BUKTI KORESPONDENSI

Lampiran	**:**	Peer review proses korespondensi submit Publikasi Jurnal Ilmiah Internasional Bereputasi
Nama Jurnal	**:**	International Journal of Applied Pharmaceutics Vol. 11 Special Issue 5 2019 Hal: 1-4
Index	**:**	Terindeks pada database internasional bereputasi dan berfaktor dampak (SCOPUS Q3)
Judul Jurnal	**:**	Antibacterial Activity of Ethanolic Extract Bawang Dayak (*Eleutherine bulbosa* (Mill.) Urb.) in Cream against *Propionibacterium acnes*

No	Item	Tanggal	Halaman
1	**Register/Submission pada konferensi internasional ICPPS 2019 (International Conference on Pharmacy and Pharmaceutical Science) di Tokyo, Jepang 28-30 Maret 2019**	09 November 2018	1
2	**Artikel accepted pada jurnal AJPCR (Asian Journal of Pharmaceutical and Clinical Research) (T0020)**	05 Desember 2018	2
3	**Notification dan Review artikel**	05 Desember 2018	3
4	**Review process, artikel accepted pada jurnal AJPCR namun jurnal tersebut masuk dalam kategori discontinued scopus sehingga panitia konferensi mengganti ke IJAP (International Journal of Applied Pharmaceutics) dengan indeks scopus Q3**	22 Juli 2019	8
5	**Article for final proof (IJAP)**	24 Juli 2019	15
6	**Article Published (IJAP)**	15 September 2019	20
7	**Ethical approval**	11 April 2018	28

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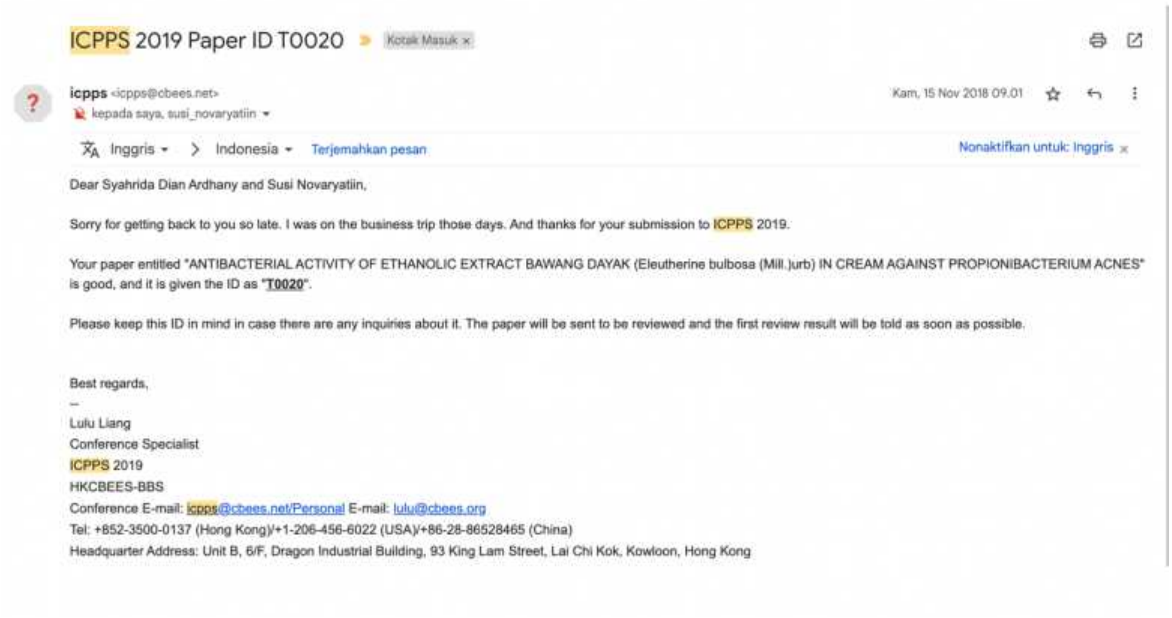

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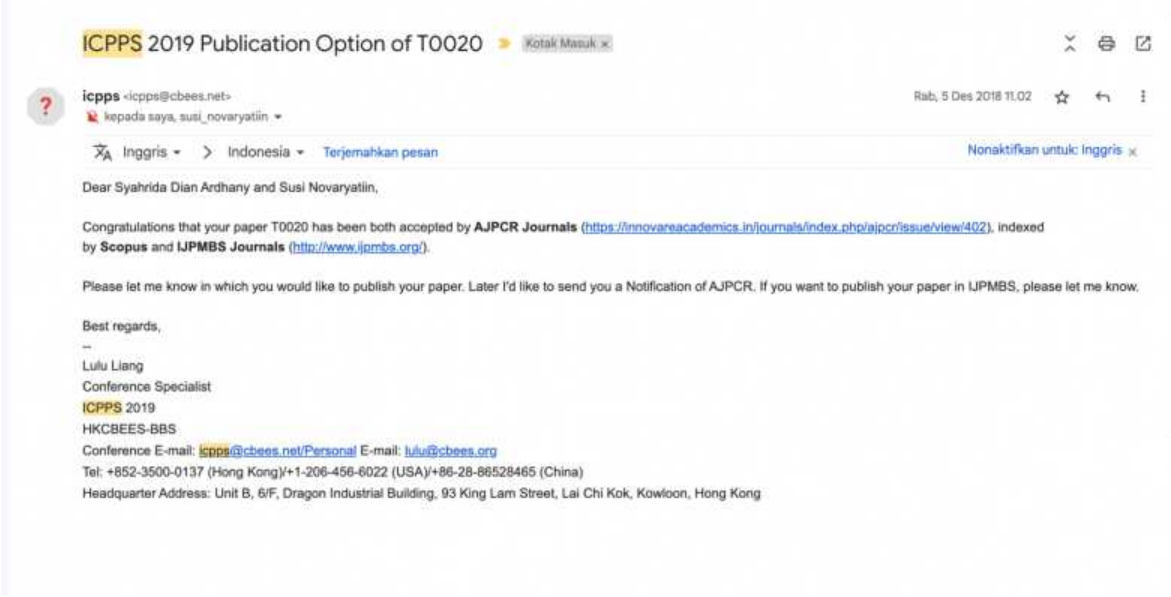

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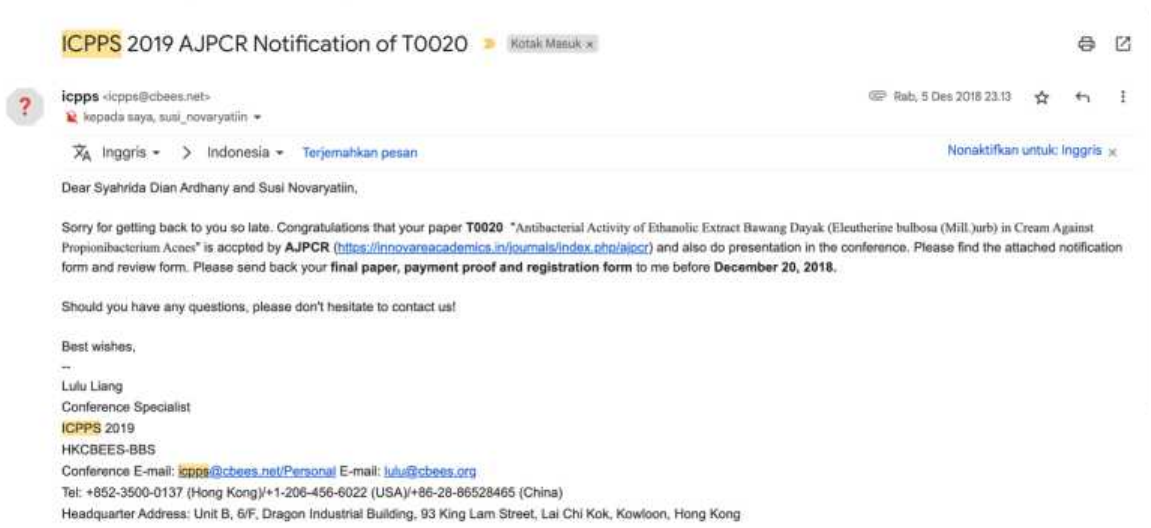

