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FORMULATION AND STABILITY OF STERILE GEL OF AGARWOOD LEAVES EXTRACT (*Gyrinops Versteeg* (*Gilg*.) *Domke*) FOR DIABETIC WOUNDS

Silvi Nurafni[1*], Antonius Padua Ratu[1], Anisya Dwi Shakil[1], Siska Fitri Herdiyanti[1]
[1]*Program Studi Farmasi Sekolah Tinggi Teknologi Industri Dan Farmasi Bogor*
**Email Corresponding : silvinurafni15@gmail.com*

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ABSTRACT

Agarwood leaves contain high levels of secondary metabolites due to increased metabolic processes in agarwood trees infected with fungi. Through this metabolic process, leaves contain secondary metabolites, flavonoids, and tannins. This causes agarwood leaves to have potential as an anti-inflammatory agent for treating diabetic wounds, aimed to formulate a sterile gel preparation of agarwood leaf extract and evaluate its quality, including sterility tests and stability tests (cycling tests) including organoleptic tests, homogeneity, spreadability, adhesive power, viscosity, and pH. A sterile gel formula was prepared with an extract concentration of 4% and variations of Carbopol 940 (gelling agent), namely 0.75%, 1.0%, and 1.25%. The results showed that F1, F2, and F3 were sterile and free of bacterial and fungal growth. The stability test before and after the cycling test in organoleptic tests F1, F2, and F3 were brown, had a distinctive odor of gaharu leaves, and had a soft texture. The homogeneity tests F1, F2, and F3 Homogeneous. The pH values before the cycling test were F1 5.63, F2 4.55, and F3 4.57, whereas after the cycling test, they were F1 5.05, F2 4.87, and F3 4.63. Adhesion time before cycling test F1 02.97 seconds, F2 03.15 seconds, F3 04.86 seconds while after cycling test F1 02.64 seconds, F2 03.04 seconds, F3 03.08 seconds. Spreadability test before cycling test F1 5.4 cm, F2 4.6 cm, F3 3.7 cm, while after cycling test F1 5.0 cm, F2 4.7 cm, F3 3.5 cm. Viscosity test before cycling test F1 14.467 cps, F2 164.000 cps, F3 260,000 cps, while after cycling test F1 7,523 cps, 66,800 cps, 148,000 cps. From the results of the research on agarwood leaf extract gel, it was concluded that F1 was the best formula.

Keywords: Agarwood, Gel, Sterile, Stability, Sterility

INTRODUCTION

Agarwood also called *Gyrinops Versteeg* (*Gilg*.) *Domke* is a plant that is famous for its aromatic resin (sapwood agarwood) and has been used in traditional medicine for centuries. In addition to agarwood sapwood, research has been conducted on agarwood leaves because they contain high levels of secondary metabolite compounds due to the increased metabolic processes of agarwood trees infected with fungi. Through this metabolic process, secondary metabolite compounds such as flavonoids are distributed not only to the tree but also to the leaves. This causes agarwood leaves to have anti-inflammatory potential, with a mechanism of inhibition of the production of pro-inflammatory agents (Reactive Nitrogen Species) by macrophage cell lines due to the active ingredient content of flavonoid glycoside compounds (Yang et al., 2012).

Based on data from a previous study, it was found that the gel formula of agarwood leaf extract with a concentration of 4% had incision wound healing activity in non-diabetic and diabetic rats. The higher the concentration of the extract, the faster the healing of the incision wound and the greater the percentage reduction in the diameter of the wound. This is because the phytochemical test results of agarwood leaves contain flavonoids and tannins so that they can heal diabetic wounds (Nurafni et al., 2022).

Diabetes wounds in patients with Diabetes Mellitus cause active ulceration associated with the incidence of infection that causes more extensive wounds, resulting in ulcers and gangrene, and even amputation if the treatment is not good (Kusumastuty and Dewi, 2020).

Flavonoids act in anti-inflammatory, anti-allergic, and antioxidant processes. Tannin compounds function as astringents or tissue contractors that can cause shrinkage of skin pores, harden the skin, stop exudate and light bleeding tocover wounds, and prevent bleeding that usually occurs in wounds (Pertiwi et al., 2020).

In this study, a sterile gel of agarwood leaf extract was formulated, and sterile gel quality testing was carried out, including a gel sterility test and gel stability test with a cycling test method including organoleptic, homogeneity, dispersion, adhesion, viscosity, and pH tests. The reason for making Sterile gel preparation is intended for the treatment of diabetic wounds because non-sterile semisolid preparations can aggravate wounds. The results of this study are expected to provide an overview of the correct formula for preparing sterile preparations of agarwood extract gels that meet the quality requirements of sterile gels.

