THE COMBINATION OF SUGAR PALM MIDRIB EXTRACT (*ARENGA PINNATA MERR.*) AND NUTGRASS (*CYPERUSROTUNDUS L.*) AS GEL FORMULATION TO INHIBIT ACNE BACTERIAS (*PROPIONIBACTERIUM ACNES* AND *STAPHYLOCOCCUS EPIDERMIDIS*)

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Introduction

Acne is a common inflammatory disease of the skin which usually occurs in teenagers and young adults. It marked with pimples, papules, pustules, and nodules. Acne vulgaris affects 85% of the world's population, especially the young people and adults (1). Although acne does not cause fatal consequences, it is quite disturbing for people who care about their look since it lessen self-confidence (2). There are some factors that may cause acne, those are; genetics, race, weather, psychic, hormones and/or bacterial infections, but the common cause is from bacterial infection. The bacteria that cause acne is *Propionibacterium acnes* and *Staphylococcus epidermidis* (3,4). According to Mulyani et al. (2017), in normal condition the bacterial is not pathogen, but if the skin changes, the bacterial will become invasive(5). Common synthetic medicine used to treat acne include benzoyl peroxide, retinoid, isotretinoin, antibiotic and oral contraceptives may have dangerous side effect if the usage is improper (6,7). Considering that new side effects are being recorded for synthetic drugs generally, demands for medicines with natural ingredients are growing recently (8). Djajadisastra et al. (2009) showed that medicines with natural ingredients were safer when used for acne treatment (9).

The midrib of sugar palm (*Arenga pinnata*) has long been known as the traditional treatment for acne. Phytochemical analysis showed identified several groups of plant secondary metabolites of which some exhibited significant antibacterial activity (10). Another study showed that there is secondary metabolite compounds in the extract of sugar palm midrib, such as saponins, steroid, triterpenoids, tannin, and phenol (11). The antimicrobial activity test results also showed that ethanol extract on the midrib of sugar palm which fractionated with 7.5% ethyl acetate fraction solvent has potential to slow both of the *Propionibacterium acnes* and *Staphylococcus aureus* bacterial with resistor diameter 14mm and tetracycline 0.005% (10). Another study by Rahim et al. (2018) indicated that nutgrass (*Cyperus rotundus L.*) contains chemical components such as essential oils, alkaloids, flavonoids, polyphenols, resins, starches, tannins, triterpenes, d-glucose, d-fructose and non-reducing sugars. There is also an antibacterial activity in nutgrass ethanol extract. The essential oil contained in nutgrass also have the potential to fight against *Staphylococcus epidermidis* bacteria that often found in skin. In her study, she examined the antibacterial activity of talcum powder. The results showed that the talcum powder of nutgrass ethanol extract has strong bactericidal effect on Staphylococcus epidermis, with a concentration of 7% b/v and a resistance diameter of 31.4mm. The antiseptic activity examination is done using replica methodology and the reduction percentage of the total number of microbial colonies is used as the basic determination of the antiseptic ability of talcum powder preparations(12).

The common method in society in using sugar palm midrib (Arenga pinnata Merr.) and nutgrass (Cyperus rotundus L.) as acne treatment is in the form of cold powder or by applying the simplicity directly to the face; either to the scars area or to the acne area. However, this method need to be developed in a more simple way with better formulation, durability, and effectiveness. One of the ways is by making a gel preparations. Gel formulation is in great demand since it is easier to be cleaned from the face and did not contain oil which can cause the damage on acne (13). Rowe et al. (2009) used gel preparation with NaCMC (*Sodium carboxymethyl cellulose*) with 3-6% concentration to produce medium viscosity to be used as the basic ingredient of gel and pasta(14). NaCMC is chosen as the gel basis since it has some advantages, including easy to flourish, can be mixed with active substance, and the appearance is more clear (15). Moreover, NaCMC is often used in medical and cosmetic product because it has high complexity and stability, low toxicity, and able to enhance the contact duration with skin which increase its effectiveness. Glycerin and propylene glycol are also used in the making of the gel preparation because both ingredients are worked as humectant or moisture lock which function is to enhance the moisture and spread ability of the preparations (16). Thus, the objective of this study is to make gel formulation from combination of sugar palm midrib extract and nutgrass extract due to slow the growth of acne bacteria – *Propionibacterium acnes and Staphylococcus epidermidis*. The combination of both of these plant extracts has purpose to enhance the antibacterial effectiveness and to obtain an optimum formula that met the requirements for a better and effective gel preparation.