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Notification of Acceptance of the ICPPS 2019

Tokyo, Japan, March 28-30, 2019

http://www.icpps.org/

Paper ID : T0020

Paper Title : Antibacterial Activity of Ethanolic Extract Bawang Dayak (Eleutherine bulbosa (Mill.)urb) in Cream Against Propionibacterium Acnes

Dear Syahrida Dian Ardhany and Susi Novaryatiin,

First of all, thank you for your concern. 2019 4th International Conference on Pharmacy and Pharmaceutical Science (ICPPS 2019) review procedure has been finished. We are delighted to inform you that your manuscript has been accepted for presentation at 2019 4th International Conference on Pharmacy and Pharmaceutical Science (ICPPS 2019) in Meiji University, Tokyo, Japan during March 28-30, 2019.. Your paper was tripling blind-reviewed and based on the evaluation. The reviewers' comments are enclosed.

The conference received papers from about 11 different countries and regions during the submission period. And there are about 69 papers accepted by our reviewers who are the international experts from all over the world. The selected papers could be published in our conference proceedings with high quality. According to the recommendations from reviewers and technical program committees, we are glad to inform you that your paper identified above has been selected for publication and oral presentation. You are invited to present your paper and studies during our ICPPS conference that would be held on March 28-30, 2019, Meiji University, Tokyo, Japan.

The ICPPS 2019 is co-sponsored by Hong Kong Chemical, Biological & Environmental Engineering Society (HKCBEES) and Biology and Bioinformatics Society (BBS).

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Again, congratulations. We are looking forward to seeing you in Tokyo, Japan.

Yours sincerely,

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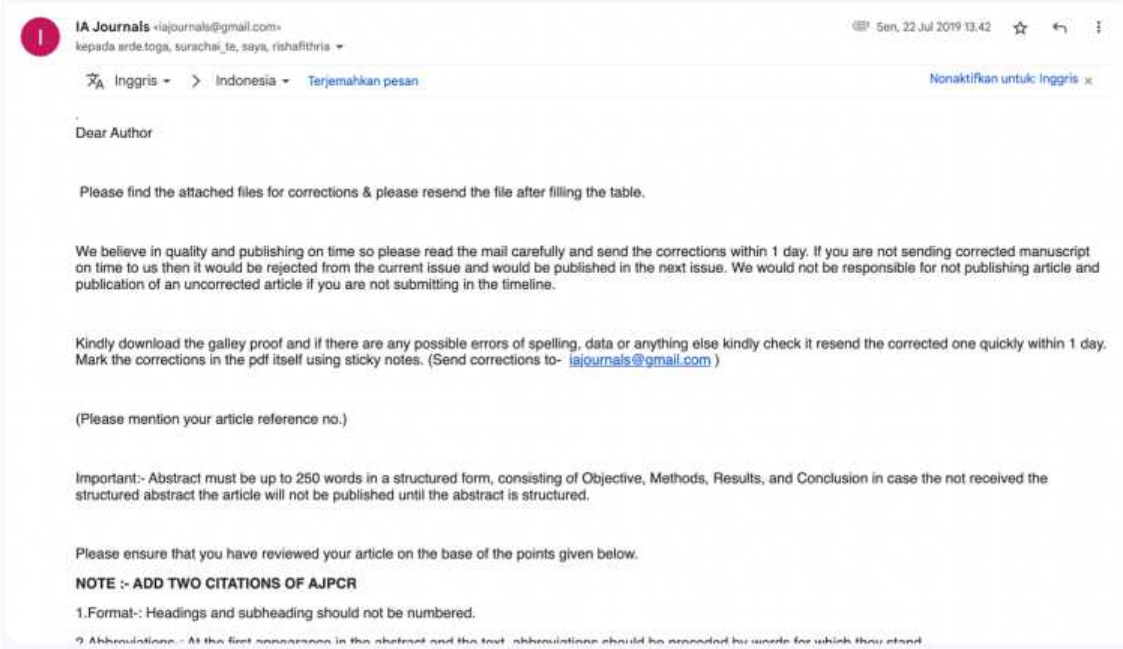

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International Journal of Applied Pharmaceutics

ISSN - 0975 - 7058 Vol 11, Special Issue 5, 2019

Research Article

ANTIBACTERIAL ACTIVITY OF ETHANOLIC EXTRACT BAWANG DAYAK (*ELEUTHERINE BULBOSA* (MILL.) URB) IN CREAM AGAINST *PROPIONIBACTERIUM ACNES*

SYAHRIDA DIAN ARDHANY*, SUSI NOVARYATIIN

Department of Pharmacy Faculty of Health Science, Muhammadiyah University of Palangkaraya, Central Kalimantan, Indonesia.
Email: chass501@gmail.com

Received: ???, Revised and Accepted: ???

ABSTRACT

Objective: The aims of this present study were to formulate antiacne cream consisting ethanolic extract of bawang dayak and evaluate antibacterial activity of cream on day 0 and day 7 to see stability activity and preparation.

Methods: Cream formula of bawang dayak was evaluated organoleptic characteristics, homogeneity, pH, adhesion test, dispersion test, and *in vitro* antibacterial against *Propionibacterium acnes*.

Results: The results of evaluate cream homogeneity were F3 and F4 on day 7 separate and non-homogen but all formula pH suitable for topical application. This antibacterial activity showed cream on day 0, F1 and F2 in category weak activity, F3 and F4 moderate activity, on day 7 zone of inhibition of all cream formula decrease but still can inhibit.

Conclusion: All cream formula potentials inhibit against *P. acnes* but this research must be improved both of preparation and stability activity.

Keywords: Acne vulgaris, Bawang dayak, Cream, *Eleutherine bulbosa*, *Propionibacterium acnes*.

 DOI: http://dx.doi.org/10.22159/ijap.2019.v11s5.T0020

INTRODUCTION

Acne vulgaris is one of the problems experienced by teenagers and adults because in this modern era, physical appearance is one of the most important things that must be considered. Acne is not a serious disease, but it can lead depression and loss of confidence. There are many causes of acne such as hormone level, fat or oil in skin, and a bacterium like *Propionibacterium acnes* [1].

Many cosmetic products that offer to improve acne problems, nature also provides a solution to these [2]. Bawang dayak is one of traditional medicines in Central Kalimantan. Based on research before, extract ethanol of bawang dayak can inhibit *P. acnes*, so in this research, ethanol extract was made in cream formulation to improve the efficiency of using traditional medicine.

METHODS

Collection of plant

Fresh plant materials, bulbs (20 kg) of bawang dayak (*Eleutherine bulbosa* (Mill.) Urb) were procured from farmer cultivation in Sei Gohong, Bukit Batu Palangka Raya Central Kalimantan.

Preparation of plant extracts

The plant materials were dried under the sun for 5–7 days. The dried plant materials were crushed by grinder. The powder of the plant materials was extracted with 96% ethanol using perkolator, and once process was finished, all extracts were concentrated in a rotary evaporator.

Formulation preparation

The formulation components used are listed in Table 1. The components consist of oil soluble (stearic acid, Adeps lanae, and paraffin liquid) and water soluble (TEA, nipagin, and aquadest). Each solution – oil soluble and water soluble – heated up to 55°C until melts. Ethanolic extract of bawang dayak dissolved in aquadest, then put into water phase and stir until homogen in mortar, oil phase add gradually, stir until the cream base is formed. The last add oleum roses stir ad homogen.