RESEARCH METHODS

Tools

Agarwood leaf (Perkebunan Gaharu, Cilendek Barat, Kecamatan Bogor Barat Kota Bogor), carbopol 940 (Sumitomo Seika Japan), glycerin (WILMAR), propylene glycol (DOW), methylparaben (UENO), triethanolamine (Merck), ethanol 96% (Brataco), ethyl acetate (HSP Pharma) aqua pro injection (Ikapharmindo putramas), aquadest (Brataco), bioplacenton^{R} (Kalbe Farma) thioglycolate media (Himedia), soybean casein media (Himedia), *Bacillus subtilis* bacteria (6051),*Candida albicans* fungus (10231), Dragendroff reagen (Sentra Teknosains Indonesia), Mayer reagen (Gifala Laboratorium Centre), Wagner reagen (Gifala Laboratorium Centre), Magnesium powder (Merck), HCl 37% (Merck), $FeCl_3$ (Merck).

Materials

Neraca analitik (Acis-AD 300i), oven (Faithful), autoclave (American 1925X), Microbiological safety cabinet (LAF type Vertical), rotary evaporator (IKA), pH meter (Xingweqiang), viscometer (Brookfield), climatic chamber (Duran), microscope binocular (SINHER), hammer mill (Elektro Motor Yuema), dehydrator (wirastar), glassware (Pyrex), waterbath (GCA Precision Scientific), mortar (Onemed), OSE, volume pipette (Iwaki), drop pipette, tube rack, incubator (Precision), porcelain cup (pyrex).

Research Procedure

1. Preparation of Agarwood Leaf Extract
   The fresh agarwood leaves were collected and washed with water. Agarwood leaves are dried with a dehydrator for 5 hours. Furthermore, the simplisia was mashed using a hammer mill tool until it became a powder and then sifted with a mesh 40 sieve to obtain fine simplisia. Then, put into a tightly closed container, Simplisia is stored in a dry, not damp place, away from direct sunlight. The process of making agarwood leaf extract uses the maceration method for 3x24 hours using 96% ethanol solvent. A total of 1.0 kg of agarwood leaf simplisia powder was put into a container, and then soaked with 96% ethanol as much as 10 L. On the 1st day soak with 96% ethanol as much as 3 L, on day 2 as much as 3 L 96% ethanol, on day 3 as much as 4 L 96% ethanol, then filtered. The resulting 96% ethanol macerate was evaporated using a rotary evaporator at ± 40 °C until a viscous extract was obtained.
2. Preparation Sterile Gel of Agarwood Leaf Extract
   Weigh Carbopol 940 and mix it with 50 mL of aquadest into a beakerglass (Mixture 1). After that dissolve methylparaben with 96% ethanol, then add glycerin and propyleneglycol stirring until homogeneous (Mixture 2) then add to the mixture 1

carbopol 940 and aquadest, stirring until homogeneous. Then, the remaining aqueous solution and triethanolamine (TEA) were added and stirred until it became a gel base. Next, the gel base is put into a beaker glass covered using aluminum foil and sterilized using an autoclave at 121ºC for 15 minutes. Agarwood leaf extract was dissolved in 96% ethanol, gradually placed into a sterile gel base, and stirred until homogeneous. Gelling was performed in a microbiological safety cabinet room (Edy et al., 2016).