Materials and Methods

Tools and Materials

The tools that used during the experiment, involving; analytical scales (LabPRO DT 224C), Homogenizer (IKA®RW 20 digital), pH meter digital (OHAUS®), Viscometer Brookfield (DV-I Prime), Oven (Wiebrock), Incubator (Mmert®), Laminar Air Flow (LAF), Mirror, Micropipette, Autoclave, inoculation needle, ruler, anaerobic jar, petri dish and others glasses tool. Whereas the materials used are; sugar palm dense extract (*Arenga pinnata* Merr.), nutgrass dense extract (*Cyperus rotundus* L.), NaCMC, propylene glycol, phenoxyethanol, glycerin, phosphate buffer solution pH 6.8, Media Brain Heart Infusion Agar (BHIA), Brain Heart Infusion Broth (BHIB), Media Tryptone Soya Agar (TSA), Tryptone Soya Broth

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(TSB), and pure strain of Propionibacterium acnes (ATCC 11827) and Staphylococcus epidermis (ATCC 12228) which obtained from Microbiology Laboratory of Biology Department, IPB.

Methods

The step in making the gel formulation from sugar palm midrib extract and nutgrass extract, can be seen below;

1. Determining the sugar palm and nutgrass plants in Center for Biological Research, Indonesian Institute of Sciences (LIPI), Cibinong
2. Making sugar palm midrib extract and nutgrass extract
3. Examining sugar palm midrib extract and nutgrass yield extract
4. Examining the combination of sugar palm midrib dense extract and nutgrass dense extract
   a. Organoleptic examination of sugar palm midrib dense extract and nutgrass extract
   b. pH examination of sugar palm midrib dense extract and nutgrass extract
   c. Phytochemical Screening of sugar palm midrib dense extract and nutgrass extract
   d. Quality parameter examination of sugar palm midrib dense extract and nutgrass extract
   e. Antibacterial activity test of sugar palm midrib dense extract and nutgrass extract
5. Making gel formulation of sugar palm midrib dense extract and nutgrass extract
6. Testing gel formulation antibacterial activity of sugar palm midrib dense extract and nutgrass extract
7. Evaluating the gel formulation of sugar palm midrib dense extract and nutgrass extract
8. Gel formulation stability test
9. Gel formulation irritation test

Results and Discussion

The determination result of sugar palm midrib and nutgrass was examined in the Research Biology Center of Indonesian Institute of Sciences (LIPI), Cibinong. The organoleptic examination showed that sugar palm midrib extract has dark brown color, odorless, and thick texture. Nutgrass extract also has dark brown color and thick texture but it has aromatic smell. While the pH examination can be seen in table 2 below;

Table 1. pH examination result of sugar palm midrib and nutgrass extract

Extract	pH
Sugar palm midrib	**6.20 ± 0.01**
Nutgrass	**4.56 ± 0.02**

From the table 2 above, it is indicated that the pH level of both sugar palm midrib and nutgrass extract are within the scale of normal for about 4.5 - 6.5 which is safe for skin.

