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FORMULATION AND TEST OF ANTIBACTERIAL ACTIVITY OF EMULGEL ESSENTIAL OIL OF CITRONELLA (CYMBOPOGON NARDUS (L.) RENDLE) AND ALOE VERA (ALOE VERA (L.) BURM. F.) EXTRACT AGAINST PROPIONIBACTERIUM ACNES

FORMULASI DAN UJI AKTIVITAS ANTIBAKTERI EMULGEL MINYAK ATSIRI SEREH WANGI (CYMBOPOGON NARDUS (L.) RENDLE) DAN EKSTRAK LIDAH BUAYA (ALOE VERA (L.) BURM. F.) TERHADAP PROPIONIBACTERIUM ACNES

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Research Report
Penelitian

A B S T R A C T

Background: *Acne is described as an abnormal skin condition caused by the disruption of excess oil production and collaboration with bacteria. Aloe vera and citronella oil are plants that have antibacterial properties, including acne-causing bacteria.* ***Purpose:*** *To obtain a formulation that has an anti-acne effect.* ***Method:*** *This research method is experimental in which the formulation of citronella oil emulgel and aloe vera extract is made as much as 10-15 grams in each formula by varying the additional ingredients in each formulation. This formula was made from three different concentrations (F1 (6%:4%), F2 (4%:6%), and F3 (5%:10%)) and tested the physical stability, among others, organoleptic, pH, homogeneity, dispersion and antibacterial activity against Propionibacterium acnes.* ***Result:*** *There was no significant difference between the organoleptic test, pH, homogeneity, and inclusion in the eligible category. In contrast, the dispersion test had a slight difference in F2 and F3, which did not meet the requirements.* ***Conclusion:*** *Inhibitory activity test of the preparations obtained the average diameter of citronella oil emulgel preparations and aloe vera extract at concentrations of F1 (6%:4%), F2 (4%:6%), and F3 (5%:10%) are 11 mm, 10.7 mm and 16 mm and the ability to inhibit bacteria by all concentrations was in a strong category. Among the three formulations known to have the most remarkable effectiveness was at F3 (5%:10%) with an inhibitory diameter of F3 16 mm.*

A B S T R A K

Latar belakang: Jerawat digambarkan sebagai kondisi abnormal kulit yang diakibatkan karena gangguan produksi minyak yang berlebih dan berkolaborasi dengan bakteri. Lidah buaya dan minyak sereh wangi merupakan tanaman yang memiliki khasiat sebagai antibakteri antara lain bakteri penyebab jerawat. **Tujuan:** Untuk mendapatkan formulasi yang memiliki efek sebagai anti jerawat. **Metode:** Metode penelitian ini adalah metode eksperimen, formulasi emulgel minyak sereh wangi dan ekstrak lidah buaya dibuat 10-15 gram di tiap formula dengan memvariasikan bahan tambahan disetiap formulasi. Pembuatan formula ini dilakukan dengan tiga konsentrasi berbeda (F1 (6%:4%), F2 (4%:6%) dan F3 (5%:10%)) serta menguji kestabilan fisik antara lain, organoleptis, pH, homogenitas, daya sebar, serta aktivitas antibakteri terhadap *Propionibacterium acnes*. **Hasil:** Tidak ada perbedaan signifikan antara uji organoleptis, pH, homogenitas dan masuk kategori memenuhi syarat, sedangkan uji daya sebar ada sedikit perbedaan pada F2 dan F3 yang tidak memenuhi syarat. **Kesimpulan:** Uji aktivitas daya hambat sediaan didapatkan diameter rata-rata sediaan emulgel minyak sereh wangi dan ekstrak lidah buaya pada konsentrasi F1 (6%:4%), F2 (4%:6%), dan F3 (5%:10%) berturut-turut 11 mm; 10,7 mm; 16 mm dan kemampuan penghambatan bakteri oleh semua konsentrasi masuk kategori kuat. Diantara ketiga formulasi diketahui yang memiliki efektivitas paling besar adalah pada F3 (5%:10%) dengan diameter hambat sebesar F3 16 mm.