3. Phytochemical Screening of Agarwood Leaf Extract
   Phytochemical screening involves the addition of reagents that are specific to several classes of chemical compounds, including alkaloids, flavonoids, saponins, tannins, and steroids/triterpenoids.
4. Gel Quality Testing
   a. Gel Sterility Test
      Sterile gel preparations were tested for sterility, including the dissolution of the test media, evaluation of the test media, and sterility testing of the preparation.
      1. Dissolution of Test Media
         Thioglycolate and soybean-casein digestion media were used for the sterility tests. Thioglycolate media is prepared by weighing 29.8 g, then dissolved in 1 L of aquadest, boiling until completely dissolved. The media is filled into a test tube, covered with cotton wrapped in gauze, and then sterilized by autoclave for 30 minutes at a temperature of 121ºC. For *Soybean-Casein Digest* media is made by weighing 30 g then dissolved into 1 L of aquadest, boiling until completely dissolved. The media is filled into test tubes covered with cotton wool wrapped in gauze, and sterilized by autoclave for 30 minutes at 121ºC (Abdassah et al., 2015).
      2. Test Media Evaluation
         The test media that has been made must be evaluated before being used in the sterility tests. Media testing included media sterility, fertility, and effectiveness. The media sterility test was carried out by taking two tubes of sterile Thioglycolate and Soybean Casein Digest media and incubated at a temperature of 30-35ºC (for Thioglycolate) and a temperature of 20-25ºC (for *Soybean-Casein Digest*) in no less than 7 days. The rest of the medium was stored in a refrigerator at 10 °C until use. Bacterial and fungal growth can be determined based on the onset of turbidity in the medium. Fertility tests were carried out by implanting *Bacillus subtilis* bacteria into two test tubes containing sterile thioglycolate media and incubated at a temperature–30-35ºC for no less than 7 days. Then, two test tubes containing *Soybean-Casein Digest* media, each implanted *with Candida albicans fungus*, were incubated at a temperature of 20-25ºC for not less than 7 days. Turbidity was observed. The effectiveness test was carried out by implanting *Bacillus subtilis* bacteria into two test tubes containing sterile thioglycolate media then each added 2 mL test preparation and then incubated at a temperature of 30-35ºC for no less than 7 days. Into two test tubes containing sterile *Soybean-Casein Digest* media, each implanted *with Candida albicans fungus* and added 2 mL of test preparation, incubated at a temperature of 20-25ºC for not less than 7 days. Turbidity was also observed (Abdassah et al., 2015).
      3. Gel Sterility Test
         Before conducting a sterility test of the preparation, the aseptic cabinet table is first wiped with 70% alcohol, then turned on an ultraviolet (UV) lamp and laminar airflow for 1 hour. Outer sterile gel packaging was cleaned with 70% alcohol. Three test tubes containing thioglycolate media, into each tube, dripped 2 mL of the test preparation, and incubated at a temperature of 30-35ºC. The same was

performed on three test tubes containing *Soybean-Casein Digest* media and incubated at a temperature of 20-25ºC. Incubation was performed for 14 days, and turbidity was observed every day. In sterility tests, it is necessary to control the sterility of the test media, positive controls, and negative controls. Positive controls, namely tubes containing thioglycolate media that have been planted with *Bacillus subtilis* indicator bacteria and tubes containing *Soybean-Casein Digest* media that have been planted with *Candida albicans* fungi, were incubated together with other test tubes. The negative control was a tube containing thioglycolate media and *a Soybean-Casein Digest* media tube, which was placed on a Bioplacenton gel and incubated together with other test tubes. Control of sterility of test media, namely tubes containing thioglycolate media and tubes containing *soybean-casein* media that are not planted but incubated with other test tubes (Abdassah et al., 2015).

b. Gel Stability Test (Cycling Test)

The preparation is stored at 4±2ºC for 24 hours, then transferred into an oven at 40±2ºC for 24 hours (one cycle). This test was carried out for 6 cycles. All quality evaluations included organoleptic, homogeneity, dispersion, adhesion, viscosity, and pH tests (Rohmani and Kuncoro 2019).

1. Organoleptic Test

   Physical observation of the gel is carried out subjectively based on the appearance of the gel, including color, odor, and texture (Edy et al., 2016).
2. Homogeneity Test

   A total of 1 g of the preparation is smeared onto the glass of the object and examined for coarse particles by palpation and observing the texture of the preparation. Homogeneous preparations are characterized by the absence of coarse particles and evenly distributed colors (Wulandari and Wahyudi, 2023).
3. Dipersion Test

   Weigh 0.5 g of the preparation and place it between 2 glass plates of the watch, At the top is placed a load of 150 grams, allowed to stand within 1 minute, and measured the diameter of the spread. This step was repeated by applying different loads until a good dispersion diameter limit was achieved. The diameter of a good cream dispersion ranges from 5-7 cm (Wulandari and Wahyudi, 2023).
4. Adhesion Time

   An adhesion test was carried out to determine how long the attachment time of the agarwood leaf ethanol extract gel was on the surface of the skin so that the active substance was in the absorbed preparations. The longer the gel adheres to the skin, the effect is caused by a large spread on the surface of the skin. A total of 0.25 grams is placed between 2 glass objects then pressed with a load of 1 kg on it and left for 5 minutes. After that, the glass object is placed on the tool and a load weighing 80 grams, the time is recorded until the glass object is released (Rohmani and Kuncoro, 2019).
5. pH Test