Evaluation of cream

Organoleptic properties

The cream was observed for color, odor, and appearance.

Homogeneity observed

The particles size was observed on the slide to find the coarse particles. Preparations should show a homogeneous composition and no visible coarse grains [3].

PH measurements

Determining pH of the preparation is done using pH meter [4].

Dispersion test

Cream with 0.5 g was placed in the middle of a round glass scale. Round glass which has been weighted placed thereon and left for 5 min. After that followed with 50 g load, let stand for 1 min and record the diameter of the spread cream, did the same thing with 100 g and 150 g [5].

Adhesion test

A total 0f 0.5 g of preparation were spread on the disc glass, on top of it, other glass object placed and pinned under 1 kg load for 1 min. Then, disc glass mounted on test equipment, load is released, and the time was recorded up to the second object of the glasses falling off [5].

Evaluation of antibacterial activity by zone of inhibition by well diffusion method

Ethanolic extract of bawang dayak was evaluated for *in vitro* antibacterial activity against acne vulgaris were caused by *P. acnes* using the disc diffusion method with different concentrations of extract in cream formula.

Table 1: Various cream formula of ethanolic extract bawang dayak

Materials	F1	F2	F3	F4
Extract ethanol of bawang dayak	5% (1250 mg)	10% (2500 mg)	15% (3750 mg)	20% (5000 mg)
Ol. Rosae	12 gtt	12 gtt	12 gtt	12 gtt
Oily phases (mg)				
Stearic acid	5000	5000	5000	5000
Adeps lanae	750	750	750	750
Paraffin liquid	6250	6250	6250	6250
Aqueous phase (mg)				
Triethanolamine	375	375	375	375
Nipagin	25	25	25	25
Aquadest ad	25,000	25,000	25,000	25,000

Table 2: Organoleptic appearance of various cream formula bawang dayak

Observation	Color	Odor	Appearance
Day 0			
F1	Brown (+)	Significant (+++)	Semi-solid
F2	Brown (++)	Significant (+++)	Semi-solid
F3	Brown (+++)	Significant (++++)	Semi-solid
F4	Brown (+++)	Significant (++++)	Semi-solid
Day 7			
F1	Brown (++)	Significant (+++)	Semi-solid
F2	Brown (+++)	Significant (+++)	Semi-solid
F3	Brown (++++)	Significant (++++)	Semi-solid
F4	Brown (++++)	Significant (++++)	Semi-solid

+: Weak, ++: Moderate, +++: Strong, ++++: Very strong

Table 3: Homogeneity test of various cream formula bawang dayak

Observation	Result
Day 0	
F1	Homogen
F2	Homogen
F3	Homogen
F4	Homogen
Day 7	
F1	Homogen
F2	Homogen
F3	Non-homogen
F4	Non-homogen

Table 4: Adhesion test of various cream formula bawang dayak

Observation	Adhesion (seconds)
Day 0	
F1	4.24
F2	4.67
F3	4.85
F4	4.55
Day 7	
F1	2.17
F2	2.76
F3	2.93
F4	2.43

The bacterial isolates were subcultured into a nutrient. The 24-hour-old bacterial culture was standardized using McFarland standard (10^6 CFU/mL of 0.5 McFarland standard). Mueller-Hinton agar (MHA) was used for bacteria bioassay. MHA was prepared by dissolving 38 g in 1000 ml of distilled water and brought to boil to completely dissolve. Sterilization was achieved by autoclaving at 121°C for 15 min [6].

MHA plates were prepared and bacterial strains were inoculated by cotton swab, and then, antibiotic and cream with various concentrations of extract bawang dayak applied in it. The plates were incubated at 37°C for 24 h, and the zone of inhibition was measured [7] and recorded later on.

Table 5: Dispersion test of various cream formula bawang dayak

Observation	First (cm)	50 g (cm)	100 g (cm)	150 g (cm)
Day 0				
F1	3.56	5.22	5.72	6.20
F2	3.03	3.49	3.78	4.07
F3	3.80	4.53	5.06	5.40
F4	3.36	4.05	4.49	4.93
Day 7				
F1	4.04	4.52	4.98	5.41
F2	3.43	4.20	4.43	4.93
F3	3.86	4.48	4.97	5.15
F4	3.27	3.51	4.04	4.38

Table 6: PH test of various cream formula bawang dayak

Observation	pH	Result (pH=4.5-6)
Day 0		
F1	6	Qualified
F2	6	Qualified
F3	6	Qualified
F4	6	Qualified
Day 7		
F1	5.7	Qualified
F2	6	Qualified
F3	6	Qualified
F4	6	Qualified

Table 7: Zone of inhibition of clindamycin

Concentration of clindamycin (%)	Zone of inhibition (mm)	Result
0.5	25.53	Strong activity
1	25.43	Strong activity
2	27.33	Strong activity
4	32.83	Strong activity

Table 8: Zone of inhibition of various cream formula bawang dayak

Various cream	Zone of inhibition (mm)	Result
Day 0		
F1	7.83	Weak activity
F2	9.53	Weak activity
F3	12.47	Moderate activity
F4	12.53	Moderate activity
Day 7		
F1	7.00	Weak activity
F2	8.20	Weak activity
F3	9.60	Weak activity
F4	9.83	Weak activity

RESULTS AND DISCUSSION

Evaluation test of cream formula

Organoleptic appearance

The results of organoleptic test on day 0 showed that F1 had a lighter brown color than other formulas, it caused the concentration of ethanolic extract bawang dayak less concentration than other formulas. On day 7, all formulations became darker than before, this was probably due to ethanolic extract of bawang dayak content antioxidant compound. The odor of F3 and F4 on day 0 has sharper odor than F1 and F2, it caused concentration of ethanolic extract, but the odor has no change on the day 7 (Table 2).

Homogeneity observation

The observation of cream bawang dayak showed on day 0 all formulation homogen, but day 7, F3 and F4 showed separation phase between the oil phase and the water phase (Table 3).

PH observation

The pH observation showed all cream formula of bawang dayak around 6 on day 0 and day 7 (Table 6). The pH that suitable for topical application is between 4.5 and 6 same with pH of skin [8].

Dispersion test

The dispersion test adding and without adding weight has an average of more than 3 cm to all creamy formula both on day 0 and day 7 (Table 5).

Adhesion test

Adhesion test of cream on day 0 was more than 4 s and time of adhesion decrease on day 7 (Table 4).

Antibacterial activity

The antibacterial activities can be classified into three levels: Weak activity (inhibition zone lower than 12 mm), moderate activity (inhibition zone between 12 and 20 mm), and strong activity (inhibition zone higher than 20 mm) [9]. The inhibitory test results on day 0 F1 have 7.83 mm inhibition zone (weak activity), F2=9.53 mm (weak activity), F3=12.47 mm (moderate activity), and F4=12.53 mm (moderate activity), while all formula which stand until 7 days have decrease zone of inhibition in category weak activity. Inhibition zone decrease on day 7 may be caused storage not in cool area like in refrigerator, so it was needed develop research further. This research showed that all formula with different concentration of ethanolic extract bawang dayak potential inhibit *P. acnes* that caused acne vulgaris although zone of inhibition smaller than clindamycin as positive control.

Inhibition of all formula against *P. acnes* because ethanolic extract of bawang dayak contains secondary metabolites such as alkaloid, flavonoid, tannin, and saponin that can be potential has antibacterial effect against *P. acnes* [10]. Research about bawang dayak with the same type of plant specifically *E. bulbosa* parallel with research that conducted in India that stated bawang dayak has significant antibacterial activity [11].

