form
- b) Color
- c) Odor

2) Homogeneity Test

Homogeneity analysis of emulgel was conducted by (Sativa, 2014):

- a) Applying the emulgel onto a glass plate or another suitable transparent material.

b) Observing the results; the preparation must show a homogeneous composition and no visible coarse particles.

3) pH Test

The pH test was carried out by (Sativa, 2014):

- a) Measuring pH using a pH meter.
- b) The instrument was calibrated using a standard buffer solution.
- c) The pH meter was washed with distilled water and dried with tissue paper.
- d) The pH meter was inserted into the emulgel preparation until the instrument showed a constant pH value.

4) Emulsion Type

The emulsion type test was conducted using electrical conductivity by (Syamsuni, 2007):

- a. Preparing cable wires, electrical plugs, and neon lamps.
- b. Inserting the cable wire into the emulsion preparation and plugging in the electrical socket.
- c. Observing the resulting neon lamp illumination.

b. Acceptability testing, including:

1) Spreadability Test

Spreadability testing was carried out by (Fujiastuti and Nining, 2015):

- a) Weighing 0.5 g of emulgel preparation and placing it in the center of a graduated circular glass plate.
- b) Covering the glass with another glass plate of known weight and allowing it to stand for 1 minute, then measuring the diameter.
- c) Adding a 50 g load on top of the glass and allowing it to stand for 1 minute, then measuring the spread diameter.

d) Adding further loads continuously after 1 minute with weights of 100 g, 150 g, 200 g, or until constant weight was achieved.

2) Adhesion Test

The adhesion test was conducted by (Murtiningsih, 2014):

- a) Weighing 0.25 g of emulgel preparation and placing it between 2 object glasses, then pressing with a 1 kg load for 5 minutes.
- b) The object glass was mounted on the test apparatus.
- c) An 80 g load was applied to the test apparatus.
- d) The release time of the emulgel was recorded.

c. Effectiveness Testing

1) Antibacterial Activity Test

Antibacterial activity testing was conducted using the disk diffusion method. The test material obtained was made into emulgel preparations with concentrations of cherry leaf ethanol extract formulation I 4%, formulation II 8%, and formulation III 12%. All tools and materials used were sterilized beforehand.

a) Sterilization of tools and materials

Glassware such as petri dishes, test tubes, tweezers, and Erlenmeyer flasks were first wrapped with aluminum foil and then sterilized in an oven at 100°C for 60 minutes. Materials such as MHA (Mueller Hilton Agar) and NB (Nutrient Broth) were sterilized in an autoclave at 121°C for 15 minutes.

b) Preparation of Mueller Hilton Agar media

The preparation of Mueller Hilton Agar media was carried out by weighing 10.2 g of MHA media, dissolving it in 300 ml of distilled water (34 g/1000 ml) using an Erlenmeyer flask. Shake until homogeneous and heat over a Bunsen burner until dissolved. The media was sterilized in an autoclave at 121°C for 15 minutes, then left in the autoclave until the pressure dropped and poured aseptically into petri dishes and allowed to solidify. Store in a refrigerator until the temperature reached $\pm 45-50^{\circ}\text{C}$.

c) Preparation of Nutrient Broth liquid media

The media was prepared by weighing 400 mg of NB media dissolved in 50 ml of distilled water, then heated and sterilized using an autoclave, followed by inoculating 1–5 loopfuls of pure *P. acnes* culture into the liquid NB media and incubating for 24 hours.

2) Antibacterial Test

The antibacterial test was conducted using the disk diffusion method. Testing was performed by soaking disks into the emulgel preparations of formulation I, formulation II, formulation III, negative control (-), and Medi-Klin® gel preparation as positive control (+). The soaked disks were left for 15 minutes. The dried disks were then placed into plates containing MHA (Mueller Hilton Agar) media, previously inoculated with *P. acnes* bacteria. The next step was incubation at 37°C for 48 hours. The greatest antibacterial activity was indicated by the largest clear zone diameter formed from the concentration.

