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Evaluation of Antimicrobial Potential using Disc Diffusion Assay of Seagrape Macroalgae Extract (*Caulerpa* sp.) in the waters of Pasaran Island, Lampung as an Anti-Inflammatory Agent

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Abstract

Sea grape (*Caulerpa* sp.) is a green seaweed species with bioactive content consisting of flavonoids, terpenoids, alkaloids, and phenols. This study evaluates the antimicrobial potential of Sea*Grape macroalgae extract (*Caulerpa* sp.) obtained from Pasaran Island, Lampung. The diffusion assay method assessed the antimicrobial activity of *Caulerpa* sp. extract against Staphylococcus aureus. *Caulerpa* sp. samples were extracted using the maceration extraction method and evaporated using two methods: water bath and rotary evaporator. The results showed that *Caulerpa* sp. extract had antimicrobial activity at a concentration of 10,000 ppm, which was resistant to Staphylococcus aureus. These findings suggest that *Caulerpa* sp. from the waters of Pasaran Island has the potential to be a source of natural antimicrobial and anti-inflammatory components if the concentration of the extract is more significant, which can be further developed for applications in the health and pharmaceutical fields.

Keywords: macroalgae; Inflammation; Seagrapes; biological agents.

INTRODUCTION

Seagrape (*Caulerpa* sp.) is a type of green seaweed that lives in tropical to subtropical areas and has high potential. This plant contains high fiber, vitamins, and minerals and is a readily available source of natural antioxidants (Ridhowati & Asnani, 2016). Macroalgae belong to the Chlorophyceae class. What distinguishes *Caulerpa* sp. from other macroalgae is its ability to be sold fresh without having to be dried first, and it can even be eaten directly as fresh vegetables (Tapotubun et al., 2020). *Caulerpa* sp. is also one of the macroalgae that has received attention for cultivation because it contains chlorophyll A and B, carotene, xanthophyll, and lutein (Darmawati, et al., 2016). In Indonesian waters, there are several types of *Caulerpa* found, including *C. racemosa, C. sertularoides, C. taxifolia, C. serrulata, C. lentillifera, C. peltata, and C. cupressiodes* (Utami et al., 2021). Various regional names, such as Latoh in Java and Lawi-Lawi in Sulawesi know Seagrapes (*Caulerpa* sp.) in Indonesia. Bulung Boni (Bali) are widely distributed in marine waters and can live in tidal locations (Ines et al., 2020). Seagrapes (*Caulerpa* sp.) can be consumed directly as vegetables and traditional food in Bali, this habit has been passed down for generations because Seagrapes are believed to have properties as healthy food for diet (Julyasih & Wirawan, 2017).

Seagrapes (*Caulerpa* sp.) contain bioactive compounds that function as antibacterial, antifungal, anti-inflammatory, antidiabetic, and antioxidant (Siagian et al., 2018; Saputri et al., 2019). These bioactive compounds include flavonoids, saponins, and triterpenoids, which are known to have the ability to be antibacterial compounds (Rusli et al., 2016; Nome et al., 2019). *Caulerpa* sp. has the potential to be used as an anticoagulant for people with circulatory diseases and thrombotic disorders and hematological analysis (Arenajo et al., 2018). According to Waji and Sugrani (2009), the compounds contained in *Caulerpa* sp. also have various important roles, including protecting the integrity of cell structures, increasing the potency of vitamin C, inhibiting inflammatory processes, maintaining bone density, and having antibiotic properties.

Inflammation is the body's response to injury or tissue damage as a protective measure. This process aims to destroy or reduce the causative agent of injury or damaged tissue (Latief et al., 2019; Wang et al., 2016). One of the chemical contents that has properties as an anti-inflammatory is flavonoid. Flavonoids can inhibit

cyclooxygenase or lipooxygenase enzymes and prevent the accumulation of leukocytes in the affected area, thus acting as an anti-inflammatory (Narande et al., 2013; Agustina et al., 2015). *Caulerpa* sp. has potential as an anti-inflammatory because it contains flavonoid bioactive compounds.