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INTRODUCTION

At the age of adolescents or adults, acne (acne vulgaris) is a worrying disease (Herwin *et al*., 2018). *Propionibacterium acnes* is a bacteria that causes acne infection, where under normal conditions, these bacteria will be non-pathogenic. However, these bacteria can change under invasive conditions if there is a change in skin condition (Mulyani *et al*., 2017), where metabolites that react with sebum will be produced, resulting in increased skin inflammation (Bota *et al*., 2015). The peak prevalence of acne occurs in the middle of adolescence (14-19 years). It is known that more than 85% occur in adulthood and decrease in adulthood and above. But acne can also arise and even persist at the age of more than 30 years (Kamal *et al*., 2018). Acne vulgaris is a self-limited disease, although this disease occurs regardless of age.

The cause of acne is multifactor, but the exact cause is unknown (Susanto *et al*., n.d.). The efficacy of oral antibiotics in acne tends to be multifactorial (Madelina *et al*., 2018). Antibiotics for acne are highly discouraged because of fears of antibiotic resistance if they are used continuously (Madelina *et al*., 2018). Several studies show that antibiotic resistance is increasing in several countries. More than 50% of *Propionibacterium acnes* strains are reported to be resistant to topical macrolides, so this antibiotic is less effective (Siber *et al*., 2019).

One of the efforts to reduce and avoid antibiotics in acne is to utilize a variety of productive plants that have secondary metabolites as antibacterials (Suhaimi *et al*., 2018). Herbal plants are widely trusted by the public to be used as a treatment for acne compared to antibiotics (Ali *et al*., 2021). Aloe vera (*Aloe vera. (L.) burm f.*) and citronella (*Cymbopogon nardus (L.) Rendle*) have been extensively collaborated on in several studies that this plant is used as a medicinal ingredient, one of which is as an antibacterial (Yenny, 2019). Citronella essential oil contains terpenes which have the best antibacterial properties. In addition, the active compounds possessed by citronella essential oil as antibacterial are geraniol, citronellal, and citronellol (Sholih *et al*., 2015). Research studies state that essential oils in citronella leaves produce good inhibition zones containing *Staphylococcus aureus*, *Escherichia coli*, and *Staphylococcus epidermidis* bacteria with concentrations of 12.5% and 15% (Puspawati *et al*., 2016).

Aloe vera contains active sterols, saponins, and acemannan, which can inhibit the growth of *Escherichia coli* bacteria and *Staphylococcus aureus* (Putriningtyas *et al*., 2013). The content of aloe vera plant is also known to contain various vitamins besides vitamin D, aloin, emodin, gum, and others such as essential oils (Kadek *et al*., 2012). Seeing the bacterial activity in the content of secondary metabolites of citronella oil and aloe vera extract, it is necessary to develop research on making anti-acne emulgel formulations from natural ingredients from citronella oil and aloe vera extract. It is hoped that this emulgel can be made to replace antibiotics in cases of acne. As is well known, the advantage of making emulgel in acne drug preparations is the process of mixing the oil phase and the water phase with the help of a gelling agent, which will act as a suitable carrier and is hydrophobic so that an emulsion preparation becomes a topical drug delivery agent that has good receptivity (Yenti *et al*., 2014). The purpose of this study was to obtain formulations that have antibacterial and anti-acne effects.

MATERIAL AND METHOD

Plant collection and determination

Fragrant citronella was collected from the Perjiwa Tenggarong Seberang Village area, East Kalimantan. Meanwhile, aloe vera was collected from gardens in the Sambutan area of Samarinda City, and then plant determination was carried out at the Dendrology Laboratory, Faculty of Forestry, Mulawarman University.

Making citronella oil

Citronella plants cleaned of dirt will then be dried using the manual method of airing them for a while. After that, it is cut into small pieces, and steam distillation is carried out for 8 hours to obtain citronella oil. The results of the oil yield are then calculated, and the refractive index value measured concerning the citronella oil quality standard according to SNI 06-3953-1995, namely with a refractive index value of 1.466–1.475. The yield of citronella oil produced is 4.67%, with a refractive index of 1.462.