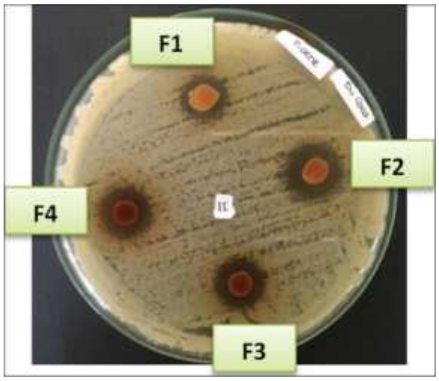

Fig. 1: Zone of inhibition all cream formula ethanolic extract of bawang dayak day 0

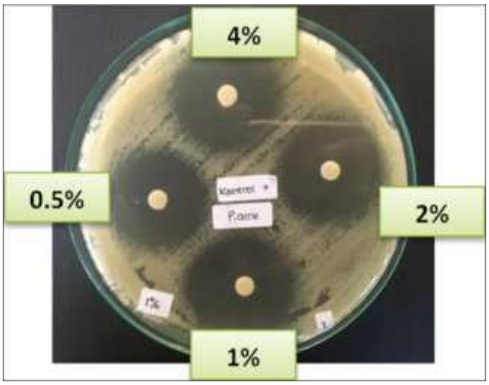

Fig. 3: Zone of inhibition clindamycin

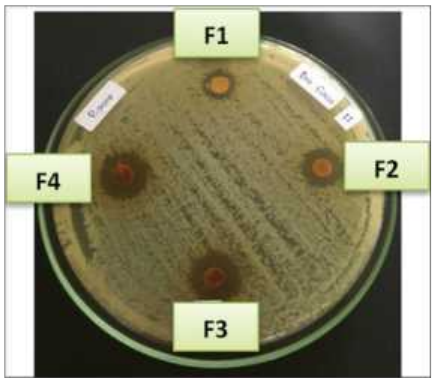

Fig. 2: Zone of inhibition all cream formula ethanolic extract of bawang dayak day 7

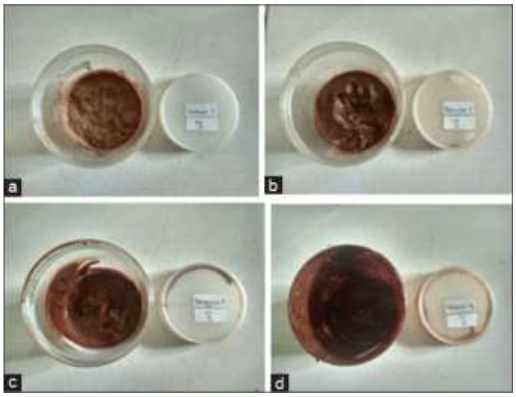

Fig. 4: Various cream formula ethanolic extract of bawang dayak; (a) F1, (b) F2, (c) F3, (d) F4

CONCLUSION

Extract ethanolic of bawang dayak in all cream formula potential inhibits *P. acnes,* but inhibitory ability decreases on day 7. This research must be developed such as cream formula and improve effectiveness and combination with another material, so as the formula not separate and the effectivity is stable.

ACKNOWLEDGMENT

The authors wish to thank the Program Bantuan Seminar Luar Negeri Ditjen Penguatan dan Pengembangan, Kemenristekdikti of Indonesia to facilitate to the 4th International Conference on Pharmacy and Pharmaceutical Science 2019 in Tokyo, Japan.

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Author Queries???
AQ1:Kindly provide history details
AQ2:Kindly review the sentence as it seems to be unclear.
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AQ4:Kindly cite figures 1-4 in the text part
AQ5:Kindly cite tables 7 and 8 in the text part and also chronological order

Vol 11 special issue 5
Article reference no: IJAP_T0020_RA
Title: Antibacterial Activity of Ethanolic Extract Bawang Dayak (Eleutherine bulbosa (Mill.) Urb) in Cream Against Propionibacterium acnes
Name & mail address of corresponding author: Syahrida Dian Ardhany and Susi Novaryatiin (chass501@gmail.com)

Highlighted Corrections

S.No.	Asked query no.	Details
1	AQ1	Received: December 5th 2018 Revised and Accepted: July 22th 2019
2	AQ2	On day 0, F1 and F2 shown antibacterial activity in category weak activity, F3 and F4 in category moderate activity, while on day 7 all formula have antibacterial activity in category weak activity
3	AQ3	Ethanolic extract of bawang dayak dissolved in aquadest, then put into water soluble and stir until homogenous in mortar, oil soluble add gradually, stir until the cream base was formed. The last add oleum roses and stir ad homogenous. Ethanolic extract of bawang dayak was evaluated for in vitro antibacterial activity against propionibacterium acnes using the disc diffusion method with different concentrations (F1= 5%, F2= 10%, F3= 15% and F4= 20%) of extract bawang dayak in a cream formula The pH that suitable for topical application is same with pH of skin, between 4.5-6
4	AQ4	**Evaluation test of cream formula** *Organoleptic appearance* The results of organoleptic test on day 0 showed that F1 had a lighter brown color than other formulas, it caused the concentration of ethanolic extract bawang dayak less concentration than other formulas. On day 7, all formulations became darker than before, this was probably due to ethanolic extract of bawang dayak content antioxidant compound. The odor of F3 and

		F4 on day 0 has sharper odor than F1 and F2, it caused concentration of ethanolic extract, but the odor has no change on the day 7 (Table 2) (Fig 4) **Antibacterial activity** The antibacterial activities can be classified into three levels: Weak activity (inhibition zone lower than 12 mm), moderate activity (inhibition zone between 12 and 20 mm), and strong activity (inhibition zone higher than 20 mm) [9]. The inhibitory test results on day 0 F1 have 7.83 mm inhibition zone (weak activity), F2=9.53 mm (weak activity), F3=12.47 mm (moderate activity), and F4=12.53 mm (moderate activity), while all formula which stand until 7 days have decrease zone of inhibition in category weak activity (Table 8) (Fig 1 and Fig 2). Inhibition zone decrease on day 7 may be caused storage not in cool area like in refrigerator, so it was needed develop research further. This research showed that all formula with different concentration of ethanolic extract bawang dayak potential inhibit *P. acnes* that caused acne vulgaris although zone of inhibition smaller than clindamycin as positive control (Table 7) (Fig 3)
5	AQ5	**Evaluation test of cream formula** *Organoleptic appearance* The results of organoleptic test on day 0 showed that F1 had a lighter brown color than other formulas, it caused the concentration of ethanolic extract bawang dayak less concentration than other formulas. On day 7, all formulations became darker than before, this was probably due to ethanolic extract of bawang dayak content antioxidant compound. The odor of F3 and F4 on day 0 has sharper odor than F1 and F2, it caused concentration of ethanolic extract, but the odor has no change on the day 7 (Table 2) (Fig 4) **Antibacterial activity** The antibacterial activities can be classified into three levels: Weak activity (inhibition zone lower than 12 mm), moderate activity (inhibition zone between 12 and 20 mm), and strong activity