The diversity of bioactive compounds from Seagrapes (*Caulerpa* sp.) has great potential as an antibacterial. Antibacterial compounds effectively control the growth of bacteria, especially bacteria that are harmful to humans. *Staphylococcus aureus* is commonly used as a target bacterium in antibacterial research. Staphylococcus aureus bacteria are pathogenic bacteria that cause disease. Therefore, it is necessary to extract natural ingredients that can be used as antibacterials to inhibit and kill these pathogenic bacteria (Marfuah et al., 2018).

Based on the description, this study aims to identify the optimal concentration of *Caulerpa* sp. extract with the best antimicrobial activity and evaluate its relationship with anti-inflammatory potential. This study is expected to provide a comprehensive understanding of the dual potential of *Caulerpa* sp. as an antimicrobial and anti-inflammatory agent for developing pharmacological natural materials.

MATERIALS AND METHODS

Materials and equipment

This research was conducted from October to December 2024 at the Oceanography Laboratory of the Marine Science Study Program, Department of Fisheries and Marine Sciences, Faculty of Agriculture, University of Lampung. The primary material used in this research was *Caulerpa* sp. macroalgae obtained from the Pasaran Island area, Teluk Betung, Bandar Lampung, Indonesia. Other materials used were technical methanol, disc paper, distilled water, Tryptone Soy Agar (Himedia), Tryptone Soya Broth (Himedia), and a *Staphylococcus aureus* bacterial culture (ACTT 6538).

The equipment used in this study are masks, latex examination gloves, blenders (Miyako), glass bottles with a capacity of 460 ml, vial bottles, funnels, analytical scales (sojilab by sojikyo), measuring cups, filter paper (Whatman), Erlenmeyer (borosil), petri dish (citotest), autoclave, tweezers, bunsen, magnetic stirrer, micropipette (DLAB), hot plate (DLAB), stirring rod, Laminar air flow, test tube rack, test tube, refrigerator, micropipette, vernier calliper, water bath (Stuart), rotary evaporator (Heidolph Laborota 4000 efficient), and aluminium foil.

Method

Sterilization of tools

The process includes preparing materials, proper packaging, and placement in an autoclave. The autoclave is filled with distilled water and set at 121°C and 15 psi pressure. Sterilization lasted for 15-20 minutes. After completion, the autoclave was turned off and allowed to stand until the pressure dropped and the temperature reached 80°C before opening.

Extraction Procedure

Sample preparation begins with the drying process, followed by making *Caulerpa* sp. macroalgae powder. After becoming a powder, extraction is carried out by the maceration method by putting the powder into two glass bottles, each as much as 50 grams. Then, 200 ml of technical methanol solvent was added, and the bottle was covered with aluminium foil. The sample was allowed to stand for 7 days.

Rotary evaporator

Samples that had been allowed to stand for 7 days were transferred into a collection flask, which was then attached to a rotary evaporator. In the water bath, the temperature was set at 70°C, and the rotation speed was 100 rpm. Slowly lower the flask into the water bath until submerged, adjusting the vacuum pressure so the sample is not mixed with condensed or contaminated solvent. When the moisture content of the sample is exhausted, turn off the machine and take the sample in the collection flask, then transfer it to the vial bottle.