4) Observation and Measurement

Observations were carried out after 48 hours of incubation. The clear zone around the paper disk indicated sensitivity to the antibacterial substance used as the test material, expressed by the width of the inhibition zone diameter measured using a caliper.

H. Data Processing and Analysis

The data analysis used in the study of the effect of cherry leaf extract concentration on the stability quality of anti-acne emulgel and antibacterial activity included:

1. Descriptive Method

The descriptive method is a method used to explain or describe the characteristics of each research variable (Notoatmodjo, 2012). Data analysis was used for observations of organoleptic tests, homogeneity tests, and emulsion type tests of anti-acne emulgel preparations.

2. One Way ANOVA Method

The obtained data were processed using the One Way ANOVA method with a 95% confidence level, conducted for pH tests, spreadability tests, adhesion tests, and antibacterial tests of emulgel preparations to determine whether there were differences among the given treatments. The data to be analyzed had to be normally distributed and homogeneous. The results of One Way ANOVA analysis, if the sig value obtained was >0.05 , indicated no significant difference, whereas if the sig value obtained was <0.05 , it indicated a significant difference, therefore a follow-up test using the LSD (Least Significant Difference) test was conducted.

CHAPTER 3: RESULTS AND DISCUSSION

Kersen (*Muntingia calabura* L.) is a wild plant commonly found growing along roadsides and widely encountered in tropical regions. Kersen leaves have antibacterial properties because they contain compounds such as flavonoids, tannins, and saponins (Zakaria et al., 2006). The purpose of this study was to determine whether the anti-acne emulgel formulation of ethanol extract of kersen leaves has antibacterial activity against *Propionibacterium acnes* bacteria and to determine differences in the antibacterial activity of the anti-acne emulgel of ethanol extract of kersen leaves on the growth of *Propionibacterium acnes* bacteria at concentrations of 4%, 8%, and 12%. Acne is a skin disease caused by several factors, namely increased sebum production, bacterial growth, and inflammation (Fissy et al., 2014). Current acne treatments widely use antibiotics. The use of antibiotics can cause resistance, therefore alternative acne treatments are needed, one of which is using kersen leaves. The kersen leaves used were first extracted and then formulated into an emulgel preparation using carbopol 940 gel base and tween 80 and span 80 emulsion bases.

The kersen leaves used in this study were first identified to ensure the identity of the leaves used. Identification was carried out at UPT Materia Medica Batu. The identification results showed that the leaves used were kersen leaves (*Muntingia calabura* L.). Extraction of kersen leaves used the maceration method. Extraction was carried out by soaking simplicia powder in

a solvent. The solvent penetrates the cell wall and enters the cell cavity containing active substances. The concentration difference between the active substance solution inside and outside the cell causes the concentrated solution to be pushed out. This process repeats until concentration equilibrium occurs between the solution outside and inside the cell (Depkes RI, 1986). Stirring during the extraction process is necessary because it aims to achieve a faster equilibrium of extract concentration into the cell fluid. This extraction process used remaceration, aiming to extract remaining chemical compounds still contained in the simplicia. The advantages of the maceration extraction method are its easy procedure, simple equipment, relatively high yield, and avoidance of compound damage because no heating is involved (Nirwana et al., 2015).

The solvent used in the extraction process was 96% ethanol. A 96% ethanol solvent is able to dissolve polar compounds, including flavonoids. The advantages of 96% ethanol as a solvent include being non-toxic, neutral, having good absorption, requiring minimal heating during concentration, and dissolving only limited interfering substances. The use of 96% ethanol as a solvent produces extracts with higher total flavonoid content compared to 70% ethanol and water solvents (Nirwana et al., 2010). The extraction of 3000 grams of simplicia powder using 30 liters of 96% ethanol solvent produced 324 grams of thick extract with a yield of 10.8%.

The ethanol-free test was carried out to determine whether the extract used was free from solvent residue, so that ethanol would not affect the antibacterial activity test. The ethanol-free test was conducted using an

esterification reaction. Extracts still containing ethanol are characterized by the smell of ester. The esterification test results showed that the obtained extract did not contain ethanol, indicated by the absence of ester odor in the extract mixed with reagents (Setyani et al., 2016).