Preparation of aloe vera ethanol extract

The aloe vera was cleaned of dirt. Then it was cut into small pieces and dried in a hot oven at 35^0C for several hours to reduce the water content contained in the aloe vera. After that, the simplicial was soaked in ethanol for seven days while stirring regularly, filtered to obtain aloe vera ethanol filtrate, and then concentrated using a rotary evaporator to produce a thick aloe vera extract. The yield of aloe vera produced is 22.4%

Preparation for making citronella oil emulgel and aloe vera extract

Emulgel formulations of fragrant citronella oil and aloe vera extract were made as much as 10-15 grams in each formula by varying the additional ingredients in each formulation. Emulgel formulation designs are presented in Table 1.

Table 1. Emulgel formula for citronella oil and aloe vera extract

Material	Formulas (F)		
	I	II	III
Citronella oil	6	4	5
Aloe vera extract	4	6	10
HPMC	6	6	6,5
Propylene glycol	10	10	10
Propyl paraben	0.1	0.1	0.1
Methyl paraben	0.1	0.1	0.1
Liquid paraffin	5	5	5
Tweens 80	0.5	0.5	0.5
Span 80	1	1	1
Aquadest	ad 100	ad 100	ad 100

Making citronella oil emulgel and aloe vera extract

The emulgel formulation of citronella oil and aloe vera was made with 3 (three) different concentrations of citronella oil and aloe vera extract. This was based on previous research used as a reference in selecting concentrations. The formulation stages are divided into two phases the preparation of the HPMC gel base and the emulsion base preparation stage. First, the gel mass was prepared by dispersing it in the HPMC method little by little using hot water so that the HPMC expands. Then, the formulation was crushed to form a gel base. After that, propylparaben and methylparaben were dissolved in propylene glycol, then mixed in a gel base. Aloe vera extract was added while grinding until the formulation was homogeneous. Likewise with citronella oil, this was mixed gradually while grinding until there was a homogeneous formulation (gel base).

Second, the emulsion mass (Tween 80 and Span 80) was formulated by heating a mixture of the oil and water phases separately at 70°C. Then, the two steps were remixed into the mortar, which already contained the gel base. After mixing, the formulation was ground for ±45 minutes until the formulation was homogeneous and an emulgel mass was formed. The finished formulation was evaluated for emulgel preparations, including organoleptic, pH, spreadability, stability, and antibacterial tests

Organoleptic test

Organoleptic testing can be assessed from the color, smell, texture, pH, and spreadability, to the homogeneity of the freshly made emulgel preparations.

pH test

The tool used for testing the pH of the emulgel used a previously calibrated pH meter. Emulgel preparations were weighed as much as 0.5 g in each formulation then diluted in 5 mL of distilled water in a beaker glass. After that, the pH meter was dipped into the preparation showing a constant pH value. In this case, the number shown by the pH meter is the pH value of each emulgel preparation.

Spreadability test

As much as 0.5 gram of the emulgel preparation was placed on a transparent glass which based on graph paper. Then, the preparation was allowed to spread and produce a certain diameter. After that, the preparation that was poured earlier was covered using transparent glass that had been given a load (1 g, 2 g, 5 g, and 10 g), and the increase in diameter measured after being given a load.

Homogeneity test

As much as 0.1 gram of the emulgel preparation was applied evenly and thinly on the transparent glass. An emulgel is said to be homogeneous if no coarse grains are visible (Dewi *et al*., 2018).

Antibacterial power test

The bacterial suspension that had been previously inoculated was then mixed into the NA tube media that had been sterilized and put into the petri dish. The NA that had solidified in the petri dish was then perforated using a cork borer which had been aseptic. The wells consisted of positive control, negative control, and emulgel with various concentration variations. Emulgel, whose concentration has been determined, was then placed in each of the available wells to cover the wells. Clindamycin phosphate 1.2% was used in this assay as a positive control and DMSO as a negative control. Then the NA medium was incubated for 24 hours at 37°C. After that, the inhibition zone formed was observed and measured using a caliper in the clear area formed minus the diameter of the wellbore made. The diameter of the inhibition that has been produced is used as the basis for observing antibacterial activity compared to the inhibition results of positive and negative controls. In this study, three repetitions were carried out.