   Done by weighing 10 grams of the preparation dissolved in 50 mL aquadest in a beaker glass, adding aquadest up to 100 mL then mix thoroughly. The pH of the solution was measured using a standardized pH meter. Measure with a pH meter and record the pH shown. The measurement results show a pH target on the skin of 4.5 – 6.5 (Ermawati et al., 2019).
6. Viscosity Test

   The viscosity test is carried out using as much as 100 mL of gel inserted into a

tubular container and then installed spindle 64. The spindle was submerged during test preparation. The viscometer is turned on and it is confirmed that the rotor can rotate at a speed of 60 rpm. The pointing needle from the viscometer was observed, pointing to the money on the viscosity scale, and then recorded and multiplied by a factor of 100 (Astuti et al., 2017).

RESULT AND DISCUSSION

1. Phytochemical Screening of Agarwood Leaf Extract

Table I shows that the Gaharu leaf extract contains alkaloid compounds, which are shown by positive results in the Mayer reagent forming a white precipitate, Wagner reagent forming a yellow-brown precipitate, and Dragendorf reagent forming a brick-red precipitate. Positive results were also shown in the test for flavonoid compounds that formed a yellow solution, tannin compounds that formed a greenish-black solution, and triterpenoid compounds that formed a brown ring. Flavonoids have anti-inflammatory, anti-allergic, and antioxidant properties. Tannin compounds function as astringents or tissue contractors that can cause shrinkage of skin pores, harden the skin, stop exudate, and cause light bleeding to cover wounds and prevent bleeding that usually arises in wounds (Pertiwi et al., 2020).

Table I. Phytochemical Screening Result

Compound	Observations
Alkaloids	
• Mayaer	+
• Wagner	+
• Dragendorf	+
Flavonoids	+
Tannins	+
Saponins	-
Steroids	-
Triterpenoids	+

2. Sterile Gel Formula

The agarwood leaf extract was then made into 3 sterile gel formulas with the same extract concentration of 4% and variations in the concentration of Carbopol 940 (gelling agent) of 0.75%, 1.0%, and 1.25%. The formula for sterile gel is shown in Table II.

Table II. Agarwood Leaf Extract Gel Formulation

Material	Function	Gel Formula %		
		F1	F2	F3
Ekstrak	Active substances	4	4	4
Carbopol 940	Gelling agents	0,75	1,0	1,25
Glycerine	Humectants	15	15	15
Propylene glycol	Humectants	5	5	5
Methylparaben	Preservatives	0,18	0,18	0,18
Triethanolamine	pH adjustment	0,9	0,9	0,9
Ethanol 96%	Solvent	5	5	5
Aquadest	Solvent	Add	Add	Add
		100	100	100