Phytochemical screening of the ethanol extract of kersen leaves was conducted to determine the compound contents through color tests for flavonoids and tannins, and foam tests for saponins. The phytochemical screening results of the ethanol extract of kersen leaves showed positive results for flavonoids, tannins, and saponins.

Flavonoid identification produced an orange-colored solution, indicating the positive presence of flavonoids in the ethanol extract of kersen leaves. Magnesium and hydrochloric acid in this test react to form bubbles which are H₂ gas, while Mg metal and concentrated HCl function to reduce the benzopyrone nucleus in the flavonoid structure, causing a color change to red or orange. If a plant extract contains flavonoid compounds, flavilium salts will form upon addition of Mg and HCl, producing a red or orange color (Setyowati et al., 2014).

Tannin identification produced positive results in the ethanol extract of the leaves with the formation of a greenish-black color in the solution. The addition of extract with 1% FeCl₃ in water causes a strong green, red, purple, or black color. The formation of a greenish-black color after addition of 1%

FeCl₃ occurs because tannins react with Fe³⁺ ions to form complex compounds (Setyowati et al., 2014).

Saponin identification in the ethanol extract of kersen leaves showed positive results evidenced by foam formation that persisted for no less than 10 minutes and did not disappear after addition of 2N HCl. The formation of foam in this test indicates the presence of glycosides that can form froth in water and hydrolyze into glucose and other compounds (Setyowati et al., 2014).

Testing using Thin Layer Chromatography (TLC) was carried out to confirm the results obtained from the phytochemical screening test. TLC is a method for separating compounds based on differences in distribution between two phases, namely the stationary phase and the mobile phase. The stationary phase used was a polar silica gel plate made from silica gel GF254 measuring 10 cm x 2 cm. The TLC silica gel GF254 plate was previously activated by oven heating at 100°C for 1 hour to remove moisture from the TLC plate (Sastrohamidjojo, 2007). The mobile phase used in this TLC was a mixture of n-butanol : glacial acetic acid : water (BAA) in a ratio of (4:1:5), which provided the best separation because the composition is highly polar and capable of separating polar flavonoid compounds. A good mobile phase is one that can separate many compounds, indicated by the appearance of spots. The spots formed should not tail and the distance between spots should be clear (Harborne, 1987). Ammonia vapor exposure on the TLC plate aimed to strengthen the resulting color intensity. The TLC test results of the ethanol extract of kersen leaves were consistent with previous studies, showing spots

visible under visible light as brownish-yellow, under UV 254 nm as black, and under UV 366 nm as blue ring curves (Manik et al., 2014). The comparison standard used was rutin and the resulting Rf value was 65.

The next stage was the preparation of emulgel formulations weighing 30 grams for each formulation. The reason for choosing emulgel dosage form was because emulgels have several advantages, including emulsion content with high penetration ability (Singla, 2012). Other advantages of topical emulgel preparations are greater stability, ease of spreading, and less oily texture (Haneefa et al., 2013). Materials used in emulsion preparation were tween 80 and span 80 because Tween 80 is a water-soluble emulsifying agent capable of forming O/W emulsions. Span 80 is a nonionic emulsifying agent with dominant lipophilic groups. Combining water-soluble and fat-soluble emulsifying agents can form and maintain emulsions more effectively compared to using a single emulsifying agent (Kim, 2005). Tween 80 and span 80 are nonionic emulsifiers that tend to have balanced hydrophilic and lipophilic properties (Syamsuni, 2007). The gel base used carbopol 940 because it is a hydrophilic gel base with greater stability, non-irritating, and non-toxic properties, making it suitable as a gel base (Rowe et al., 2009). Addition of TEA in the formulation aimed to neutralize the acidic nature of carbopol 940 and improve its clarity. Propylene glycol was added as a solvent, gel stabilizer, and humectant or skin moisturizer in pharmaceutical and cosmetic preparations. Liquid paraffin was added as an emollient to help maintain skin softness and smoothness, while distilled water was used as a

solvent because it is neutral, does not affect other ingredients, is clear, odorless, tasteless, and colorless (Depkes RI, 1979).