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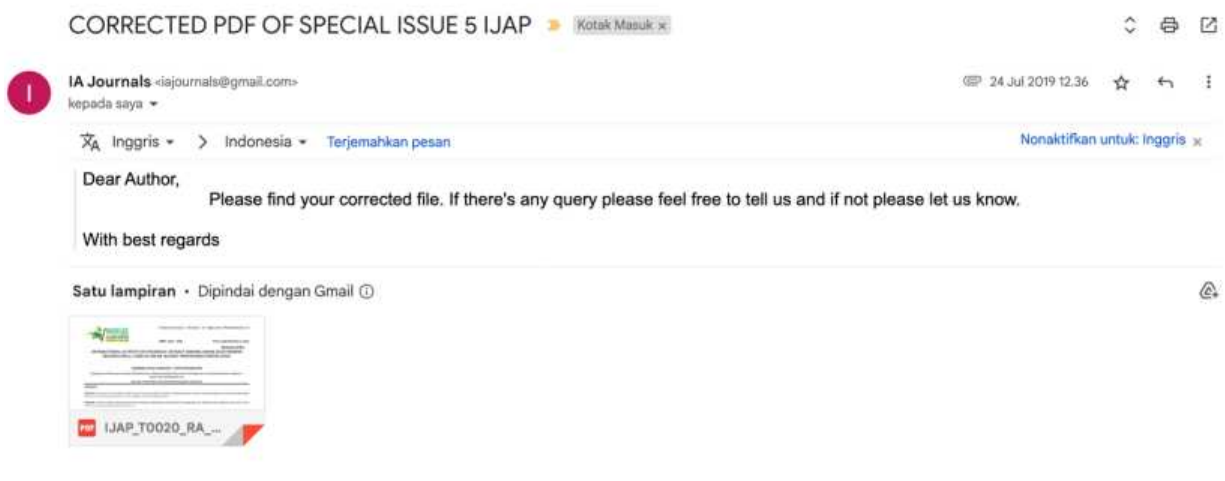

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Research Article

ANTIBACTERIAL ACTIVITY OF ETHANOLIC EXTRACT BAWANG DAYAK (*ELEUTHERINE BULBOSA* (MILL.) URB) IN CREAM AGAINST *PROPIONIBACTERIUM ACNES*

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Received: 05 December 2018, Revised and Accepted: 22 July 2019

ABSTRACT

Objective: The aims of this present study were to formulate antiacne cream consisting ethanolic extract of bawang dayak and evaluate antibacterial activity of cream on day 0 and day 7 to see stability activity and preparation.

Methods: Cream formula of bawang dayak was evaluated organoleptic characteristics, homogeneity, pH, adhesion test, dispersion test, and *in vitro* antibacterial against *Propionibacterium acnes*.

Results: The results of evaluate cream homogeneity were F3 and F4 on day 7 separate and non-homogen but all formula pH suitable for topical application. On day 0, F1 and F2 shown antibacterial activity in category weak activity, F3 and F4 in category moderate activity, while on day 7 all formula have antibacterial activity in category weak activity.

Conclusion: All cream formula potentials inhibit against *P. acnes* but this research must be improved both of preparation and stability activity.

Keywords: Acne vulgaris, Bawang dayak, Cream, *Eleutherine bulbosa*, *Propionibacterium acnes*.

 DOI: http://dx.doi.org/10.22159/ijap.2019.v11s5.T0020

INTRODUCTION

Acne vulgaris is one of the problems experienced by teenagers and adults because in this modern era, physical appearance is one of the most important things that must be considered. Acne is not a serious disease, but it can lead depression and loss of confidence. There are many causes of acne such as hormone level, fat or oil in skin, and a bacterium like *Propionibacterium acnes* [1].

Many cosmetic products that offer to improve acne problems, nature also provides a solution to these [2]. Bawang dayak is one of traditional medicines in Central Kalimantan. Based on research before, extract ethanol of bawang dayak can inhibit *P. acnes*, so in this research, ethanol extract was made in cream formulation to improve the efficiency of using traditional medicine.

METHODS

Collection of plant

Fresh plant materials, bulbs (20 kg) of bawang dayak (*Eleutherine bulbosa* (Mill.) Urb) were procured from farmer cultivation in Sei Gohong, Bukit Batu Palangka Raya Central Kalimantan.

Preparation of plant extracts

The plant materials were dried under the sun for 5–7 days. The dried plant materials were crushed by grinder. The powder of the plant materials was extracted with 96% ethanol using perkolator, and once process was finished, all extracts were concentrated in a rotary evaporator.

Formulation preparation

The formulation components used are listed in Table 1. The components consist of oil soluble (stearic acid, Adeps lanae, and paraffin liquid) and water soluble (TEA, nipagin, and aquadest). Each solution – oil soluble and water soluble – heated up to 55°C until melts. Ethanolic extract of bawang dayak dissolved in aquadest, then put into water soluble and stir until homogenous in mortar, oil soluble add gradually, stir until the cream base was formed. The last add oleum roses and stir ad homogenous.

Evaluation of cream

Organoleptic properties

The cream was observed for color, odor, and appearance.

Homogeneity observed

The particles size was observed on the slide to find the coarse particles. Preparations should show a homogeneous composition and no visible coarse grains [3].

PH measurements

Determining pH of the preparation is done using pH meter [4].

Dispersion test

Cream with 0.5 g was placed in the middle of a round glass scale. Round glass which has been weighted placed thereon and left for 5 min. After that followed with 50 g load, let stand for 1 min and record the diameter of the spread cream, did the same thing with 100 g and 150 g [5].

Adhesion test

A total 0f 0.5 g of preparation were spread on the disc glass, on top of it, other glass object placed and pinned under 1 kg load for 1 min. Then, disc glass mounted on test equipment, load is released, and the time was recorded up to the second object of the glasses falling off [5].

Evaluation of antibacterial activity by zone of inhibition by well diffusion method

Ethanolic extract of bawang dayak was evaluated for in vitro antibacterial activity against propionibacterium acnes using the disc diffusion method with different concentrations (F1=5%, F2=10%, F3=15% and F4=20%) of extract bawang dayak in a cream formula.

Table 1: Various cream formula of ethanolic extract bawang dayak

Materials	F1	F2	F3	F4
Extract ethanol of bawang dayak	5% (1250 mg)	10% (2500 mg)	15% (3750 mg)	20% (5000 mg)
Ol. Rosae	12 gtt	12 gtt	12 gtt	12 gtt
Oily phases (mg)				
Stearic acid	5000	5000	5000	5000
Adeps lanae	750	750	750	750
Paraffin liquid	6250	6250	6250	6250
Aqueous phase (mg)				
Triethanolamine	375	375	375	375
Nipagin	25	25	25	25
Aquadest ad	25,000	25,000	25,000	25,000

Table 2: Organoleptic appearance of various cream formula bawang dayak

Observation	Color	Odor	Appearance
Day 0			
F1	Brown (+)	Significant (+++)	Semi-solid
F2	Brown (++)	Significant (+++)	Semi-solid
F3	Brown (+++)	Significant (++++)	Semi-solid
F4	Brown (+++)	Significant (++++)	Semi-solid
Day 7			
F1	Brown (++)	Significant (+++)	Semi-solid
F2	Brown (+++)	Significant (+++)	Semi-solid
F3	Brown (++++)	Significant (++++)	Semi-solid
F4	Brown (++++)	Significant (++++)	Semi-solid

+: Weak, ++: Moderate, +++: Strong, ++++: Very strong

Table 3: Homogeneity test of various cream formula bawang dayak

Observation	Result
Day 0	
F1	Homogen
F2	Homogen
F3	Homogen
F4	Homogen
Day 7	
F1	Homogen
F2	Homogen
F3	Non-homogen
F4	Non-homogen

Table 4: Adhesion test of various cream formula bawang dayak

Observation	Adhesion (seconds)
Day 0	
F1	4.24
F2	4.67
F3	4.85
F4	4.55
Day 7	
F1	2.17
F2	2.76
F3	2.93
F4	2.43

Table 5: Dispersion test of various cream formula bawang dayak

Observation	First (cm)	50 g (cm)	100 g (cm)	150 g (cm)
Day 0				
F1	3.56	5.22	5.72	6.20
F2	3.03	3.49	3.78	4.07
F3	3.80	4.53	5.06	5.40
F4	3.36	4.05	4.49	4.93
Day 7				
F1	4.04	4.52	4.98	5.41
F2	3.43	4.20	4.43	4.93
F3	3.86	4.48	4.97	5.15
F4	3.27	3.51	4.04	4.38