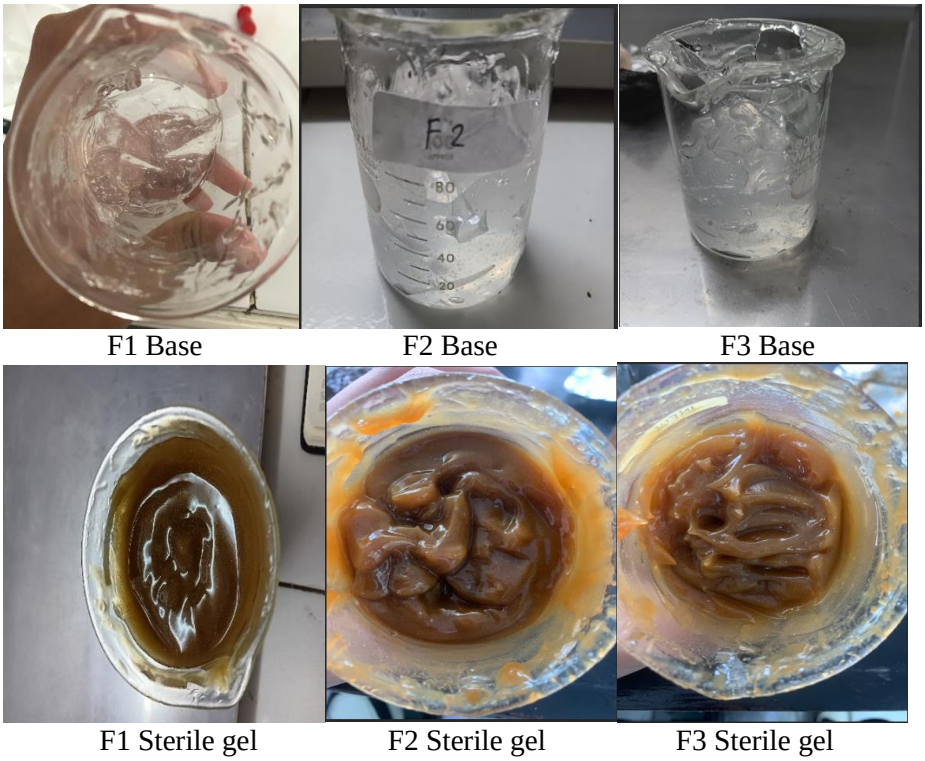

Figure 1. Sterile Gel Preparation of Agarwood Extract

3. Sterility Test

a. Media Evaluation Test

Before conducting a preparation sterility test, media evaluation tests were carried out, including sterility, fertility, and effectiveness tests on growth media.

Table III. Media Evaluation Test

Day	Soyaben Casein Digest Media (*Candida albican*)					Tiogikolat Media (*Bacillus subtilis*)				
	Sterility	Fertility	Effectiveness			Sterility	Fertility	Effectiveness		
			F1	F2	F3			F1	F2	F3
1	-	+	+	+	+	-	+	+	+	+
3	-	+	+	+	+	-	+	+	+	+
5	-	+	+	+	+	-	+	+	+	+
7	-	+	+	+	+	-	+	+	+	+

In Table III, it can be seen that the results of the media sterility test showed no growth of both bacteria and fungi, indicating that the media was sterile. The results of the media fertility test showed the growth of *Bacillus subtilis* on thioglycolate media and *Candida albicans* on *Soybean Casein Digest* media, indicating that the media was fertile. The results of testing the effectiveness of the growth media showed turbidity in Thioglycolate and *Soybean Casein-Digest* media after planting indicator germs and sterile preparations, indicating that the media can grow microorganisms even though they contain test preparations. So it can be concluded that both media can be used for further sterility testing (Abdassah et al., 2015).

b. Gel Sterility Test

After the results of the media evaluation test met the requirements, sterility tests were carried out on sterile gel preparations of agarwood leaf extract with thioglycolate

media for bacterial growth and *Soyabean Casein Digest* media for fungal growth. In sterility tests, it is necessary to control the sterility of the test media (MSC), positive control (PC), and negative control (NC). Positive control (PC), namely tubes containing thioglycolate media that have been planted with *Bacillus subtilis* indicator bacteria and tubes containing *Soybean-Casein Digest* media that have been planted with *Candida albicans* fungi, were then incubated together with other test tubes. The negative control (NC) was a tube containing thioglycolate media and *a Soybean-Casein Digest media* tube that had been given Bioplacenton gel and incubated together with other test tubes. Control of sterility of test media (MSC), namely tubes containing thioglycolate media and tubes containing *soybean-casein* media that are not planted, but incubated with other test tubes. The sterility test results of agarwood extract sterile gel preparations can be seen in Table IV and Table V showing that there was no growth of microorganisms, both bacteria and fungi, during the 14 days of sterility test testing. Sterility of wound-healing preparations is one of the conditions that must be met (Edy et al., 2016).

Table IV. Sterility Test on Thioglycolate Media

Day	MSC	PC	NC	F1			F2			F3		
				1	2	3	1	2	3	1	2	3
1	-	+	-	-	-	-	-	-	-	-	-	-
2	-	+	-	-	-	-	-	-	-	-	-	-
3	-	+	-	-	-	-	-	-	-	-	-	-
4	-	+	-	-	-	-	-	-	-	-	-	-
5	-	+	-	-	-	-	-	-	-	-	-	-
6	-	+	-	-	-	-	-	-	-	-	-	-
7	-	+	-	-	-	-	-	-	-	-	-	-
8	-	+	-	-	-	-	-	-	-	-	-	-
9	-	+	-	-	-	-	-	-	-	-	-	-
10	-	+	-	-	-	-	-	-	-	-	-	-
11	-	+	-	-	-	-	-	-	-	-	-	-
12	-	+	-	-	-	-	-	-	-	-	-	-
13	-	+	-	-	-	-	-	-	-	-	-	-
14	-	+	-	-	-	-	-	-	-	-	-	-