The emulgel preparations made included negative control emulgel (without ethanol extract of kersen leaves), formulation I (4% concentration), formulation II (8% concentration), and formulation III (12% concentration). The purpose of making the negative control emulgel was as a comparison in antibacterial testing and to determine whether the emulgel base itself had antibacterial activity.

The prepared emulgels were then tested for stability, acceptability, and effectiveness. Stability testing included organoleptic examination, pH, homogeneity, and emulsion type. Acceptability testing included spreadability and adhesion tests. Effectiveness testing involved antibacterial testing against *Propionibacterium acnes* bacteria, followed by statistical data analysis using One Way ANOVA. Data analysis aimed to determine the effect of independent variables on dependent variables. Before conducting One Way ANOVA, normality and homogeneity tests were performed because these are absolute requirements for ANOVA analysis. If the significance value in normality and homogeneity tests was >0.05 , the analysis proceeded to One Way ANOVA. This test aimed to determine whether there were significant differences among the tested samples. If a significant difference was found with $\text{sig} < 0.05$, it was followed by LSD (Least Significant Difference) testing to determine differences between individual samples.

Organoleptic examination was conducted visually to observe physical appearance including form, color, and odor. Based on the results obtained, all emulgel formulations were semi-solid in form. Formulations I, II, and III were greenish-brown in color. The odor produced by all formulations was characteristic of kersen leaf extract. The color and odor of the emulgel preparations depended on the concentration of ethanol extract of kersen leaves used. The higher the concentration used, the stronger the characteristic odor and the darker the color (Yulianti, 2015).

Homogeneity testing is a parameter indicating the quality of the preparation because it affects the therapeutic effect of the preparation. The test was conducted to determine whether the preparation was homogeneous. Results showed that all tested preparations met emulgel homogeneity requirements, namely no coarse particles were visible on the object glass (Kumesan et al., 2013).

The pH test aimed to determine the safety of the emulgel preparation during use so that it would not irritate the skin. Results showed that the pH of the emulgel preparations fell within the skin pH range of 4.5–6.5 (Kumesan et al., 2013) and also matched the relatively acidic facial skin pH range of 4.0–5.5 (Priani, 2014). A pH value that is too low can cause skin irritation, while a pH that is too high can cause skin scaling (Murtiningsih, 2014).

Analysis of the pH test results showed that the Shapiro-Wilk normality test produced significance values of 0.637 for formulation I, 0.637

for formulation II, and 1.000 for formulation III, indicating normal distribution because $\text{sig} > 0.05$ for each formulation. The homogeneity test showed homogeneous distribution with a sig value of 0.203 (> 0.05). Since the pH test data were normally distributed and homogeneous, One Way ANOVA could be performed. The One Way ANOVA test produced a sig value of 0.047 (< 0.05), indicating significant differences in pH values among formulations. Therefore, LSD testing was conducted to determine differences between formulations. LSD results showed a significant difference (sig < 0.05) between formulation II and formulation III with a sig value of 0.019. LSD results also showed no significant differences (sig > 0.05) between formulation I and II with a sig value of 0.72, and between formulation I and III with a sig value of 0.359.

Emulsion type testing aimed to determine whether the emulgel preparation was O/W or W/O type. Based on conductivity testing using a neon lamp, the lamp lit up in all formulations, indicating that the emulgel preparations were O/W emulsions because they could conduct electricity (Syamsuni, 2007).

Spreadability testing aimed to determine the spreading ability of the emulgel preparation when applied to the skin. The larger the spreadability value, the wider the surface area that can be covered by the preparation. Good spreadability for semi-solid preparations ranges from 5–7 cm (Kumesan et al., 2013). The spreadability test results for all emulgel formulations met the requirements because they remained within the good spreadability range.

