International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 17, Special Issue 3, 2025

Original Article

EFFECTIVENESS TEST OF WOUND HEALING ACTIVITY OF ETHANOL EXTRACT OF SEA GRAPE (*CAULERPA RACEMOSA*) GEL ON WISTAR RATS

SRI HARYANTI[1*], ATHIKA DARUMAS PUTRI[2], MUTMAINAH[3], MONICA CAHYANI[1]

[1]Department of Pharmacology and Clinical Pharmacy, Stifar Yaphar Semarang. [2]Department of Pharmaceutical Chemistry, Stifar Yaphar Semarang. [3]Department of Pharmaceutical Technology, Stifar Yaphar Semarang
[*]Corresponding author: Sri Haryanti; [*]Email: yantif2_stifar@yahoo.com

Received: 02 Apr 2025, Revised and Accepted: 06 Jul 2025

ABSTRACT

Objective: This study aimed to investigate the effect of varying concentrations of ethanol extract of Caulerpa racemosa on the physicochemical properties of gel formulations and their efficacy as wound healing agents, given the plant's reported antibacterial, antioxidant, and anti-inflammatory activities.

Methods: The extraction of *C. racemosa* was carried out through maceration for 3 × 24 hours using 96% ethanol as the solvent. The resulting ethanol extract was incorporated into three gel formulations containing 0.4%, 1.0%, and 1.6% extract concentrations, respectively. The formulations were evaluated for physicochemical properties, including organoleptic characteristics, homogeneity, pH, spreadability, adhesion, and viscosity. Wound healing efficacy was assessed using a wound healing model in male Wistar rats, and statistical analysis was performed to determine the significance of observed differences. Additionally, in silico analysis was conducted to assess skin permeability (logKp) of the extract compounds.

Results: Increasing the concentration of *C. racemosa* extract in the gel led to a decrease in pH, viscosity, and adhesion, while spreadability increased. Notably, at 1.6% extract concentration, the pH dropped from 7.99 to 4.62, and viscosity decreased from 54.669 cps to 13.629 cps. Wound healing time was significantly improved with higher extract concentrations: F1 (11.4 d), F2 (9.8 d), F3 (8.2 d), compared to the negative control (14.4 d) and the positive control (7.6 d). Statistical analysis showed a significant difference in healing times ($p < 0.05$), although no significant difference was observed between F3 and the positive control ($p > 0.05$). In silico findings indicated that most compounds in the extract had logKp values within the acceptable range for skin permeability (>-3.0 cm/s).

Conclusion: The ethanol extract of *C. racemosa* influenced the physicochemical properties of gel formulations and enhanced wound healing activity in a concentration-dependent manner. A 1.6% concentration was found to be the most effective, showing wound healing efficacy comparable to that of the positive control, suggesting its potential as a natural alternative for topical wound healing treatment.

Keywords: *Caulerpa racemosa*, Ethanol extract, Gel formulation, Wound healing, Physical characterization

© 2025 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (https://creativecommons.org/licenses/by/4.0/)
DOI: https://dx.doi.org/10.22159/ijap.2025.v17s3.09 Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Open wounds can lead to infection by microorganisms, potentially developing into chronic wounds characterized by prolonged healing times. Treatment is necessary to prevent chronic wound formation. One popular treatment approach is traditional medicine using local plants [1]. *Caulerpa racemosa*, or sea grape, is a relatively underutilized plant with potential medicinal properties. Phytochemical analysis of *C. racemosa* revealed the presence of saponins, steroids, alkaloids, tannins, carbohydrates, flavonoids, proteins, and caulerpin [2].

Caulerpin (100 µmol/kg, p. o.) derived from *C. racemosa* exhibited significant anti-inflammatory activity in a carrageenan-induced peritonitis model, reducing the number of recruited inflammatory cells by 48.3% [3]. *C. racemosa* has also been shown to possess analgesic and anti-inflammatory properties at oral doses of 25 and 50 mg/kg body weight [4]. Previous research has shown that *C. racemosa* is capable of killing 50% of larvae that had LC_{50} value of 44.070 ppm, indicating its potential as a larvicide [5]. Topical formulations are considered to have lower toxicity and higher efficacy due to their ability to penetrate the skin directly, making them suitable for local treatment of skin diseases [6]. Gel formulations are a preferred choice for treating external wounds. The phytochemical composition of *C. racemosa*, which is mostly polar and semipolar, makes it suitable for formulation into a hydrophilic gel base. The advantages of gel formulations include ease of application, non-greasy texture, cooling sensation upon application, and deeper penetration compared to creams [7]. Therefore, it is necessary to conduct a study to investigate the effect of *C. racemosa* extract concentration on the characteristics of gel formulations and their efficacy as wound healing agents. This study is the first to explore a gel formulation made from *C. racemosa* extract for its potential use in managing wound healing, offering a new perspective on the therapeutic applications of algal species.