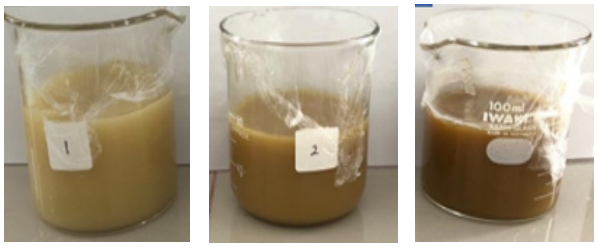
Data analysis test

Antibacterial activity test data were tested for normality with the *Shapiro-Wilk* using SPSS 23. The purpose of the normality test was to determine whether there were data that were not normally distributed. The test results are normal if the significance value is (*p-value*>0.05). If the values obtained are normally distributed, then the data will be analyzed using the *One-way* ANOVA statistical test. Then it was analyzed based on the hypothesis in the form of H_0, namely the emulgel formula with concentrations F1 (6%:4%), F2 (4%:6%), and F3 (5%:10%) did not have effectiveness as an anti-acne and H_1, namely the emulgel formula with concentrations of F1 (6%:4%), F2 (4%:6%) and F3 (5%:10%) have effectiveness as anti-acne. Decision-making can accept and reject the hypothesis by comparing calculated F_{value} and F_{table}. In this case, the conditions that apply are if the estimated F_{value} is less than the F_{table}, then H_0 is accepted. and H_1 is rejected. If the calculated F is more significant than F_{table}, then H_0 is rejected, and H_1 is accepted.

RESULT

Organoleptic observations

Organoleptic observations on the three emulgel preparations showed emulgel F1 in semi-solid form with a little runniess. This was due to the aqueous nature of citronella oil which had a yellow color, so the higher the concentration of citronella oil, the preparation became diluted resulting in the brownish-yellow color (Figure 1).



(a) (b) (c)

Figure 1. Emulgel citronella oil and aloe vera extract F1(a), F2(b), F3(c)

Emulgel preparations F2 and F3 are semi-solid and viscous. The color of the preparation was different from that of the F1 emulgel because the concentration of aloe vera extract used in the F2 and F3 emulgel preparations was higher than that of citronella. For the odor observation, the three emulgel preparations had the same odor: the distinctive aromatic smell of fragrant citronella. Emulgel preparations were stored for more than two weeks, and there were no significant changes during storage. That is, the preparations were said to be stable both before and after storage, and during the storage period, the components in the preparation did not experience any reaction between the ingredients one and another.

pH test

Using citronella oil and aloe vera extract of different concentrations will change the pH value of the formulations. However, as shown in Table 2, all emulsion formulations still meet normal skin pH standards, namely 4.5–6.5, so the resulting emulsion is considered safe for use on the skin (Yani *et al*., 2016).

The skin's pH is indicated by the level of acidity from the formation of fatty acids, amino acids, and oil secretion in the skin. The more alkaline it can cause dry skin. However, inflammatory problems such as eczema, psoriasis, or skin irritation result from the high level of acidity of an ingredient or preparation that will touch the skin (Handayani *et al*., 2015; Laverius, 2011; Afianti *et al*., 2015).

Spreadability test

This spreadability test aims to determine how much force is needed for the emulgel to spread on the skin or to find out how much the ability of the emulgel preparation to lay on the skin when applied. Emulgel preparations must have good spreadability and make it easy to apply emulgel preparations to the skin. It is known that the range of 3-5 cm is the result of good spreading power used for emulgel preparations. In Table 2, it is known that only the F1 preparation has good spreading power, and F2 and F3 do not have good spreading power. It is stated that the higher the concentration of citronella oil, the better the dispersion and the better the viscosity (Brooks *et al*., 2008).