Analysis of spreadability test results showed that the Shapiro-Wilk normality test indicated normal distribution with sig values >0.05 , namely 1.000 for formulation I, 1.000 for formulation II, and 1.000 for formulation III. The homogeneity test showed homogeneous distribution with a sig value of 1.000 (>0.05). Since the data were normally distributed and homogeneous, One Way ANOVA could be conducted. The One Way ANOVA test produced a sig value of 0.000 (<0.05), indicating significant differences in spreadability values among formulations, so LSD testing was conducted. LSD results showed significant differences between formulation I and II with a sig value of 0.003 (<0.05), between formulation I and III with a sig value of 0.000 (<0.05), and between formulation II and III with a sig value of 0.010 (<0.05). Therefore, it can be concluded that there were significant differences among the three formulations.

The next test was adhesion testing, which aimed to determine the adhesion ability of the kersen leaf extract emulgel preparation on the skin. Adhesion ability is inversely proportional to spreadability; emulgel preparations with lower spreadability have higher adhesion. High adhesion affects drug absorption because longer skin contact allows maximum absorption, enabling the expected therapeutic effect to be achieved. Adhesion test results showed values greater than 1 second for all emulgel formulations, which met the requirement for semi-solid preparations according to previous studies (Ariesti et al., 2013).

Analysis of adhesion test results showed that the Shapiro-Wilk normality test produced sig values of 0.567 for formulation I, 0.843 for formulation II, and 1.000 for formulation III, indicating normal distribution because $\text{sig} > 0.05$ for each formulation. The homogeneity test showed homogeneous distribution with a sig value of 0.787 (> 0.05). Since the adhesion test data were normally distributed and homogeneous, One Way ANOVA could be performed. The One Way ANOVA test produced a sig value of 0.000 (< 0.05), indicating significant differences in adhesion values among formulations. Therefore, LSD testing was conducted. LSD results showed significant differences ($\text{sig} < 0.05$) among formulations, namely formulation I with II ($\text{sig} 0.000$), formulation I with III ($\text{sig} 0.000$), and formulation II with III ($\text{sig} 0.000$).

The next test was antibacterial activity testing of the ethanol extract emulgel of kersen leaves against *Propionibacterium acnes* bacteria. This test aimed to determine the inhibitory power of the emulgel preparation against *Propionibacterium acnes* bacteria. Antibacterial testing was conducted using the agar diffusion method to measure inhibition. Since emulgel is a semi-solid preparation, paper discs were used to facilitate the diffusion process (Arifin et al., 2015). The antibacterial test results of the emulgel preparations showed inhibitory activity in all preparations, indicated by the formation of clear zones around the discs. Negative and positive controls were used to compare inhibitory activity with emulgel formulations containing various concentrations of kersen leaf ethanol extract. The negative control did not show antibacterial activity because no clear zone formed around the disc. This

occurred because the negative control formulation contained no antibacterial substances and consisted only of the emulgel base, proving that the antibacterial activity originated from the kersen leaf extract without influence from the emulgel base.

The positive control used in the antibacterial test was Medi-Klin® gel, a commercially available preparation commonly used for topical acne treatment. Medi-Klin® gel was chosen because it contains clindamycin. Clindamycin is an antibiotic from the lincosamide group that works by inhibiting bacterial protein synthesis. Clindamycin inhibits the growth of *Propionibacterium acnes* on the skin surface and reduces free fatty acid concentration in sebum (Indriani, 2015).

According to the Clinical and Laboratory Standards Institute (CLSI), inhibition response classification for the disk diffusion method using clindamycin is resistant ≤ 14 mm, intermediate 15–16 mm, and sensitive ≥ 17 mm (CLSI, 2012). The antibacterial activity test results against *P. acnes* showed that formulation I (4% concentration) had resistant antibacterial inhibition with an average inhibition zone of 12.07 mm, formulation II (8% concentration) had intermediate inhibition with an average inhibition zone of 15.52 mm, and formulation III (12% concentration) had sensitive inhibition with an average inhibition zone of 18.57 mm. The antibacterial test results showed that higher concentrations of ethanol extract of kersen leaves produced larger inhibition zone diameters.