Testing the Yield

After making the extract of sugar palm midrib and nutgrass, the yield extract is tested using ethanol. The result of testing the yield extract can be seen in table 2 and 3 below;

Table 2. The result of testing yield extract of sugar palm midrib and nutgrass ethanol extract

No	Simplicity	Weight powder (g)	Ethanol Volume (L)	Weight extract (g)	Yield (%)
1.	**Sugar palm midrib**	**5000**	**50**	**253**	**5.06**
2.	**Nutgrass**	**5000**	**50**	**283**	**5.66**

Table 3. The result of quality extract parameter test

Standard simplicity parameter	Standard MMI (%)	Examination Result (%)	
		Sugar palm extract	Nutgrass extract
Specific			
Water Essence	**≥ 18%**	**21.26**	**18.25**
Ethanol Soluble Content	**≥ 6.30%**	**38.55**	**47.62**
Nonspecific			
Water content	**≤ 10%**	**9.72**	**8.70**
Ash content	**≤ 10%**	**2.68**	**Non-detected**
Non soluble ash content acid	**≤ 12.6%**	**Non-detected**	**Non-detected**
Remaining solvent (ethanol)	**≤ 1%**	**0.02**	**0.26**
Flavonoid	**≥ 1.96%**	**3.85**	**5.25**

Phytochemical Screening

The phytochemical screening result can be seen in table 4 below;

Table 4. Phytochemical screening result

Phytochemical Screening	Sugar palm midrib extract	Nutgrass extract
Alkaloid	+	+
Saponin	+	+
Tannin	+	+

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Phenolic	+	+
Flavonoid	+	+
Steroid	-	-
Glycoside	+	+

Notes: (+) positive: bacteria grow; (-) negative: bacteria did not grow

Formulation of Gel Preparation

Gel formulation is made using the combination of 4% NaCMC, 5% Glycerin, and 10% Propylene Glycol. NaCMC has function as gelling agent, while propylene glycol used as basis and humectant. The other ingredients, glycerin, is used to keep the water content within the preparation. The gel preparation formulation can be seen in following table 5 below;

Table 5. Gel Preparation Formulation

Ingredients	Amount (%)					
	F1	F2	F3	F4	F5	K-
Sugar Palm Midrib Extract (Arenga pinnata Merr.)	40	-	10	20	40	-
Nutgrass Extract (Cyperus rotundusL.)	-	25	25	25	25	-
Na CMC	4	4	4	4	4	4
Propylene glycol	10	10	10	10	10	10
Glycerin	5	5	5	5	5	5
Phenoxyetanol	0,8	0,8	0,8	0,8	0,8	0,8
Aquadest	ad 100	ad 100	ad 100	ad 100	ad 100	ad 100

In defining the minimum inhibitory concentration, broth dilution method is applied. This method is intended to determine the amount/minimum concentration of an antibacterial substance that able to slow the growth of target bacteria, the result can be seen in table 6 and 7 below;

Table 6. Minimum Inhibitory Concentration (MIC) of Sugar Palm Midrib Extract

Concentration (%)	P. acnes	S. epidermis
50	-	-
40	-	-
30	+	+
20	+	+
15	+	+
10	+	+

Notes: + (positive) = colony bacteria grow ; - (negative) = colony bacteria did not grow

Table 7. Minimum Inhibitory Concentration (MIC) of Nutgrass Extract

Concentration (%)	P. acnes	S. epidermidis
25	-	-
12.5	+	-
6.25	+	+
3.125	+	+
1.56	+	+
0.78	+	+
0.39	+	+

Notes:+ (positive) = colony bacteria grow ;- (negative) = colony bacteria did not grow

Meanwhile, the result of inhibitory power diameter test on sugar palm midrib and nutgrass extract can be seen in table 8 and 9 below;

Table 8. Inhibitory Power Diameter on Sugar Palm Midrib Extract

CONCENTRATE (%)	Average IPD on Sugar Palm Midrib Extract, ($\bar{X} \pm$ SD) mm			
	P.acnes	Category	S.epidermidis	Category
40	11.54 ± 0.73	Strong	11.10 ± 0.07	Strong
30	9.53 ± 0.68	Medium	9.13 ± 0.11	Medium
K+	20.10 ± 0.07	Strong	25.08 ± 0.04	Very Strong

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K-	0.00	-	0.00	-

Notes: Positive Control (+) = Clindamycin 200 ppm; Negative Control (-) = DMSO 10%; SD = Standard Deviation