Homogeneity test

The purpose of carrying out the homogeneity test on this emulgel preparation is to find out the mixability of the preparations that are made to be mixed homogeneously or not. Table 2 shows that the emulgel preparations F1, F2, and F3 have good homogeneity. The results of the homogeneity test showed that each emulgel formula gave homogeneous results marked by the absence of clumps of solid particles on the slide and the color equation that was spread and evenly distributed (Handayani *et al*., 2015).

Antibacterial power test

Antibacterial activity test on emulgel preparations was carried out using the good method against *Propionibacterium acnes* bacteria (Figure 2). The diffusion method employing wells was used in this study because the preparations inserted in each hole had a greater contact time so that an osmolarity process occurred to inhibit bacterial growth from becoming stronger.

Table 2. Results of physical test of citronella oil emulgel formula and aloe vera extract

No.	Testing	Formula I	Formula II	Formula III	Status
1	Organoleptic				
	Color	Brownish yellow	Light brown	Dark brown	MS
	Smell	Lemongrass aromatic	Lemongrass aromatic	Fragrant lemongrass scent	MS
	Texture	Finew	Fine	Fine	MS
2	pH	5.2	5.3	5.5	MS
3	Spread power	3.3 cm	2.8 cm*	2.9 cm *	TMS
4	Homogeneity	Homogeneous	Homogeneous	Homogeneous	MS

Note: *TMS = Not eligible; MS = Qualified

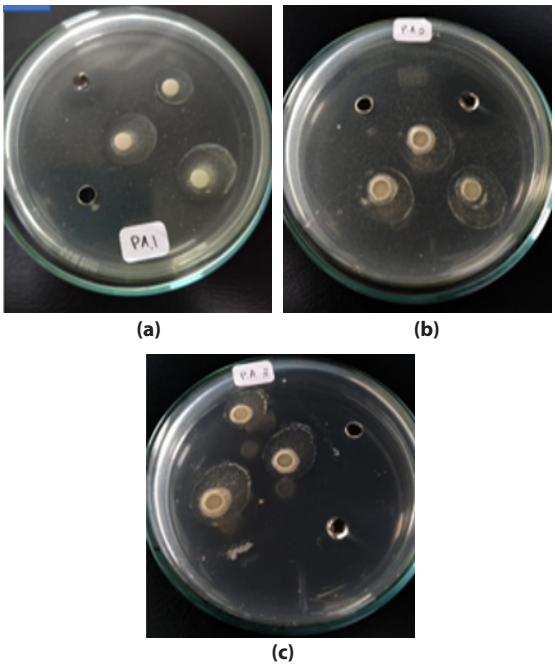


Figure 2. Emulgel antibacterial activity test with well diffusion method F1(a), F2(b), F3(c)

The concentration of citronella oil and aloe vera extract used is different. F1 (6%:4%), F2 (4%:6%) and F3 (5%:10%). DMSO as a negative control and 1.2% clindamycin gel preparation as a positive control. It is known that each emulgel formula with concentration variations carried out three times repetition in the results of this inhibition test showed differences in inhibition on the growth of *Propionibacterium acnes* bacteria compared to positive control clindamycin and negative control (Table 3).

Table 3. Antibacterial test results for emulgel preparations of citronella oil and aloe vera extract *P. acnes* bacteria

Formulation	Diameter of inhibition area(mm)				
	Test			Average	Std Dev.
	I	II	III		
Control (-)	0	0	0	0	0
Control (+)	28	25	26	26.3	1.53
Formula 1	13	9	11	11	2.00
Formula 2	13	9	10	10.7	2.08
Formula 3	17	18	13	16	2.65

The Minimum Inhibitory Concentration (MIC) or the diameter of the inhibition zone in F1 was an average of 11 mm, F2 was 10.7 mm, and F3 was 16 mm. Meanwhile, the positive control of 1.2% clindamycin gel showed that the resulting inhibition zone was 26.3 mm, more significant than the emulgel preparation. This is because clindamycin is a broad-spectrum antibiotic or antimicrobial like lincomycin. However, the antimicrobial activity of clindamycin was more significant in sensitive organisms such as *Staphylococcus aureus*, *Streptococcus pyogenes*, *D. pneumoniae*, and *Streptococci* except for *Streptococcus faecalis* (Davis *et al*., 1971) and DMSO as negative controls which did not have antibacterial activity against *Propionibacterium acnes* bacteria.