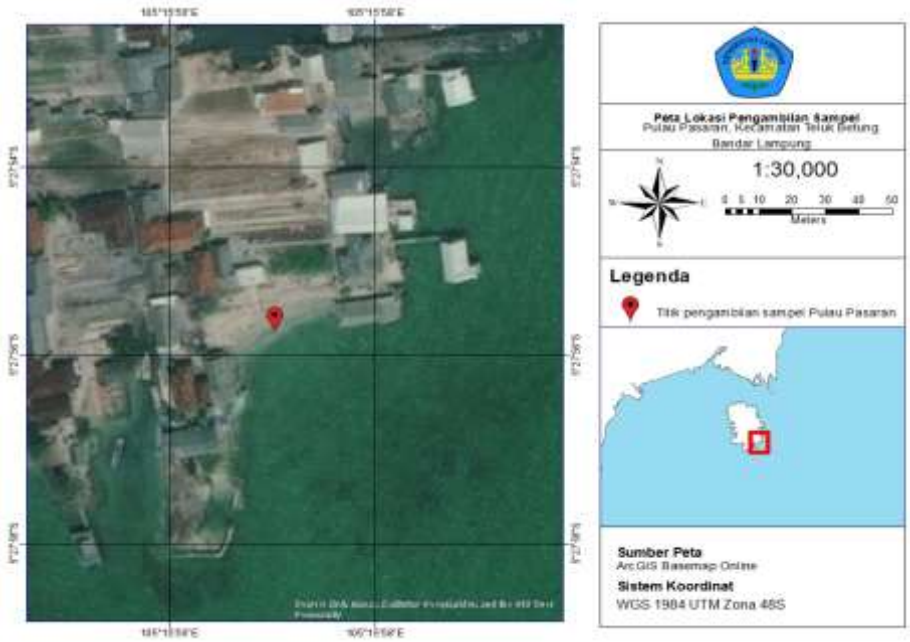

Figure 1. Map of sampling locations.

Water bath
Next, perform the water bath process, fill the water bath with enough water, and then turn it on. After reaching 70°C, put the sample bottle into the water bath. To prevent precipitation, stir the sample once every 30 minutes for 24 hours. If there is shrinkage in the sample, separate the pulp and liquid using a sieve.

Preparation of TSA and TSB media
Preparation of TSA (Tryptone Soya Agar) and TSB (Tryptone Soya Broth) begins with dissolving 4 grams of TSA powder with 100 ml of distilled water and 1.5 grams of TSB with 50 ml of distilled water. TSA was heated on a hotplate for 15 minutes, while TSB was homogenized. Both media were sterilized in an autoclave (121°C, 15 minutes). Sterilized TSA was poured into Petri dishes to solidify, while TSB was poured into test tubes. TSA was used for the activity test, and TSB was used for *Staphylococcus aureus* culture.

Staphylococcus aureus bacterial culture
Staphylococcus aureus bacteria were cultured on Tryptone Soya Broth (TSB) media. The reculturing process was done by inoculating 0.1 ml of pure isolate of *Staphylococcus aureus* into TSB media using a sterilized micropipette. The bacterial culture was then incubated in an incubator for 24 hours at an optimal temperature of 37°C to support the growth and multiplication of bacterial cells.

Disc-diffusion assay
Antibacterial testing was carried out using TSA (Tryptone Soya Agar) media with the disc diffusion method. *Caulerpa* sp. samples as much as 0.05 grams were dissolved in 5 ml of distilled water. The sample solution was then diluted to make test concentrations of 10,000, 5,000, 1,000, 100, and 10 ppm. The test bacterial isolate was *Staphylococcus aureus*, grown on TSA media. Paper dishes that have been soaked in the test solution are placed on the media containing bacteria. After that, the media was placed in an incubator. Observations were made every 24 hours for 3 days.

Minimum inhibitory zone observation
The zone of inhibition was measured every 24 hours using a caliper. Measurements were taken horizontally, vertically, and diagonally.

RESULTS AND DISCUSSION

Sample Properties
The waters of Pasaran Island became the sampling location for green macroalgae, especially *Caulerpa* sp. Table 1 shows the number of samples taken.

Table 1. Sample weight (*Caulerpa* sp.).

wet weight	dry weight	powder weight	weight of extract
4 kg	200 gram	100 gram	2,3 g (rotary) 100 ml (water bath)

The sample of *Caulerpa* sp. can be shown in Figure 2.

Profile inhibition zone
The antibacterial activity test revealed that the Seagrape (*Caulerpa* sp.) extract showed an inhibitory effect on the growth of *Staphylococcus aureus*; however, the inhibition zone formed was relatively small in size.

Observation of the diameter of the inhibition zone was carried out for three consecutive days at 24-hour intervals, and the detailed measurement results are presented in Table 2 to Table 7.