Table 6: PH test of various cream formula bawang dayak

Observation	pH	Result (pH=4.5-6)
Day 0		
F1	6	Qualified
F2	6	Qualified
F3	6	Qualified
F4	6	Qualified
Day 7		
F1	5.7	Qualified
F2	6	Qualified
F3	6	Qualified
F4	6	Qualified

Table 7: Zone of inhibition of clindamycin

Concentration of clindamycin (%)	Zone of inhibition (mm)	Result
0.5	25.53	Strong activity
1	25.43	Strong activity
2	27.33	Strong activity
4	32.83	Strong activity

Table 8: Zone of inhibition of various cream formula bawang dayak

Various cream	Zone of inhibition (mm)	Result
Day 0		
F1	7.83	Weak activity
F2	9.53	Weak activity
F3	12.47	Moderate activity
F4	12.53	Moderate activity
Day 7		
F1	7.00	Weak activity
F2	8.20	Weak activity
F3	9.60	Weak activity
F4	9.83	Weak activity

The bacterial isolates were subcultured into a nutrient. The 24-hour-old bacterial culture was standardized using McFarland standard (10^6 CFU/mL of 0.5 McFarland standard). Mueller-Hinton agar (MHA) was used for bacteria bioassay. MHA was prepared by dissolving 38 g in 1000 ml of distilled water and brought to boil to completely dissolve. Sterilization was achieved by autoclaving at 121°C for 15 min [6].

MHA plates were prepared and bacterial strains were inoculated by cotton swab, and then, antibiotic and cream with various concentrations of extract bawang dayak applied in it. The plates were incubated at 37°C for 24 h, and the zone of inhibition was measured [7] and recorded later on.

RESULTS AND DISCUSSION

Evaluation test of cream formula

Organoleptic appearance

The results of organoleptic test on day 0 showed that F1 had a lighter brown color than other formulas, it caused the concentration of ethanolic extract bawang dayak less concentration than other formulas. On day 7, all formulations became darker than before, this was probably due to ethanolic extract of bawang dayak content antioxidant compound. The odor of F3 and F4 on day 0 has sharper odor than F1 and F2, it caused concentration of ethanolic extract, but the odor has no change on the day 7 (Table 2 and Fig. 1).

Homogeneity observation

The observation of cream bawang dayak showed on day 0 all formulation homogen, but day 7, F3 and F4 showed separation phase between the oil phase and the water phase (Table 3).

PH observation

The pH observation showed all cream formula of bawang dayak around 6 on day 0 and day 7 (Table 6). The pH that suitable for topical application is same with pH of skin, between 4.5-6 [8].

Dispersion test

The dispersion test adding and without adding weight has an average of more than 3 cm to all creamy formula both on day 0 and day 7 (Table 5).

Adhesion test

Adhesion test of cream on day 0 was more than 4 s and time of adhesion decrease on day 7 (Table 4).

Antibacterial activity

The antibacterial activities can be classified into three levels: Weak activity (inhibition zone lower than 12 mm), moderate activity (inhibition zone between 12 and 20 mm), and strong activity (inhibition zone higher than 20 mm) [9]. The inhibitory test results on day 0 F1 have 7.83 mm inhibition zone (weak activity), F2=9.53 mm (weak activity), F3=12.47 mm (moderate activity), and F4=12.53 mm (moderate activity), while all formula which stand until 7 days have decrease zone of inhibition in category weak activity (Table 8 and Figs. 2 and 3). Inhibition zone decrease on day 7 may be caused storage not in cool area like in refrigerator, so it was needed develop research further. This research showed that all formula with different concentration of ethanolic extract bawang dayak potential inhibit *P. acnes* that caused acne vulgaris although zone of inhibition smaller than clindamycin as positive control (Table 7 and Fig. 4).

Inhibition of all formula against *P. acnes* because ethanolic extract of bawang dayak contains secondary metabolites such as alkaloid, flavonoid, tannin, and saponin that can be potential has antibacterial effect against *P. acnes* [10]. Research about bawang dayak with the same type of plant specifically *E. bulbosa* parallel with research that conducted in India that stated bawang dayak has significant antibacterial activity [11].

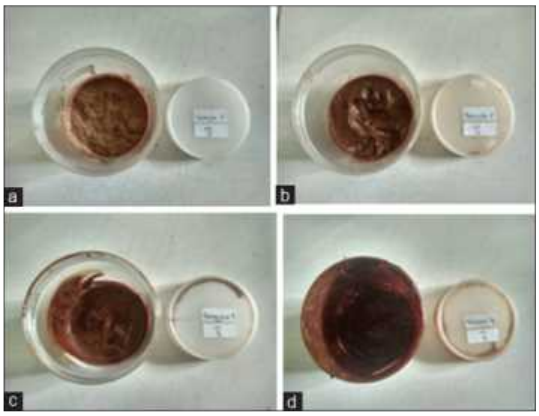

Fig. 1: Various cream formula ethanolic extract of bawang dayak; (a) F1, (b) F2, (c) F3, (d) F4

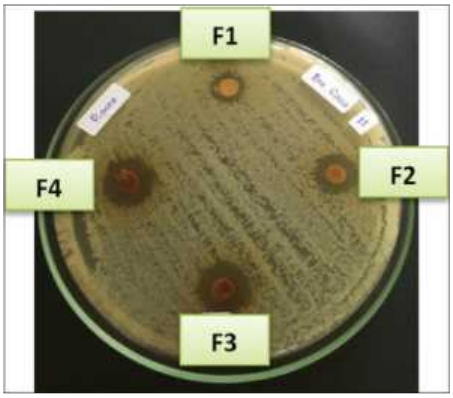

Fig. 3: Zone of inhibition all cream formula ethanolic extract of bawang dayak day 7

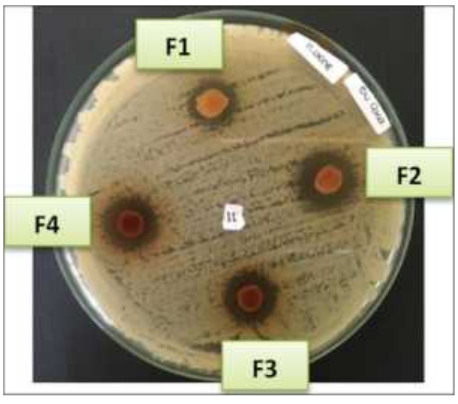

Fig. 2: Zone of inhibition all cream formula ethanolic extract of bawang dayak day 0

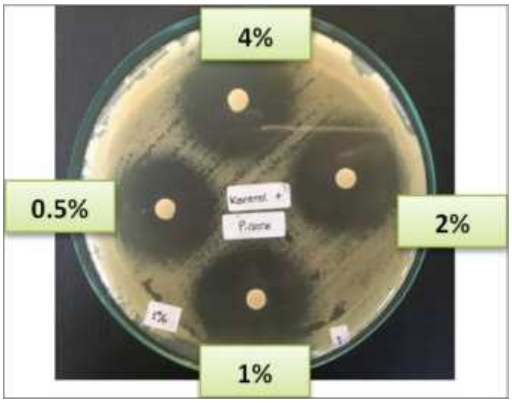

Fig. 4: Zone of inhibition clindamycin

CONCLUSION

Extract ethanolic of bawang dayak in all cream formula potential inhibits *P. acnes,* but inhibitory ability decreases on day 7. This research must be developed such as cream formula and improve effectiveness and combination with another material, so as the formula not separate and the effectivity is stable.