When viewed from the diameter of the inhibitory power, Fl, F2, and F3 preparations are included in the criteria for solid inhibitory power. This is adjusted to the requirements for inhibition of bacteria according to Davis and Stout (1971) which states several criteria for inhibition of a bacterium, namely:diameter >20 mm where this diameter means that the inhibition produced is very strong. Meanwhile, a diameter of 10–20 mm means that the inhibition power is in a strong category, a diameter of 5–10 mm means that the inhibition power produced is sufficient, and a diameter <5 mm means that the inhibition produced is weak (Wirawan, 2019).

The inhibition of the bacterial formulation was adjusted from the concentration of a sample used, namely citronella oil and aloe vera extract. Citronellal, citronellol, and geraniol compounds present in citronella oil are known to function as antibacterial agents, and these three compounds have antibacterial solid properties (Lertsatitthanakorn *et al*., 2008; Fani and Kohanteb, 2012). This is because citronella plants have secondary metabolites consisting of phenolics and terpenoids, where the mechanism of action of these metabolites will denature and inactivate proteins which cause enzymes not to be produced, causing the bacterial cell wall to be damaged due to decreased permeability and disruption of transport of essential organic ions, which enters into the bacterial cell (Irianto *et al*., 2020; Nurdianti, 2018). This disrupts the metabolism of bacterial cells or makes the bacterial cells die. Aloe vera has also been shown to have antibacterial activity because it contains anthraquinone emodin secondary metabolites. It is known that anthraquinone compounds can inhibit bacterial cell protein synthesis so that bacteria cannot live in any media contained in aloe vera extract (Sholih *et al*., 2015).

DISCUSSION

The normality test results showed that the significance value of F1 was 1, F2 was 0.463, and F3 was 0.36 (*p-value*>0.05), which stated that the data obtained had been normally distributed. This is based on the *One-way* ANOVA test results through the concentration obtained by the calculated F_{value} of 5.239 sig 0.048.

Determination of the value of F_{table} 1 uses a confidence level of 95%, α = 5%. From the data, the F_{table} is 5.14, so the calculated F_{value} is more than the F_{table} (5.239 > 3.48). Based on this, the results of the accepted hypothesis are that the concentrations of F1 (6%:4%), F2 (4%:6%), and F3 (5%:10%) have effectiveness as antibacterial causes of acne.

Combining these two ingredients in the emulgel formulation can produce an alternative solution to using natural ingredients as acne antibacterial, especially with the concentration of aloe vera extract used. The higher the concentration of aloe vera in emulgel, the antibacterial activity against *Propionibacterium acnes* bacteria is higher.

CONCLUSION

The optimal formulation of anti-acne emulgel preparations is with a concentration of F1 (6%:4%) and F3 (5%:10%), fulfilling the requirements for organoleptic test parameters, pH, spreadability, and homogeneity. For the antibacterial activity test against *Propionibacterium acnes* bacteria, emulgel preparations F1 (6%:4%), F2 (4%:6%), and F3 (5%:10%) had antibacterial effectiveness with an average diameter of F1 11 mm, F2 10.7 mm, and 16 mm F3 which are categorized as vital and can be productive as anti-bacterial. Among the three available formulations, the greatest effectiveness is at F3 (5%:10%) with an inhibitory diameter of 16 mm F3.

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REFERENCE

Afianti, H.P., Murrukmihadi, M., 2015. Pengaruh Variasi Kadar Gelling Agent Antibakteri Sediaan Gel Ekstrak Etanolik Kemangi (Ocimum basilicum L . forma citratum back .). Maj. Farm. Vol. 11(2), Pp. 307-315.