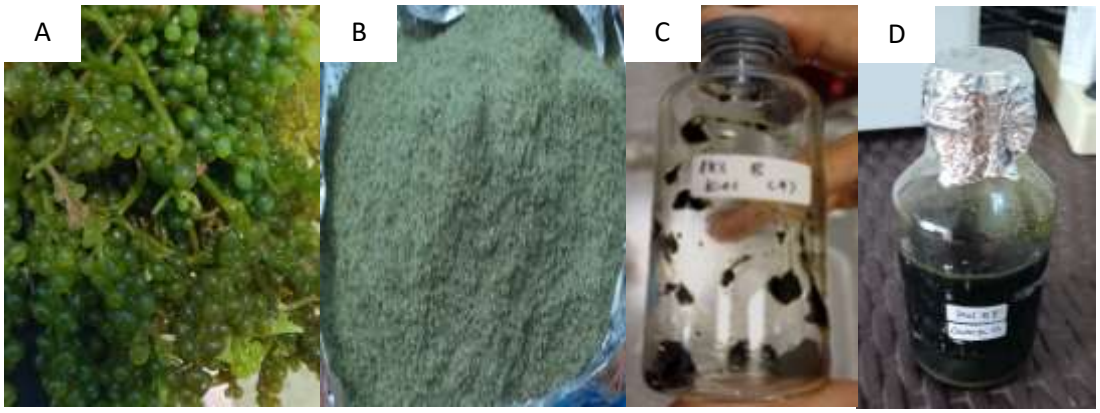

Figure 2. A: Fresh *Caulerpa* sp. sample, B: Powdered *Caulerpa* sp. sample, C: *Caulerpa* sp. sample extract results rotary evaporator method, D: *Caulerpa* sp. sample extract results water bath method.

Table 2. 24-hour observation of inhibition zone from the results extract in a rotary evaporator.

C	H	V	D	Average
10000	1,2	1,2	1,1	1,17
5000	1	1	1	1,00
1000	1	1	1	1,00
100	1	1	1	1,00
10	1,4	1,7	1,5	1,53

Description: (C): concentration; (H): horizontal; (V): vertical; (D): diagonal.

Table 3. 48-hour observation of inhibition zone from the results extract in a rotary evaporator.

C	H	V	D	Average
10000	1,4	1,5	1,4	1,43
5000	0,8	0,8	0,8	0,80
1000	0,5	0,5	1	0,67
100	0,2	0,5	0,5	0,40
10	1	1,4	1	1,13

Description: (C): concentration; (H): horizontal; (V): vertical; (D): diagonal.

Table 4. 72-hour observation of inhibition zone from the results extract in a rotary evaporator.

C	H	V	D	Average
10000	1,1	1,6	1	1,23
5000	0,7	1,2	0,6	0,83
1000	0,7	0,8	1	0,83
100	0,2	1,3	0,2	0,57
10	0,6	1,2	0,8	0,87

Description: (C): concentration; (H): horizontal; (V): vertical; (D): diagonal.

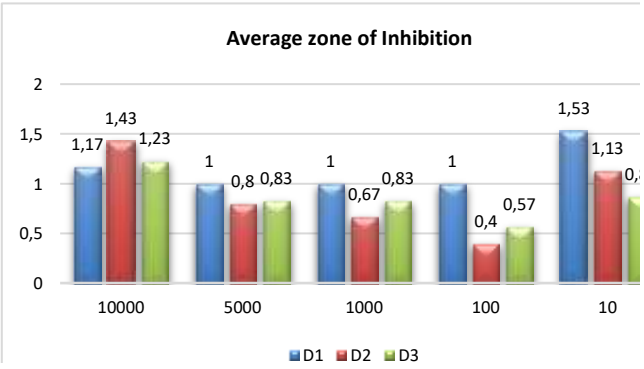

Figure 3. Average diameter of zone of inhibition by Rotary Evaporator method. Description: D1: day one observation, D2: day two observation, D3: day three observation.

Table 5. 24-hour observation of inhibition zone from the results extract in a water bath.

C	H	V	D	Average
10000	1,4	1,3	1,4	1,37
5000	1,2	1,2	1,2	1,20
1000	1,1	1,1	1,1	1,10
100	1,2	1,2	1,1	1,17
10	1,1	1,4	1,4	1,30

Description: (C): concentration; (H): horizontal; (V): vertical; (D): diagonal.

Table 6. 48-hour observation of inhibition zone from the results extract in a water bath.

C	H	V	D	Average
10000	1	1,6	0,9	1,17
5000	0,7	0,8	0,7	0,73
1000	1,3	1,3	0,7	1,10
100	1	1	0,3	0,77
10	1	0,6	1	0,87

Description: (C): concentration; (H): horizontal; (V): vertical; (D): diagonal.

Table 7. 72-hour observation of inhibition zone from the results extract in a water bath.