MATERIALS AND METHODS

Instruments

Rotary evaporator (Heidolph) rotation speed: 10-280 rpm and water bath temperature accuracy: ±1 °C, viscometer Brookfield (dv-i prime) which has speed specifications (0.3, 0.5, 0.6, 1, 2, 4, 6, 10, 20, 50, 100 rpm), pH meter (Hanna Instrument) with pH range: 0.01 to 12.00, digital balance (O'Hauss) with an accuracy of 0.01 gs, a set of surgical tools (scalpel, surgical scissors), a set of surgical instruments (scalpel, surgical scissors), bandage, GF 254 silica plate and TLC chamber. For pharmacokinetic prediction of Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET), http://www.swissadme.ch/ and https://biosig.lab.uq.edu.au/deeppk/ were employed (the default settings were utilized to perform the prediction calculation).

Materials

Fresh sea grapes, the materials used are ethanol 96% technical grade. The ingredients for formulation are pharmaceutical-grade ingredients such as Carbopol 940 (Cosroma), Glycerin (Wilmar) and Triethanolamine (Petromas Chemicals). The materials used for phytochemical screening with technical grade were Mg powder (Merck), HCl (p) (Sigma-Aldrich), amyl alcohol (Merck), H2SO4 (Merck), FeCl3 (Merck), Dragendrof's reagent, Mayer's reagent, Bauchard's reagent, acetic acid (Merck). Bauchardat reagent, anhydrous acetic acid, n-hexane. Materials for KLT with pro analysis grade are n-butanol (Merck), methanol (Merck), ethyl acetate (Merck), acetic acid (Merck) and chloroform.

Preparation of extracts

The drying method of sea grape was carried out by air-drying in a room until dry and brittle. The dried sea grape was ground and sieved using a 30/40 mesh sieve. One hundred grams of sea grape powder (*C. racemosa*) was extracted using the maceration method with 96% ethanol as the solvent (1000 ml) for 3 × 24 h with occasional stirring. The macerate was filtered using a cotton cloth. The residue was remacerated with the addition of 96% ethanol and left for 24 h. The second macerate was filtered using a cotton cloth. The residue was remacerated for another 24 h. The obtained filtrate was evaporated using a rotary evaporator at 40 °C with a speed of 50 rpm and evaporated on a water bath until thick [8].

Formulation and preparation of gel

The gel formulation was prepared by weighing and sprinkling carbopol 940 on heated aquades and stirring quickly in a mortar until a gel mass formed. TEA was added to the formed gel mass and stirred until homogeneous. Glycerin was added to the mortar and stirred until homogeneous. The ethanol extract of sea grape was added according to the concentration of 0.4%, 1%, and 1.6%, and stirred until homogeneous [9].

Treatment of experimental animals

The experimental animals used in this study were 2-3 mo old male wistar rats weighing 100-200 g. The animals were housed in rat cages containing 5 rats per cage. The animals were provided with food and water in the form of pellets. The rats' backs were shaved at least 24 h before testing. The shaved skin area was disinfected with 70% alcohol. The area to be incised was anesthetized using ethyl chloride. The anesthetized rat's back was wounded using a surgical blade, 1 cm in length and approximately 2 mm in depth. The wound depth was ensured to be approximately 2 mm by calibrating the surgical blade, measuring 2 mm from the tip, and marking it with a marker [10].

Statistical

GraphPad Prism software (ver. 10.4.2, San Diego, Canada) was employed to analyse the statistical significances in this study. In order to determine the statistical significance of differences between the treatment and controls groups, one-way ANOVA of repeated measures analysis was performed (wound healing time). Tukey's test was used to determine multiple comparisons test (Post Hoc test). If $p<0.05$, the difference was considered statistically significant. Furthermore, data were presented in means±standard deviation (SD).

RESULTS

The extraction of sea grape using 96% ethanol solvent resulted in a yield of 5.92% whereas a study by Sherley *et al.* (2023) showed that ultrasonic and Soxhlet extraction methods yielded 16.03% and 17.85%, respectively [11]. The results of phytochemical screening and confirmation tests showed that the sea grape extract contained alkaloids, flavonoids, saponins, tannins, and steroids. The compounds alkaloids, flavonoids, saponins, tannins, and steroids are suspected to have potential as wound healing agents. Physical characterization testing of the gel included organoleptic tests, homogeneity, pH, spreadability, adhesion, and viscosity. The gel base had a pH of 7.99±0.21, which decreased upon addition of sea grape extract, resulting in pH values of 6.28±0.43 for F1, 5.58±0.30 for F2, and 4.62±0.27 for F3. The spreadability of the gel formulations increased with the addition of sea grape extract, ranging from 2.98±0.16 for the base gel to 4.45±0.25, 5.39±0.08, and 6.46±0.27 for F1, F2, and F3, respectively (fig. 1).