Table 9. Inhibitory Power Diameter on Nutgras Extract

CONCENTRATE (%)	Average IPD on Nutgrass Extract ($\bar{X} \pm$ SD) mm			
	P.acnes	Category	S.epidermidis	Category
25.00	12.06± 0.01	Strong	12.06 ± 0.06	Strong
12.50	10.08± 0.04	Medium	11.15 ± 0.07	Strong
6.25	8.13 ± 0.11	Medium	9.51 ± 0.01	Medium
3.12	7.08 ± 0.04	Medium	8.08 ± 0.04	Medium
K+	20.15 ± 0.07	Strong	25.06 ± 0.06	Very strong
K-	00.00	-	00.00	-

Notes: Positive Control (+) = Clindamycin 200 ppm; Negative Control (-) = DMSO 10%; SD = Standard Deviation

Table 9 and 10 above shows that IPD of sugar palm midrib extract on MIC (40% concentrate) toward P.acnes bacteria is 12.02 ± 0.09mm (strong) and toward S. epidermis bacteria is 11.8 ± 0.11mm (strong). While the IPD of nutgrass extract on MIC (25% concentration) toward *P.acnes* bacteria is 12.06 ± 0.01mm (strong) and toward *S.epidermis* bacteria is 12.06 ± 0.06mm (strong). Moreover, both IPD of sugar palm midrib and nutgrass extract have very strong category in K+ (positive control). The bacterial activity test on gel preparation of sugar palm midrib and nutgrass extract can be seen in table 11 below;

Table 11. The result of IPD gel formulation test

Formulation	IPD mean ($\bar{X} \pm$ SD) mm			
	P.acnes	Category	*S.epidermidis*	Category
F1	26.08 ± 0.04	Very strong	15.13 ± 0.04	Strong
F2	30.03 ± 0.03	Very strong	24.13 ± 0.11	Very strong
F3	21.08 ± 0.03	Very strong	27.09 ± 0.01	Very strong
F4	22.07 ± 0.02	Very strong	28.08 ± 0.10	Very strong
F5	23.08 ± 0.10	Very strong	29.10 ± 0.07	Very strong
K+	23.11 ± 0.06	Very strong	30.07 ± 0.02	Very strong
K-	0.00	-	0.00	-

Notes: F1 = Sugar palm midrib gel extract 40% ; F2 = Nutgrass gel extract 25%; F3 = Sugar palm midrib gel extract 10%; Nutgrass gel extract 25; F4 = Sugar palm midrib gel extract 20%; Nutgrass gel extract 25%; F5 = Sugar palm midrib gel extract 40%; Nutgrass gel extract 25%; K+= positive control (+), Nutrifor® Acne Gel (*Gel that sold in market with ingredients, such as Willow Bark Extract, 4-terpineol,* and *Barosma betulina leaf extract);* K- = negative control (-), Basis Gel

Table 11 showed that the highest combination of IPD is in the F2 formulation (activity of nutgrass extract). The result on two ways ANOVA test also showed sig value for 0.000 < 0.05 which means there is influence among the formulations with concentrated variation of sugar palm midrib and nutgrass extract toward bacteria inhibitory power. Due to see which formulations, F1; F2; F3; F4; and F5, that have the best inhibitory power then Duncan test is applied. The Duncan test result indicated that the highest mean value is in F2 for 27.00mm, whereas the lowest mean value is in F1 for 20.50mm.

Gel Stability Test Result

Stability test is done to know the physical and chemical stabilization from each gel formulations, including organoleptic test, pH test, homogeneity test, spread ability test, and viscosity test. The stability test on F2 is done in 8 weeks saving with room temperature for 25-30ºC. The stability test on gel preparation also done using an oven (Wiebrock) in 40ºC temperature. The observation is done every two weeks, started from the 2nd week, 4th week, 6th week, and 8th week. The gel declared as stable if there is no significant differentiation on the parameter result.

Organoleptic Stability Test Result

The result showed that there is no physical transformation on gel preparation, such as the color, smell, and texture either in room temperature 25-30ºC or in oven temperature 40ºC.