ACKNOWLEDGMENT

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6. **Article Published (IJAP)**

ANTIBACTERIAL ACTIVITY OF ETHANOLIC EXTRACT BAWANG DAYAK (Eleutherine bulbosa (Mill.)urb) IN CREAM AGAINST PROPIONIBACTERIUM ACNES

SYAHRIDA DIAN ARDHANY[1*] & SUSI NOVARYATIIN[1]
[1]Department of Pharmacy Faculty of Health Science, Muhammadiyah University of Palangkaraya, Central Kalimantan, Indonesia.
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ABSTRACT

Objective: The aims of this present study were to formulate anti acne cream consist ethanolic extract of bawang dayak and evaluate antibacterial activity of cream on day-0 and day-7 to see stability activity and preparation

Methods: Cream Formula of Bawang dayak was evaluated organoleptic characteristics, homogenity, pH, adhesion test, dispersion test and in vitro antibacterial against *P.acnes*

Results: The results of evaluate cream homogeneity was F3 and F4 on day-7 separate and non homogen but all formula pH suitable for topical application. This antibacterial activity showed cream on day-0, F1 and F2 in category weak activity, F3 and F4 moderate activity, on day-7 zone of inhibition of all cream formula decrease but still can inhibit.

Conclusion: All Cream Formula potential against *P.acnes* but this research must be improved both of preparation and stability activity

Keywords: Acne vulgaris, Bawang dayak, Cream, Eleutherine bulbosa, *Propionicaterium acnes*

INTRODUCTION

Acne Vulgaris is one of the problems experienced by teenagers and adults because in this modern era physical appearance is one of the most important things that must be considered. Acne is not a serious disease but it can lead depression and loss of confidence. There are many causes of acne such as hormone level, fat or oil in skin and a bacterium like *Propionibacterium acnes* [1].

Many cosmetic products that offer to improve acne problems, nature also provides a solution to these [2]. Bawang dayak is one of traditional medicine in Central Kalimantan. Based on research before, extract ethanol of bawang dayak can inhibit *P.acnes*, so in this research ethanol extract was made in cream formulation to improve the efficiency of using traditional medicine.

MATERIAL AND METHODS

Collection of Plant

Fresh plant materials bulbs (20 kg) of Bawang dayak (Eleutherine bulbosa (Mill.)Urb) were procured from farmer cultivation in Sei Gohong, Bukit Batu Palangka Raya Central Kalimantan.

Preparation of Plant Extracts

The plant materials were dried under the sun for 5-7 days. The dried plant materials were crushed by grinder. The powder of the plant materials was extracted with 96% ethanol by using perkolator and once process was finished all extracts were concentrated in a rotary evaporator.

Formulation Preparation

The formulation components used were listed in Table I. The components consist of oil soluble (stearic acid, Adeps lanae, paraffin liquid) and water soluble (TEA, nipagin and aquadest). Each solution oil soluble and water soluble heated up to 55ºC until melts. Ethanolic extract of bawang dayak dissolved in aquadest, then put into water phase and stir until homogen in mortar, oil phase add gradually, stir until the cream base is formed. The last add oleum roses stir ad homogen.

Table 1. Various Cream Formula of Ethanolic Extract Bawang Dayak

Materials	F1	F2	F3	F4
Extract Ethanol of Bawang Dayak	5% (1250 mg)	10% (2500 mg)	15% (3750 mg)	20% (5000mg)
Ol. Rosae	12 gtt	12 gtt	12 gtt	12 gtt
Oily Phases:				
Stearic Acid	5000 mg	5000 mg	5000 mg	5000 mg
Adeps Lanae	750 mg	750 mg	750 mg	750 mg
Paraffin Liq	6250 mg	6250 mg	6250 mg	6250 mg
Aqueous Phase:				
Triethanolamin	375 mg	375 mg	375 mg	375 mg
Nipagin	25 mg	25 mg	25 mg	25 mg
Aquadest ad	25000 mg	25000 mg	25000 mg	25000 mg

Evaluation of Cream

a. Organoleptic Properties
   The cream was observed for color, odor and appearance
b. Homogenity Observed
   The particles size was observed on the slide to find the coarse particles. Preparations should show a homogeneous composition and no visible coarse grains [3].
c. pH Measurements
   Determining pH of the preparation is done by using pH meter [4].
d. Dispersion Test
   Cream with 0.5 grams was placed in the middle of a round glass scale. Round glass which has been weighted placed there on and left for 5 minutes. After that followed with 50 grams load, let stand for 1 minutes and record the diameter of the spread cream, did the same thing with 100 grams and 150 grams [5].

e. Adhesion Test
   A total 0f 0.5 grams of preparation was spread on the disc glass, on top of it other glass object placed and pinned under 1 kg load for 1 minute. Then disc glass mounted on test equipment, load is released and the time was recorded up to the second object of the glasses falling off [5].

Evaluation of Antibacterial Activity by Zone of Inhibition by Well Diffusion Method

Ethanolic extract of Bawang dayak were evaluated for in vitro antibacterial activity against Acne vulgaris were caused by *Propionibacterium acnes* using the disc diffusion method with different concentrations of extract in cream formula.

The bacterial isolates were subcultured into a nutrient the 24-hour-old bacterial culture was standardized using McFarland standard (10^6cfu/mL of 0.5 McFarland standard). Mueller Hinton Agar (MHA) was used for bacteria bioassay. MHA was prepared by dissolving 38g in 1000ml of distilled water and brought to boil to completely dissolve. Sterilization was achieved by autoclaving at 121^o C for 15 minutes [6].

MHA plates were prepared and bacterial strains were inoculated by cotton swab and then antibiotic and cream with various concentration of extract bawang dayak applied in it. The plates were incubated at 37^o C for 24 hours and the zone of inhibition was measured [7] and recorded later on.

RESULTS AND DISCUSSION

Evaluation Test of Cream Formula

A. Organoleptic Appearance

The results of organoleptic test on day-0 showed that F1 had a lighter brown color than other formulas, it caused the concentration of ethanolic extract bawang dayak less concentration than other formulas. Day-7 all formulations became darker than before, this was probably due to ethanolic extract of bawang dayak content antioxidant compound. The odor of F3 and F4 on day-0 have sharper odor than F1 and F2 it caused concentration of ethanolic extract, but the odor has no change on the day-7 (Table 2).

Table 2. Organoleptic Appearance of Various Cream Formula Bawang Dayak

Observation	Color	Odor	Appearance
Day-0			
F1	Brown (+)	Significant (+++)	Semi-solid
F2	Brown (++)	Significant (+++)	Semi-solid
F3	Brown (+++)	Significant (++++)	Semi-solid
F4	Brown (+++)	Significant (++++)	Semi-solid
Day-7			
F1	Brown (++)	Significant (+++)	Semi-solid
F2	Brown (+++)	Significant (+++)	Semi-solid
F3	Brown (++++)	Significant (++++)	Semi-solid
F4	Brown (++++)	Significant (++++)	Semi-solid

+:Weak; ++ :Moderate; +++ :Strong; ++++:Very Strong

B. Homogenity Observation

The Observation of cream bawang dayak showed on day-0 all formulation homogen, but day-7 F3 and F4 showed separation phase between the oil phase and the water phase (Table 3).

Table 3. Homogenity Test of Various Cream Formula Bawang Dayak

Observation	Result
Day-0	
F1	Homogen
F2	Homogen
F3	Homogen
F4	Homogen
Day-7	
F1	Homogen
F2	Homogen
F3	Non Homogen
F4	Non Homogen

C. pH Observation

The pH observation showed all cream formula of bawang dayak around 6 on day-0 and day-7 (Table 6). The pH that suitable for topical application is between 4.5-6 same with pH of skin [8].

D. Dispersion Test

The dispersion test adding and without adding weight has an average of more than 3 cm to all creamy formula both on day-0 and day-7 (Table 5).