The addition of extract led to a reduction in adhesiveness, with F1, F2, and F3 exhibiting values of 3.89±0.04, 2.57±0.07, and 1.18±0.10, respectively, which were lower than the base gel's adhesiveness of 5.62±0.08. Upon incorporation of extract, the gel's viscosity decreased significantly, ranging from 36.015±983.979 for F1 to 25410.8±427.184 for F2 and 13629±426.502 for F3, compared to the base gel's viscosity of 54669±2.145.932 (fig. 1).

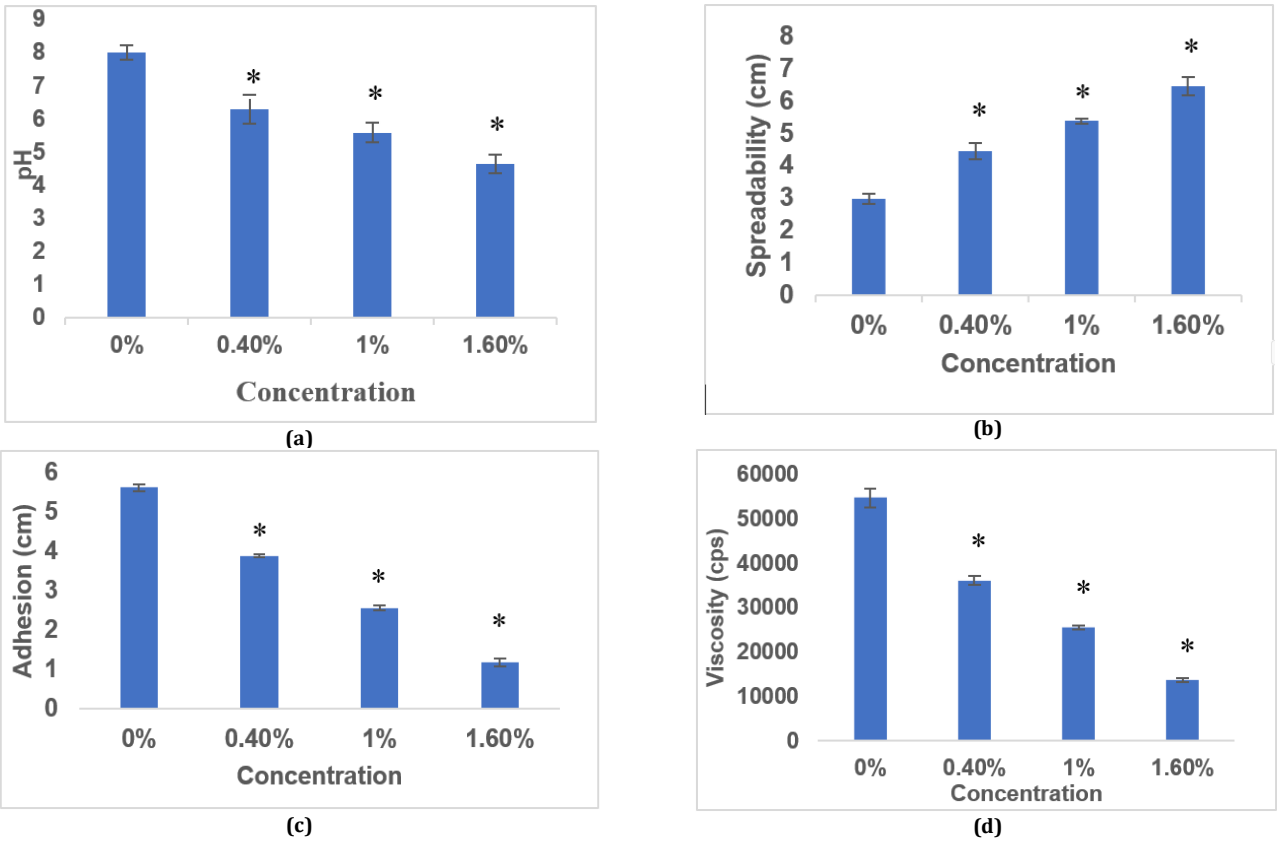

Fig. 1: Characteristics of gel (a) pH of gel ethanol extract of sea grapes (b) Spreadability of gel ethanol extract of sea grapes (c) Adhesion of gel ethanol extract of sea grapes (d) Viscosity of gel ethanol extract of sea grapes