K	H	V	D	Average
10000	0,6	2,1	1,3	1,33
5000	1	0,8	0,7	0,83
1000	0,5	0,5	0,9	0,63
100	1	0,7	1	0,90
10	0,8	1,3	1,1	1,07

Description: (C): concentration; (H): horizontal; (V): vertical; (D): diagonal.

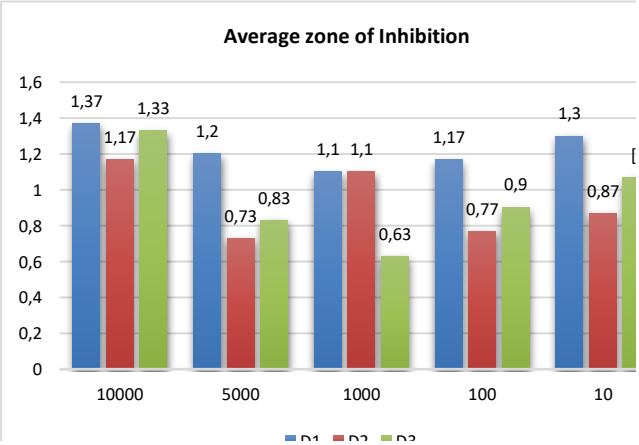

Figure 4. Average diameter of inhibition zone of water bath method. Description: D1: Day one observation, D2: Day two observation, D3: Day three observation.

Discussion

Table 1 shows the weight change of *Caulerpa* sp. samples from wet to extracted. There is a significant weight loss from the wet sample (4 kg) to powder (100 grams). After the extraction process, the sample weight was further reduced to 2.3 grams for the rotary evaporator method and 100 ml for the water bath method.

The observation results of Seagrape extract (*Caulerpa* sp.) obtained through the rotary evaporator method are presented in Tables 2, 3, and 4. On the first day of observation, the average inhibition zone measured at extract concentrations of 10,000, 5,000, 1,000, 100, and 10 respectively showed results of 1.17 mm, 1.00 mm, 1.00 mm, 1.00 mm, and 1.53 mm. Observations on the second day in order, from the highest to the lowest concentration of 10,000, 5,000, 1,000, 100, and 10, the average zone of inhibition measured was 1.43 mm, 0.80 mm, 0.67 mm, 0.40 mm, and 1.13 mm. On the third day, the average zone of inhibition measured sequentially at concentrations of 10,000, 5,000, 1,000, 100, and 10 showed results of 1.23 mm, 0.83 mm, 0.83 mm, 0.57 mm, and 1.87 mm.

The observation results of Seagrape (*Caulerpa* sp.) extract obtained through the water bath method are presented in Tables 5, 6, and 7. On the first day of observation, the average zone of inhibition varied according to the concentration of the extract. Concentrations of 10,000, 5,000, 1,000, 100, and 10 showed an average inhibition zone of 1.37 mm, 1.20 mm, 1.10 mm, 1.17 mm, and 1.30 mm, respectively. Observations on the second day showed changes in the average zone of inhibition for each concentration. Sequentially, from the highest to the lowest concentrations of 10,000, 5,000, 1,000, 100, and 10, the average inhibition zones measured were 1.17 mm, 0.73 mm, 1.10 mm, 0.77 mm, and 0.87 mm. On the third day, the average zone of inhibition sequentially at concentrations of 10,000, 5,000, 1,000, 100, and 10 showed results of 1.33 mm, 0.83 mm, 0.63 mm, 0.90 mm, and 1.07 mm.

Research conducted by Rusli et al. (2016) revealed that *Caulerpa* sp. is rich in various bioactive compounds, including flavonoids, terpenoids, alkaloids, and phenols. According to Lahay & Amiin (2023), flavonoids have a broad spectrum of health benefits. These compounds play a role in protecting the integrity of cell structures, increasing the potency of vitamin C, inhibiting inflammatory processes, maintaining bone density, and having antibiotic properties.

Staphylococcus aureus is a pathogenic microorganism capable of inducing various pathological conditions (Amiin & Lahay, 2023). Infections caused by this bacterium are characterized by specific characteristics, including inflammation, tissue death (necrosis), and abscess formation. Symptoms range from mild skin lesions such as furuncles to infections (Subekti et al., 2019).