Thus, it can be said that the gel preparation is stable and can last until 8 weeks.

pH Gel Stability Test

pH stability test indicated that there is a decrease in pH value in temperature saving 40ºC. This occurred due to some factors, such as temperature, container, and active substance that oxidize during the saving. However, this decrease is still within the range of normal skin pH for 4.5-6.5. Thus, it can

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be concluded that the gel formulation has fulfilled the pH skin requirements.

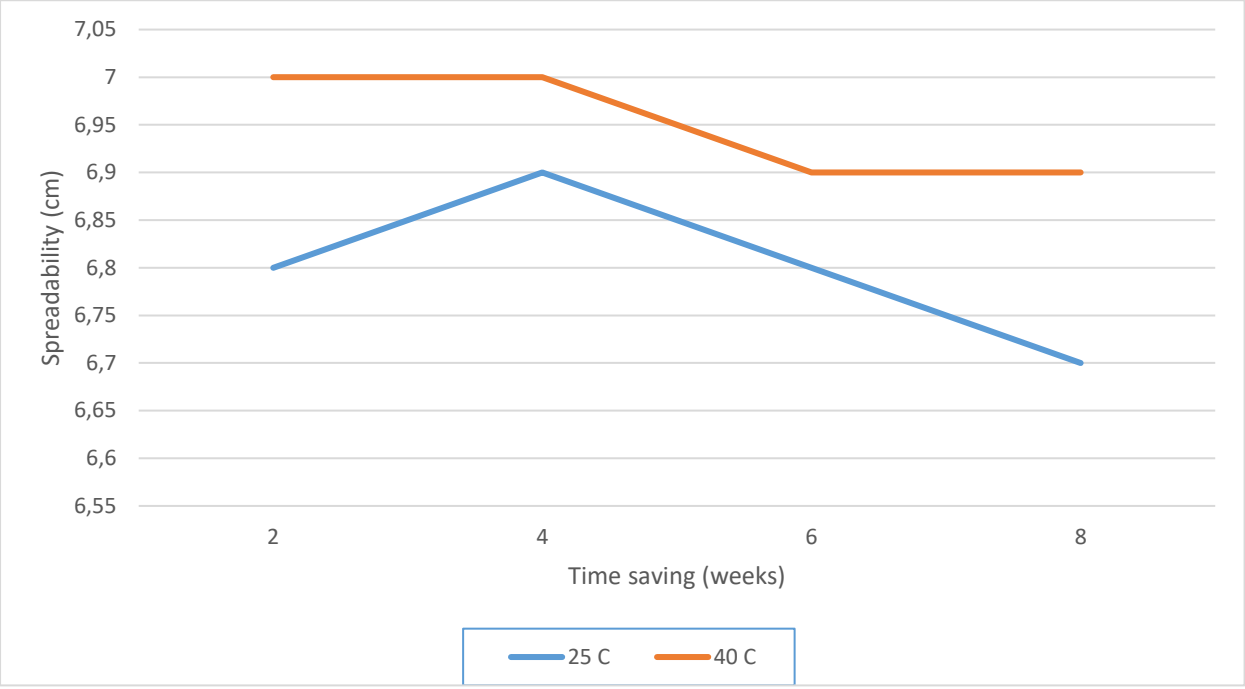

Figure 1. Spreadability ability test

Homogeneity Gel Stability Test Result

The observation found that there is no transformation on homogeneity either in room temperature or in 40ºC temperature, in which the gel preparation still having smooth surface, no rough grains, and homogeny. This happened because between the basis, the addition substance and the addictive substance, is blended evenly.

Spreadability Gel Stability Test Result

Spreadability test is done to guarantee the equalization of the gel when it is applied to the skin. The spread ability test is one of the requirement in forming the gel preparation. A good spread ability power is between 5-7 cm. the result can be seen in figure 1 below;

Viscosity Gel Stability Test

The gel viscosity stability test showed that there is viscosity reduction toward the time and temperature saving. The viscosity reduction can happen due to various factors, one of them is the preparation container that is less air-tight which allows the presence of humectant in the preparation, such as propylene glycol and glycerin, that able to absorb the moisture from outside. Based on the statistic result of the 2 ways ANOVA test, it is obtained the sig value for 0.034 < 0.05. This indicated that there is interaction between temperature and time saving. Hence, it can be concluded that there is influence between temperature and time saving

toward viscosity or the value of preparation consistency.