The observations showed that the ethanol extract of kersen leaves had activity in inhibiting the growth of acne-causing bacteria, namely *Propionibacterium acnes*. The antibacterial activity mechanism of the ethanol extract of kersen leaves can be explained based on bacterial cell wall structure, where the tested bacteria are gram-positive bacteria with relatively simple cell wall structures consisting only of peptidoglycan and teichoic acid components that are highly polar, making them easily penetrated by the also polar extract (Fissy et al., 2014).

The study results showed that kersen leaf extract contains flavonoids, tannins, and saponins that function as antibacterial agents. The antibacterial mechanism of flavonoids can be divided into three: inhibiting nucleic acid synthesis, inhibiting cell membrane function, and inhibiting energy metabolism. Flavonoids inhibit nucleic acid synthesis because rings A and B play important roles in intercalation or hydrogen bonding with nucleic acid bases, thereby inhibiting DNA and RNA formation. Hydroxyl groups at positions 2',4' or 2',6' on ring B and 5,7 on ring A are important for flavonoid antibacterial activity. This causes damage to bacterial cell wall and lysosome permeability. Second, flavonoids inhibit cell membrane function by forming complex compounds with extracellular proteins, damaging the cell membrane and causing leakage of intracellular compounds. Third, flavonoids inhibit energy metabolism by inhibiting bacterial oxygen utilization (Taufik et al., 2015).

The antibacterial mechanism of tannins works by shrinking the cell wall or membrane, thereby disrupting bacterial cell permeability. Disruption of bacterial cell permeability prevents the cell from carrying out life activities, thereby inhibiting growth or even causing death (Setyani et al., 2016).

The antibacterial mechanism of saponins works because saponins have soap-like properties and are strong surface-active compounds that reduce surface tension. Saponins absorbed on the cell surface cause membrane damage through increased membrane permeability or cell leakage, leading to cell death due to loss of essential cellular materials (Setyani et al., 2016).

Analysis of antibacterial testing results showed that the Shapiro-Wilk normality test indicated normal distribution with sig values >0.05 , namely 0.220 for positive control, 0.194 for formulation I, 0.554 for formulation II, and 0.637 for formulation III. The homogeneity test showed homogeneous distribution with a sig value of 0.095 (>0.05). Since the antibacterial test data were normally distributed and homogeneous, One Way ANOVA could be conducted. The One Way ANOVA test produced a sig value of 0.000 (<0.05), indicating significant differences in antibacterial activity among formulations. Therefore, LSD testing was conducted. LSD results showed significant differences (sig <0.05) among preparations, namely negative control with positive control (sig 0.000), negative control with formulation I (sig 0.000), negative control with formulation II (sig 0.000), negative control with formulation III (sig 0.000), positive control with formulation I (sig 0.000), positive control with formulation II (sig 0.000), positive control with formulation III (sig 0.000), formulation I with formulation II (sig 0.000),

formulation I with formulation III (sig 0.000), and formulation II with formulation III (sig 0.000).

CHAPTER 4: NEXT STAGE PLAN

The next research plan is to continue and develop this research to the stage of multivariate data analysis and carry it out in every elementary school at Kediri. Meanwhile, the output of this research will be published in an International Journal.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

Based on the research that has been conducted, it can be concluded that:

1. There is antibacterial activity in the anti-acne emulgel formulation of cherry leaf ethanol extract against the bacteria *Propionibacterium acnes*, indicated by the formation of a clear zone around the disk, which represents inhibitory activity against the bacteria.
2. There are differences in the antibacterial activity of the anti-acne emulgel of cherry leaf ethanol extract against the growth of *Propionibacterium acnes* bacteria, with average inhibition zones at a concentration of 4% measuring 12.07 mm, at 8% measuring 15.52 mm, and at 12% measuring 18.57 mm. The higher the concentration of cherry leaf ethanol extract used, the greater the inhibitory effect.

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**IMPLEMENTATION OF AGREEMENT
JOINT RESEARCH PROGRAM**



BETWEEN

Institut Ilmu Kesehatan Bhakti Wiyata Kediri

AND

MAHSA University

No. 2435769/IK/E.2342/V/2025

This Arrangement sets forth Joint Research Agreement is made on this day by and between (Lia Agustina., Institut Ilmu Kesehatan Bhakti Wiyata Kediri) and (M Dayoob, MAHSA University), hereinafter referred to singularly as “the Party” and collectively as “the Parties”.