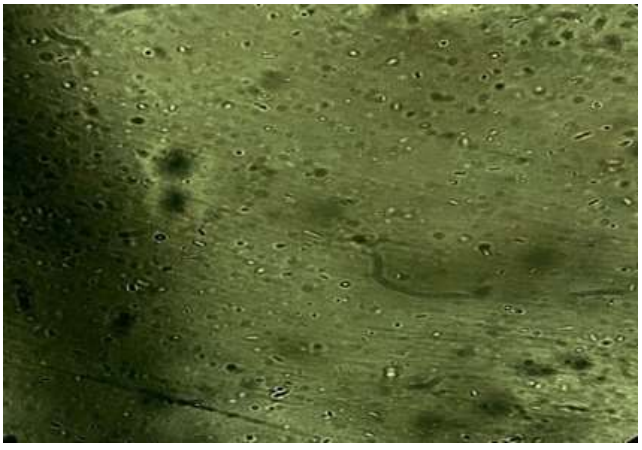

Figure 5. *Staphylococcus aureus* in the microscope

In the study of the inhibition zone test of *Caulerpa* sp. extract against *Staphylococcus aureus* bacteria using the disc diffusion assay method. The results of the inhibition zone measurement were compared with the criteria set by Lewis et al. (2023), as listed in Table 8. The results showed the level of resistance to *Caulerpa* sp. extract at the largest concentration of 10,000 ppm. The water bath method produced an average diameter of the inhibition

zone on the first, second, and third days of 1.37 mm, 1.17 mm, and 1.33 mm, respectively. Meanwhile, the rotary evaporator method produced an average inhibition zone diameter of 1.17 mm, 1.42 mm, and 1.23 mm. Based on these results, it can be concluded that the metabolite compounds contained in Seagrapes (*Caulerpa* sp.) with a concentration of 10,000 ppm tend to have less inhibitory effect on *Staphylococcus aureus* bacteria.

Resistant materials are materials that have the ability of bacteria to neutralize and weaken the performance of antibiotics (Fernandez, 2013). The nature and ability of resistant materials that can neutralize antibiotics is called the nature of resistance. Exposure to antibiotics is the initial stage of resistance (Frieri et al., 2017). The problem faced by the world today is that many microorganisms are resistant to several anti-inflammatory agents (Diaz-Granadoz et al., 2008). The increasing number of bacterial resistance in all regions of the world is a major concern of the World Health Organization (WHO), to deal with this situation WHO issued the Global Strategy for Containment of Antimicrobial Resistance, a document intended for policymakers to urge governments to take action and various efforts to prevent the occurrence of antibiotic resistance (Fernandez, 2013).

Table 8. Standardized zone of inhibition.

Inhibition Zone Diameter (mm)		
Sensitive	**Intermediet**	**Resistent**
≥ 21	16-20	≤ 15

(Lewis et al., 2023)

The inhibition zone produced tends to show an increase along with the increase in concentration from 100 to 10,000 ppm; however, at a concentration of 10 ppm, the inhibition zone produced is greater than the concentration of 100 ppm. According to Ariyanti et al. (2012), the diameter of the inhibition zone is influenced by various factors, including the rate of diffusion, characteristics of the agar medium, number of organisms inoculated, bacterial growth rate, chemical concentration, and incubation conditions. Furthermore, Elifah (2010) observed that an increase in antibacterial concentration is not always directly proportional to an increase in inhibition zone diameter. This phenomenon may be caused by variations in the diffusion speed of antibacterial compounds on agar media, as well as differences in the types and concentrations of antibacterial compounds that can produce inhibition zones with various diameters. Based on this statement, it can be concluded that the larger inhibition zone at a concentration of 10 ppm compared to 100 ppm and 1000 ppm is not always directly related to the concentration. Instead, it may be more influenced by the speed of diffusion of bioactive compounds from the *Caulerpa* sp. sample itself in the agar medium.

Based on the mean values shown in graphs 1 and 2, a comparison of the results of the methods used illustrates the varying inhibition effectiveness depending on the concentration (Achmadi et al., 2021). Although the differences between the methods are not very significant, there is a general trend of increasing inhibition zones as the concentration increases. This variation in effectiveness is evident at the various concentration levels tested, suggesting that both the concentration and the method used affect the inhibition results.