E. Adhesion Test

Adhesion test of cream on day-0 was more than 4 second and time of adhesion decrease on day-7 (Table 4).

Table 4. Adhesion Test of Various Cream Formula Bawang Dayak

Observation	Adhesion (seconds)
Day-0	
F1	4.24
F2	4.67
F3	4.85
F4	4.55
Day-7	
F1	2.17
F2	2.76
F3	2.93
F4	2.43

Table 5. Dispersion Test of Various Cream Formula Bawang Dayak

Observation	First (cm)	50 g (cm)	100 g (cm)	150 g (cm)
Day-0				
F1	3.56	5.22	5.72	6.20
F2	3.03	3.49	3.78	4.07
F3	3.80	4.53	5.06	5.40
F4	3.36	4.05	4.49	4.93
Day-7				
F1	4.04	4.52	4.98	5.41
F2	3.43	4.20	4.43	4.93
F3	3.86	4.48	4.97	5.15
F4	3.27	3.51	4.04	4.38

Table 6. pH Test of Various Cream Formula Bawang Dayak

Observation	pH	Result (pH=4.5-6)
Day-0		
F1	6	Qualified
F2	6	Qualified
F3	6	Qualified
F4	6	Qualified
Day-7		
F1	5.7	Qualified
F2	6	Qualified
F3	6	Qualified
F4	6	Qualified

Table 7. Zone of Inhibition of Clindamycin

Concentration of Clindamycin	Zone of Inhibition (mm)	Result
0.5%	25.53	Strong activity
1%	25.43	Strong activity
2%	27.33	Strong activity
4%	32.83	Strong activity

Table 8. Zone of Inhibition of Various Cream Formula Bawang Dayak

Various Cream	Zone of Inhibition (mm)	Result
Day-0		
F1	7.83	Weak activity
F2	9.53	Weak activity
F3	12.47	Moderate activity
F4	12.53	Moderate activity
Day-7		
F1	7.00	Weak activity
F2	8.20	Weak activity
F3	9.60	Weak activity
F4	9.83	Weak activity

Antibacterial Activity

The antibacterial activities can be classified into three levels: weak activity (inhibition zone lower than 12 mm), moderate activity (inhibition zone between 12 and 20 mm) and strong activity (inhibition zone higher than 20 mm) [9]. The inhibitory test results on day-0 F1 have 7.83 mm inhibition zone (weak activity), F2 = 9.53 mm (weak activity), F3 = 12.47 mm (moderate activity) and F4 = 12.53 mm (moderate activity), while all formula which stand until 7 days have decrease zone of inhibition in category weak activity. Inhibition zone decrease on day-7 may be caused storage not in cool area like in refrigerator, so it was needed develop research further. This research showed that all formula with different concentration of ethanolic extract bawang dayak potential inhibit *Propionibacterium acnes* that caused acne vulgaris although zone of inhibition smaller than clindamycin as positive control.

Inhibition of all formula againts *P.acnes* because ethanolic extract of bawang dayak containt secondary metabolites such as alkaloid, flavonoid, tanin and saponin that can be potential have antibacterial effect against *P.acnes* [10]. Research about bawang dayak with same type of plant specifically Eleutherine bulbosa parallel with research that conducted in India that stated bawang dayak have significant antibacterial activity [11].

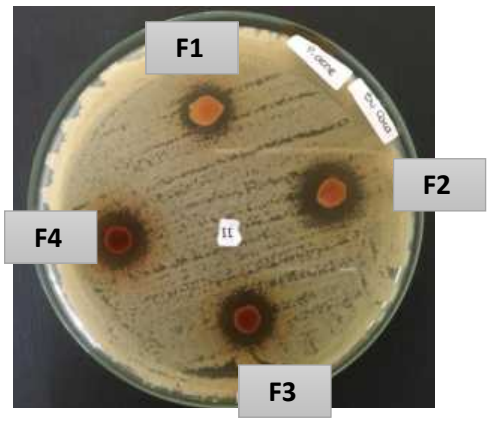

Fig 1. Zone of inhibition All Cream Formula Ethanolic Extract of Bawang Dayak Day-0

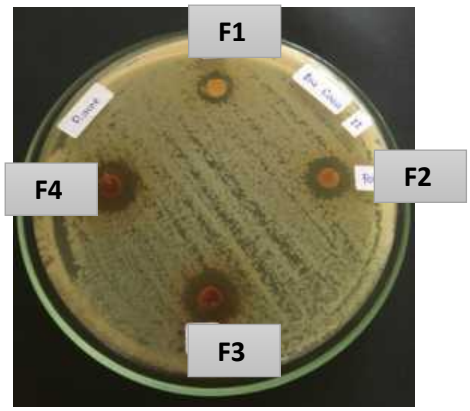

Fig 2. Zone of inhibition All Cream Formula Ethanolic Extract of Bawang Dayak Day-7

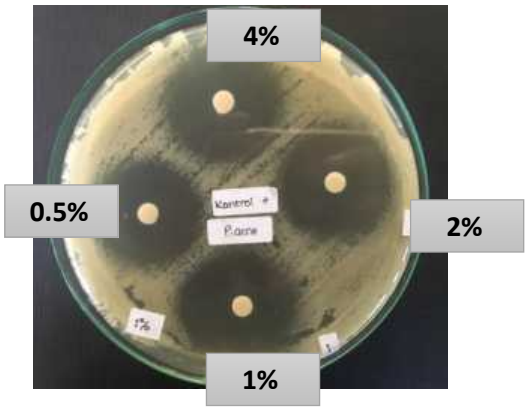

Fig 3. Zone of inhibition clindamycin

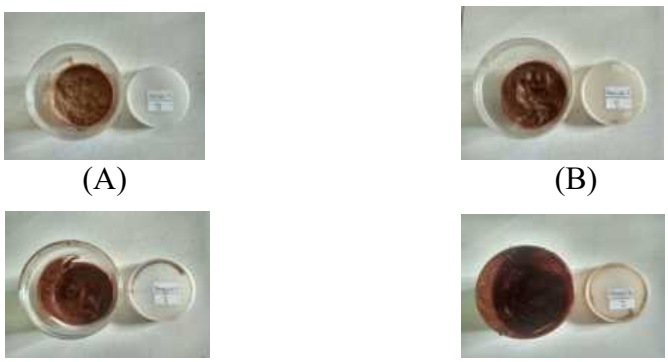

Fig 4. Various Cream Formula Ethanolic Extract of Bawang Dayak,
(A)= F1; (B) = F2; (C) = F3; (D) = F4

CONCLUSION

Extract ethanolic of bawang dayak in all cream formula potential inhibit *Propionibacterium acnes,* but inhibitory ability decrease on day-7. This research must be developed such as cream formula, improve effectiveness and combination with another material, so as the formula not separate and the effectivity is stable.

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Banjarmasin, 11 April 2018

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Lampiran : -
Perihal : Rekomendasi Penelitian

Sehubungan dengan telah dilaksanakannya sidang Etik Penelitian kepada:

Nama Ketua : Syahrida Dian Ardhany
NIK : 14.0601.033
Anggota : Susi Novaryatiin
Judul : Uji aktivitas antibakteri formulasi sediaan krim ekstrak etanol umbi Bawang Dayak (*Eleutherine bulbosa* (Mill.) Urb.) terhadap bakteri *Propionibacterium acnes*

Telah **DISETUJUI** untuk dilanjutkan penelitiannya.

Demikian surat persetujuan ini diterbitkan untuk dipergunakan dengan penuh tanggung jawab.

Menyetujui
An. Ketua
Sekretaris Komite Etik Penelitian

Ali Rakhman Hakim, M.Farm., Apt
NIK. 19.44.2015.100