Table V. Sterility Test on Soybean Casein Digest Media

Day	MSC	PC	NC	F1			F2			F3		
				1	2	3	1	2	3	1	2	3
1	-	+	-	-	-	-	-	-	-	-	-	-
2	-	+	-	-	-	-	-	-	-	-	-	-
3	-	+	-	-	-	-	-	-	-	-	-	-
4	-	+	-	-	-	-	-	-	-	-	-	-
5	-	+	-	-	-	-	-	-	-	-	-	-
6	-	+	-	-	-	-	-	-	-	-	-	-
7	-	+	-	-	-	-	-	-	-	-	-	-
8	-	+	-	-	-	-	-	-	-	-	-	-
9	-	+	-	-	-	-	-	-	-	-	-	-
10	-	+	-	-	-	-	-	-	-	-	-	-
11	-	+	-	-	-	-	-	-	-	-	-	-
12	-	+	-	-	-	-	-	-	-	-	-	-
13	-	+	-	-	-	-	-	-	-	-	-	-
14	-	+	-	-	-	-	-	-	-	-	-	-

4. Sterile Gel Stability Test

a. Organoleptic Test

Organoleptic tests were carried out by observing various changes (color, odor, and texture) in the preparations.

Table VI. Organoleptic Test

Cycle to	Organoleptic								
	Color			Odor			Texture		
	F1	F2	F3	F1	F2	F3	F1	F2	F3
0	Brown	Brown	Brown	Typical agarwood leaves	Typical agarwood leaves	Typical agarwood leaves	Soft	Soft	Soft
1	Brown	Brown	Brown	Typical agarwood leaves	Typical agarwood leaves	Typical agarwood leaves	Soft	Soft	Soft
2	Brown	Brown	Brown	Typical agarwood leaves	Typical agarwood leaves	Typical agarwood leaves	Soft	Soft	Soft
3	Brown	Brown	Brown	Typical agarwood leaves	Typical agarwood leaves	Typical agarwood leaves	Soft	Soft	Soft
4	Brown	Brown	Brown	Typical agarwood leaves	Typical agarwood leaves	Typical agarwood leaves	Soft	Soft	Soft
5	Brown	Brown	Brown	Typical agarwood leaves	Typical agarwood leaves	Typical agarwood leaves	Soft	Soft	Soft
6	Brown	Brown	Brown	Typical agarwood leaves	Typical agarwood leaves	Typical agarwood leaves	Soft	Soft	Soft

Description: Cycle to 0: Color, odor, and texture of gel before *cycling test*

In organoleptic tests, it can be seen that before and after cycling tests on all formulas, the color, odor, and texture of sterile gels did not change when the gel was brown, had the characteristic odor of agarwood leaves, and had a soft texture.

b. Homogeneity Test

Based on the results of the homogeneity tests on sterile gel preparations, agarwood leaf extract before and after cycling tests on all formulas showed that the preparations were homogeneous. This is indicated by the absence of coarse grains when the preparation was applied to transparent glass. The homogeneity test aims to determine whether the active ingredients are homogeneously mixed with the base ingredients and additives during the preparation manufacturing process (Annisa et al., 2021).

Table VII. Homogeneity Test

Cycle to	Homogeneity		
	F1	F2	F3
0	Homogenous	Homogenous	Homogenous
1	Homogenous	Homogenous	Homogenous
2	Homogenous	Homogenous	Homogenous
3	Homogenous	Homogenous	Homogenous
4	Homogenous	Homogenous	Homogenous
5	Homogenous	Homogenous	Homogenous
6	Homogenous	Homogenous	Homogenous

Description: Cycle to 0: Homogeneity of gel before cycling test

c. Dispersion Test

Dispersion tests on sterile gel preparations of agarwood leaf extract before and after *cycling tests* found only F1 was qualified where the diameter of F1 dispersion ranged from 5-6 cm. F2 and F3 are not eligible. The dispersion test determines the ability of the gel to spread on the surface of the skin where it is expected that the gel can spread easily when applied to the palm, the dispersion of 5-7 cm shows a semisolid consistency that is very comfortable in use (Manus and YamLean, 2016).