Ali, T.A.M., Muti'ah, M., Roihatul Roihatul Suryadinata, A., 2021. Literature Review Evaluasi Sediaan Ekstrak Daun Lidah Buaya (Aloe Vera (L.) Webb) sebagai Anti Jerawat pada Uji Pra Klinis dan Uji Klinis. Universitas Islam Negeri Maulana Malik Ibrahim.

Bota, W., Rondonuwu, M.M.F.S., 2015. Potensi Senyawa Minyak Sereh Wangi (Citronella oil) dari Tumbuhan Cymbopogon Nardus L. sebagai Agen Antibakteri. In: Prosding Seminar Nasional Sains Dan Teknologi. Fakultas Teknik Universitas Muhammadiyah Jakarta, Jakarta, Pp. 1-8.

Brooks, G.F., Butel, J.S., Morse, S.A., Hartanto, H., 2008. Jawetz, Melnick, dan Adelberg Mikrobiologi Kedokteran: Edisi XXII, 23rd ed. EGC Penerbit Buku Kedokteran, Jakarta.

Davis, W.W., Stout, T.R., 1971. Disc Plate Method of Microbiological Antibiotic Assay. II. Novel Procedure Offering Improved Accuracy. Appl. Microbiol. Vol. 22(4), Pp. 666-670.

Dewi, C., Saleh, A., Awaliyah, N.H., Hasnawati, H., 2018. Eevaluasi Formula Emulgel Lendir Bekicot (Achatina fulica) dan Uji Aktivitas Antibakteri terhadap Bakteri Staphylococcus epidermidis Penyebab Jerawat. J. Mandala Pharmacon Indones. Vol. 4(2), Pp. 122-134.

Fani, M., Kohanteb, J., 2012. Inhibitory Activity of Aloe Vera Gel on Some Clinically Isolated Cariogenic and Periodontopathic Bacteria. J. Oral Sci. Vol. 54(1), Pp. 15-21.

Handayani, M., Mita, N., Ibrahim, A., 2015. Formulasi dan Optimasi Basis Emulgel Carbopol 940 dan Trietanolamin dengan Berbagai Variasi Konsentrasi. Proceeding Mulawarman Pharm. Conf. (Prosiding Semin. Nas. Kefarmasian) Vol. 15(1), Pp. 53-60.

Herwin, H., Sari, Z.P., Nuryanti, S., 2018. Aktivitas Antibakteri Ekstrak Etanol Daun dan Ampas Teh Hijau (Camellia Sinensis L.) terhadap Bakteri Penyebab Jerawat (Propionibacterium acne dan Staphylococcus epidermidis) secara Difusi Agar. As-Syifaa J. Farm. Vol. 10(2), Pp. 247-254.

Irianto, I.D.K., Purwanto, P., Mardan, M.T., 2020. Aktivitas Antibakteri dan Uji Sifat Fisik Sediaan Gel Dekokta Sirih Hijau (Piper betle L.) sebagai Alternatif Pengobatan Mastitis Sapi. Maj. Farm. Vol. 16(2), Pp. 202-210.

Kadek, A.N., Gede, D.I.B., Ketut, S.S., 2012. Daya Hambat Ekstrak Kulit Daun Lidah Buaya (Aloe barbadensis miller) terhadap Pertumbuhan Bakteri Staphylococcus aureus ATCC 25923 dan Escherichia coli ATCC 25922. J. Biol. Udayana. Vol. 16(1), Pp. 1-4.

Kamal, S.E., Saputri, D.S., 2018. Uji Aktivitas Infusa Daun Lidah Buaya (Aloe Vera L.) terhadap Propionibacterium acnes Penyebab Jerawat. J. Farm. Sandi Karsa Vol. 7(4), Pp. 1-4.

Laverius, M.F., 2011. Optimasi Tween 80 dan Span 80 sebagai Emulsifying Agent serta Carbopol sebagai Gelling Agent dalam Sediaan Emulgel Photoprotector Ekstrak Teh Hijau (Camellia sinensis L.). Universitas Sanata Dharma.