Seagrape (*Caulerpa* sp.) has flavonoid antioxidant compounds that can be anti-inflammatory (Palaniyappan et al., 2023). A fractionation (purification) process was carried out to obtain Seagrape (*Caulerpa* sp.) extract.) This process produces metabolite compounds that can be used as antiviral, antihelmintic, antibacterial, antifungal, antioxidant, anticancer, and anti-inflammatory (Pérez et al., 2016). *Caulerpa* sp. contains metabolite compounds as caulerpin; this compound makes *Caulerpa* sp. act as an anti-inflammatory agent (Palaniyappan et al., 2023). If more significant anti-inflammatory effects can be observed at higher concentrations of *Caulerpa* sp. extract than those used in the current assay, then it is likely that *Caulerpa* sp. has the potential to be developed as an anti-inflammatory agent. However, further studies are needed to confirm its effectiveness and safety at various concentration levels.

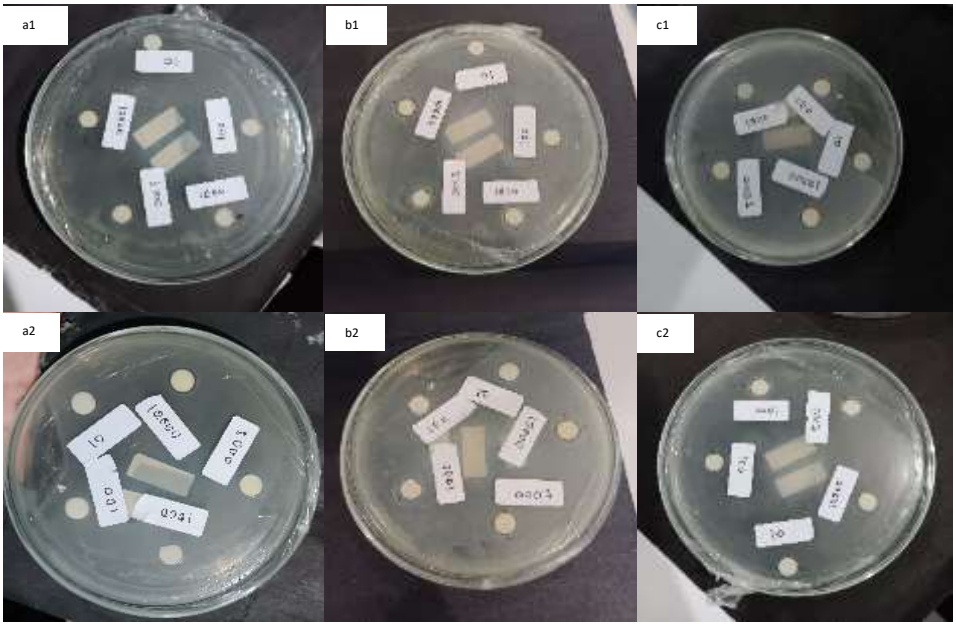

Figure 6. Observation days 1-3 a1: first-day rotary evaporator observation, b1: second-day rotary evaporator observation, c1: third-day rotary evaporator observation. a2: first-day water bath observation, b2: second day water bath observation, c2: third day water bath observation.

CONCLUSION

The results showed that in *Caulerpa* sp. extract in the water bath method, the average value of the largest inhibition zone reached 1.37 mm at a concentration of 10,000 ppm in 24-hour observation, while the smallest value was 0.63 mm at a concentration of 1,000 ppm in 72-hour observation. The rotary evaporator method produced the largest average inhibition zone value of 1.43 mm at a concentration of 10,000 ppm in 24 hours of observation, with the smallest value of 0.40 mm at a concentration of 100 ppm in 48 hours of observation. Based on the inhibition zone sensitivity standard, this study indicates that *Caulerpa* sp. extract is classified as resistant in the antibacterial activity test against *Staphylococcus aureus*. The complexity of the interaction between the extract, bacteria, and test environment emphasizes the importance of comprehensively interpreting the results. Although *Caulerpa* sp. has anti-inflammatory and antibacterial potential, its effectiveness at the tested concentrations is limited. Further studies with higher concentrations are needed to evaluate the potential of this extract as an alternative to antibiotics in the face of global resistance.

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Competing Interests: The authors state that there are no competing interests.

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