Table VIII. Dispersion Test

Cycle to	Dispersion (cm)		
	F1	F2	F3
0	5,4	4,6	3,7
1	5,0	4,1	3,7
2	5,0	4,8	4,0
3	5,4	4,0	3,7
4	5,0	3,7	3,5
5	5,0	3,5	3,5
6	5	4,7	3,5

Description: Cycle to 0: Gel Dispersion Power Before Cycling Test

d. Adhesion Time

The adhesion time was determined to determine its ability to adhere to the gel on the skin surface. The results of the adhesion time before and after the cycling test showed that the three formulas met the requirements, namely, adhesion within a range of 1-5 seconds. There are no special requirements regarding the adhesion of gel preparations; however, the adhesion of gel preparations should be more than 1 second (Sukartiningsih et al., 2019). The adhesion time results of formulations 1 to 3 increased owing to the use of carbopol, which varied with higher concentrations in each formula, causing the consistency of the gel to be thicker and causing the adhesion of the gel to increase along with the increase in carbopol concentration (Wasiaturrahmah and Jannah, 2018).

Table IX. Adhesion Time

Cycle to	Adhesion (Second)		
	F1	F2	F3
0	02.97	03.15	04.86
1	03.01	03.20	04.63
2	02.56	03.34	03.69
3	01.37	02.41	02.56
4	01.87	02.38	03.71
5	01.42	02.90	04.85
6	02.64	03.04	03.08

Description: Cycle to 0: Gel Adhesion Before Cycling Test

e. pH Test

The pH test results obtained before and after *the cycling tests* from the three formulas ranged from pH to 4-6. These results indicate that all three formulas meet the skin pH criteria of 4-8 (Wasiaturrahmah and Jannah, 2018).

Table X. pH Test

Cycle to	pH		
	F1	F2	F3
0	5,63	4,55	4,57
1	5,57	4,89	4,57
2	5,73	5,41	4,57
3	5,85	5,09	4,53
4	5,23	4,93	4,75
5	5,15	4,91	4,49
6	5,05	4,87	4,63

Description: Cycle to 0: Gel pH Before Cycling Test

f. Viscocity Test (Cps)
The viscosity test results obtained before and after the *cycling test* for formulas 1, 2, and 3 are qualified, which are in the range of 7,000 – 260,000 cps (centipoise). The addition of carbopol can increase viscosity, whereas the reduction of carbopol can decrease viscosity. The viscosity test is intended so that, at the time of application, the gel feels comfortable on the skin because an excessively thick viscosity will cause difficulty in coming out of the container and its application to the hands (Wasiaturrahmah and Jannah, 2018). The viscosity test results are shown in Figure 2 below.

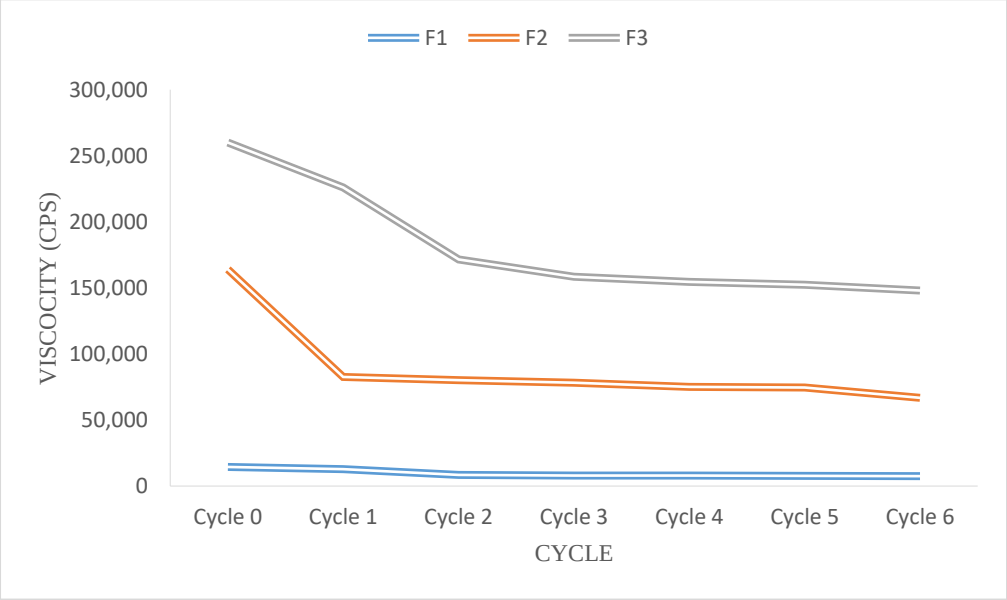

Figure 2. Viscocity Test Chart

CONCLUSION

Based on the research data that has been done, it can be concluded that the best sterile gel of agarwood leaf extract meets the gel quality requirements is formula 1 with a concentration of carbopol 940 as much as 0.75%.