WHEREAS, the Parties have decided to conduct a Joint Research Program on **Formulation And Evaluation Of Antibacterial Activity Of Emulgel Preparation Containing Muntingia Calabura L. Leaves Extract** NOW, therefore, in consideration of the mutual promises recited herein, the parties agree as follows:

I. Period of Services

(Lia Agustina) from Institut Ilmu Kesehatan Bhakti Wiyata Kediri and (M Dayoob) from MAHSA University agree to conduct a joint research program on **Formulation And Evaluation Of Antibacterial Activity Of Emulgel Preparation Containing Muntingia Calabura L. Leaves Extract** for the period of 2024/2025

II. Employee Status

During the term of this agreement, Lia Agustina will remain at all times an employee of Institut Ilmu Kesehatan Bhakti Wiyata. Institut Ilmu Kesehatan Bhakti Wiyata will be responsible for continuing and making all appropriate employee payrolls for Lia Agustina For no purpose will joint research program.

III. Funding

Each Party will each bear any costs, expenses, or other charges of whatever nature incurred by such Party and which are not expressly detailed in the approved Joint Research.

IV. JOINT INTELLECTUAL PROPERTY

- a) The protection of intellectual property rights shall be enforced in conformity with the respective national laws, rules and regulations of the Parties and with other international agreements signed by both Parties.
- b) The use of the name, logo and/or official emblem of any of the Parties on any publication, document and/or paper is prohibited without the prior written approval of either Party.
- c) The ownership of all intellectual property arising of the work or any project under this Agreement (hereinafter referred to as “Joint Intellectual Property”) shall be shared equally between both Parties.
- d) Either Party may, by giving a prior written notice to the other Party and upon certain payment, the amount of which to be agreed later by the Parties, to the other Party abandon its own share in the Joint Intellectual Property and transfer its share in the Joint Intellectual Property to the other Party.

V. PUBLICATIONS POLICY

Both Parties shall have the right to use and publish any information derived from the work or project under this Agreement provided that written consent is obtained from the other Party. In the event that any Parties, wishes to publish, disclose and/ or present (in any form of disclosure) the data and/ or outcome arising from this Agreement, the Party shall submit a draft of each such publication or presentation to the other Party and give the right to the other Party to have certain parts of the said publication. In any such publications, the contribution of both Parties shall be acknowledged.

VI. Duration of Agreement

This Agreement is valid for a year and becomes effective on the date that it is signed by the official representatives of both institutions. This Agreement may be terminated according to the same terms set forth in the Joint Research Agreement between Institut Ilmu Kesehatan Bhakti Wiyata Kediri and MAHSA University. If either institution intends to terminate or to modify this Agreement, a written notice should be given to the other institution 30 days prior to the desired effective date of termination.

VII. Force Majeure

If, as a result of an act of force majeure, including without limitation, an act of God, war, riot, labor dispute, strike or threat thereof, intervention of a government agency or instrumentality or other occurrence beyond the control of either party, either party is substantially hindered in performing its obligations hereunder then, in such event, that party shall have the right, upon notifying the other of the occurrence of force majeure as herein defined, to suspend performance of the cooperative activity pursuant to this Agreement and any contract based on this Agreement until the force majeure has passed

IN WITNESS WHEREOF, the parties hereto have executed this agreement as of the date fit written above.

Approved by,

Academic Director

Institut Ilmu kesehatan Bhakti
Wiyata



Ninis Yuliati, S.Si., M.Kes

NIK. 1996.0064

Principal Investigator

MAHSA University

Prof. Dato' Dr. Ikram S. Ismail FASc
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Chancellery
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Level 10, Unity Building,
Jalan SP 2, Bandar Saujana Putra,
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A handwritten signature in blue ink, corresponding to the name of the Vice Chancellor of MAHSA University.