Irritation Test

Irritation test is done to animal to find out the irritation effect on skin and to evaluate the characteristic of a substance if it is exposed to the skin. The gel formulation used in this test is F2 with 0.5 gr dosage given to rabbit. The observation result can be seen in table 12;

Table 12. Irritation Primary Score

Group	Erythema Score			Edema Score			Mean
	24 hours	42 hours	72 hours	24 hours	42 hours	72 hours	
Rabbit 1	0,0	0,0	0,0	0,0	0,0	0,0	0,0± 0,0
Rabbit 2	0,0	0,0	0,0	0,0	0,0	0,0	0,0± 0,0
Rabbit 3	0,0	0,0	0,0	0,0	0,0	0,0	0,0± 0,0
Irritation Index 0,0± 0,0							

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From table 12 above, it is seen that in rabbit 1, 2, and 3 during 24 hours times, there is no redness in the area and no bruises (edema) in the edge of the area. These also happen in the next 48 and 72 hours. Therefore, the gel preparation is safe to use in skin.

Conclusions

In summary, the sugar palm midrib extract with 40% b/v gives concentration of minimum resistance towards *Propionibacterium acnes* for 11.54 ± 0.73mm (strong) and *Staphylococcus epidermis* for 11.10 ± 0.07mm (strong) of resistor diameter. While the nutgrass extract with 25% b/v gives minimum concentration resistance on *Propionibacterium acnes* for 12.06 ± 0.01mm (strong) and the nutgrass effect with 12.2% b/v gives minimum concentration resistance to *Staphylococcus epidermis* for 11.15 ± 0.07mm (strong). The gel formulation extract of the combination of sugar palm midrib and nutgrass extract can fulfill the physic and chemical evaluation test against *Propionibacterium acnes* and *Staphylococcus epidermis* bacteria. This gel formulation has an antagonist effectiveness in resisting the growth of *Propionibacterium acnes* and a synergic effectiveness on *Staphylococcus epidermis*. Moreover, in its statistical test, it showed that the stability test results had no effect on temperature and saving duration toward the pH value and spread power, but there is an influence on temperature and saving duration toward the viscosities value.

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The Combination of Sugar Palm Midrib Extract (*Arenga pinnata Merr.*) and Nutgrass (*Cyperusrotundus L.*) as Gel Formulation to Inhibit Acne Bacterias (*Propionibacterium acnes* and *Staphylococcus epidermidis*)

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Abstract: This study aims to determine the effectiveness of the combination gel preparation of the two extracts in inhibiting the growth of acne-causing bacteria (*Propionibacterium acnes* and *Staphylococcus epidermidis*), also to test the gel formula to meet physical and chemical parameters as well as stability to temperature and storage time, and the primary irritation test for rabbits. Each extract with different concentrations was given a positive control (clindamycin) and a negative control (sterile aquabidest), incubated, then the minimum inhibitory concentration of the two extracts was determined to determine the lowest level of the extract that still gave antibacterial activity against the tested bacteria. Then the inhibition zone was measured, then the combination of the extract was formulated in a gel preparation with excipients NaCMC, Propylene glycol, Phenoxyetanol, glycerin and Aquadest. The antibacterial activity test for gel preparations used the well method with positive gel control on the market. Then the formula evaluation includes physical, chemical and microbiological evaluations. Data were analyzed using the Two-Way Anova test. The results showed that the combination gel preparation of sugar palm midrib extract and nutgrass extract had activity against *P. acne* and *S. epidermidis* at concentrations of 25% w/v and 40% w/v. The combination gel preparation of the two extracts compared to the single extract gel preparation had increased effectiveness against *S. epidermidis* and decreased against *P. acnes* bacteria. The gel formula can meet physical and chemical parameters and is stable to temperature and storage time. The primary irritation index results obtained an irritation index score of 0.0± 0.0 which is not irritating.

Keywords: sugar palm midrib; nutgrass; acne

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