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REFERENCES

Abdassah, M., Noviardani, T., Levita, J., Suherman, S.E., 2015. Formulation and Stability Study of Sulfacetamide Eyedrops. IJPST 2, 33–44. https://doi.org/10.15416/ijpst.v2i1.7808

Annisa, A., Kawareng, A.T., Indriyanti, N., 2021. Formulasi Sediaan Masker Gel Peel Off dari Minyak Atsiri Sereh (Cymbopogon citratus): Formulation of the Preparation of Peel Off Gel Mask from Cymbopogon Citratus Essential Oil (Cymbopogon citratus). Proc. Mul. Pharm. Conf. 14, 348–353. https://doi.org/10.25026/mpc.v14i1.599

Astuti, D.P., Husni, P., Hartono, K., 2017. Formulasi Dan Uji Stabilitas Fisik Sediaan Gel Antiseptik Tangan Minyak Atsiri Bunga Lavender 15.

Edy, H.J., Wahyuono, S., Nugroho, A.E., 2016. Formulasi Dan Uji Sterilitas Hidrogel Herbal Ekstrak Etanol Daun Tagetes erecta L. Jurnal Pharmacon 5.

Ermawati, D., Nurbaiti, V., Chasanah, U., 2019. Formulation of marigold (Tagetes erecta L.) flower extract in peel-off masks using polyvinyl alcohol and polyethylene glycol 6000 as the bases 9.

Kusumastuty, H., Dewi, N.S., 2020. Penggunaan Terapi Komplementer dalam Modern Wound Dressing pada Pasien dengan Luka Diabetes: Literature Review. Holistic Nursing and Health Science 3, 81–91. https://doi.org/10.14710/hnhs.3.2.2020.81-91

Manus, N., YamLean, P.V.Y., 2016. Formulasi Sediaan Gel Minyak Atsiri Daun Sereh 5.

Nurafni, S., Ratu, A.P., Marliana, T., Rahmawati, E., 2022. Uji Aktivitas Obat Herbal Gel Ekstrak Daun Gaharu (Gyrinops versteegii (Gilg.) Domke) Terhadap Luka Diabetes Pada Tikus Putih Jantan (Rattus norvegicus). JIIS 7, 360–369. https://doi.org/10.36387/jiis.v7i2.1002

Pertiwi, R., Manaf, S., Supriati, R., Saputra, H.M., Ramadhanti, F., 2020. Pengaruh Pemberian Salep Kombinasi Ekstrak Daun Morinda citrifolia dan Batang Euphorbia tirucalli terhadap Penyembuhan Luka. JFIKI 7, 42. https://doi.org/10.20473/jfiki.v7i12020.42-50

Rohmani, S., Kuncoro, M.A.A., 2019. Uji Stabilitas dan Aktivitas Gel andsanitizer Ekstrak Daun Kemangi. J. Pharm. Sci. Clin. Res. 4, 16. https://doi.org/10.20961/jpscr.v4i1.27212

Sukartiningsih, Y.N.N.T., Edi, H.J., Siampa, J.P., 2019. Formulasi Sediaan Gel Ekstrak Etanol Daun Kaliandra (Calliandra surinamensis Benth) Sebagai Antibakteri. Pha 8, 801. https://doi.org/10.35799/pha.8.2019.29356

Wasiaturrahmah, Y., Jannah, R., 2018. Formulation And Physical Properties Test Of Hand Sanitizer Gel From Bay Leaf Extract.

Wulandari, S., Wahyudi, A., 2023. Formulasi Dan Evaluasi Masker Gel Peel Off Dari Ekstrak Etanolik Kopi Robusta (Coffea Canephora Pierre Ex. A Froehner) Peaberry Sangrai: Formulation And Evaluation Of Gel Peel Off Mask From Ethanolic Extract Roasted Peaberry Robusta Coffee (Coffea canephora Pierre ex. A Froehner). MS 8, 529–538. https://doi.org/10.37874/ms.v8i2.556

Yang, X.-B., Feng, J., Yang, X.-W., Zhao, B., Liu, J.-X., 2012. Aquisiflavoside, a new nitric oxide production inhibitor from the leaves of Aquilaria sinensis. J Asian Nat Prod Res, 14 9, 867–72. https://doi.org/10.1080/10286020.2012.701209