Lertsatitthanakorn, P., Arunyanart, S.T.C., Khunkitti, C.A.W., 2008. Effect of Citronella Oil on Time Kill Profile, Leakage, and Morphological Changes of Propionibacterium acnes. J. Essent. Oil Res. Vol. 22(3), Pp. 270-294.

Madelina, W., Sulistiyaningsih, S., 2018. Review: Resistensi Antibiotik pada Terapi Pengobatan Jerawat. J. FARMAKA Vol. 16(2), Pp. 105-117.

Mulyani, T., Wahyu, Y., Hidayat, D., Isbiantoro, I., Fatimah, Y., 2017. Ekstrak Daun Katuk (Sauropus Androgynus (L) Merr) sebagai Antibakteri terhadap Propionibacterium acnes dan Staphylococcus epidermidis. JFL J. Farm. Lampung Vol. 6(2), Pp. 46-54.

Nurdianti, L., 2018. Evaluasi Sediaan Emulgel Anti Jerawat Tea Tree (Melaleuca alternifolia) Oil dengan menggunakan HPMC sebagai Gelling Agent. J. Pharmacopolium Vol. 1(1), Pp. 23-31.

Puspawati, N.M., Suirta, I.W., Bahri, S., 2016. Isolasi, Identifikasi, serta Uji Aktivitas Antibakteri pada Minyak Atsiri Sereh Wangi (Cymbopogon winterianus jowitt). J. Kim. (Journal Chem. Vol. 10(2), Pp. 219-227.

Putriningtyas, D., Kuswandi, M., Munawaroh, R., 2013. Aktivitas Antibakteri Minyak Atsiri Daun Sirih Merah (Piper crocatum ruiz & Pav.) dan Minyak Atsiri Daun Sereh Wangi (Cymbopogon Nardus (L.) Rendle) Asal Tawangmangu terhadap Bakteri Staphylococcus Aureus dan Escherichia Coli. Universitas Muhammadiyah Surakarta.

Sholih, M.G., Muhtadi, A., Saidah, S., 2015. Rasionalitas Penggunaan Antibiotik di Salah Satu Rumah Sakit Umum di Bandung Tahun 2010. J. Farm. Klin. Indones. Vol. 4(1), Pp. 64-70.

Siber, H.T., Putra, I.W.A., Anggraini, D.I., 2019. Tata Laksana Terkini Acne Vulgaris. JK Unila J. Kedokt. Univ. Lampung Vol. 3(2), Pp. 313-319.

Suhaimi, S., Indrawati, T., Kumala, S., 2018. Uji Aktivitas Kombinasi Ekstrak Kering Lidah Buaya (Aloe Vera. (L) Brum. F.) dan Ekstrak Kental Daun Sirih Merah (Piper crocatum ruiz & Pav) untuk Antibakteri Penyebab Jerawat. J. Ilmu Farm. Farm. Klin. Vol 15(1), Pp. 7-14.

Susanto, A.A.M.I., Pramuningtyas, R., n.d. Review Analisis Efektivitas Terapi Antibiotik Acne Vulgaris Derajat Berat. In: Medical Research For Better Health In Pandemic. Pp. 192-200.

Wirawan, E., 2019. Potensi Serai Wangi sebagai Pestisida Nabati.

Yani, T.N., Anwar, E., Saputri, F.C., 2016. Formulasi Emulgel yang Mengandung Ekstrak Etanol Daun Binahong (Anredera cordifolia (Ten.) Steenis) dan Uji Aktivitasnya terhadap Propionibacterium acnes secara in Vitro. J. Kefarmasian Indones. Vol. 6(2), Pp. 89-97.

Yenny, S.W., 2019. Antibiotic Resistaince in Acne Vulgaris. West Sumatera, Indonesia.

Yenti, R., Afrianti, R., Qomariah, S., 2014. Formulasi Emulgel Ekstrak Etanol Daun Dewa (Gynura Pseudochina (L.) Dc) untuk Pengobatan Nyeri Sendi terhadap Tikus Putih Jantan. In: Prosiding Seminar Nasional Dan Workshop "Perkembangan Terkini Sains Farmasi Dan Klinik IV. Pp. 56-53.