Table 1: Formulation of gel ethanol extract of sea grapes

Component	K (-)	F1	F2	F3
Ethanol extract of sea grapes	-	0.4%	1.0%	1.6%
Carbopol	2%	2%	2%	2%
Triethanolamine	2.75%	2.75%	2.75%	2.75%
Glycerin	15%	15%	15%	15%
Aquadest ad	100%	100%	100%	100%

Description: F1: Gel ethanol extract of sea grapes 0.4%, F2: Gel ethanol extract of sea grapes 1.0%, F3: Gel ethanol extract of sea grapes 1.6%, K (-): Gel base

A wound was considered completely healed when it had fully closed [1]. The efficacy of sea grape ethanol extract gel in wound healing was evaluated in male rats, showing a complete close (fig. 2).

The effectiveness of wound healing is indicated by the average wound healing time. Based on the test results, there was a significant difference in wound healing time among each treatment. The average wound healing time is expressed in days. The average wound healing time can be seen in fig. 3.

F3 and K(+) did not yield a statistically significant difference (p = 0.3691). The F3 treatment demonstrated wound healing efficacy that was nearly equivalent to the positive control. In contrast, the F1 and F2 treatments exhibited wound healing effects, but they were less pronounced compared to the positive control. The negative control group had the longest wound healing time. The statistical analysis revealed a significant difference in healing time ($p<0.05$) (table 2).

(a) (b) (c)

Fig. 2: Incision wound after F1 treatment. (a) First day wound (b) Wound after 6 d (c) Healed wound

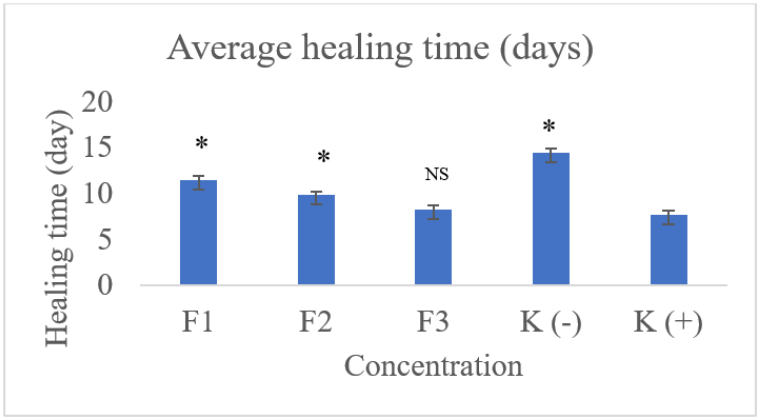

Fig. 3: Average healing time; *p<0.0001, NS = non-significant, n=5, one-way ANOVA followed by Tukey's test), Description: F1: Sea grape ethanol extract gel 0.4%, F2: Sea grape ethanol extract gel 1%, F3: Sea grape ethanol extract gel 1.6%, K (-): Negative control (Gel base), K (+): Positive control (Binasol gel)

Table 2: Results of statistical analysis on wound healing time

Treatment	Adjusted p-value
F1 VS F2	0.0006
F1 VS F3	<0.0001
F2 VS F3	0.0006
F1 VS K(-)	<0.0001
F2 VS K(-)	<0.0001
F3 VS K(-)	<0.0001
F1 VS K(+)	<0.0001
F2 VS K(+)	<0.0001
F3 VS K(+)	0.3691 (NS)
K(-) VS K(+)	<0.0001

Description: F1: Sea Grape Ethanol Extract Gel 0.4%, F2: Sea Grape Ethanol Extract Gel 1%, F3: Sea Grape Ethanol Extract Gel 1.6%, K (-): Negative Control (Gel Base), K (+): Positive Control (Binasol Gel)

One-way ANOVA followed by Tukey's post-hoc test revealed statistically significant differences among the treatment groups, typically toward negative control group K(-) with all p-values<0.0001. These results indicate the reliability of the observed effects and validate the outcomes of the gel formula of sea grape extract to accelerate wound healing time compared to K(-). In addition, positive cotrol and F3 group showed no significant difference, as the healing times were nearly identical. This suggests that F3 formula can accelerate wound healing to a similar extent as K(+).

Table 3: ADMET calculation of estimated compounds of sea grape ethanolic extract

Compound	Property	Model name	Predicted value (log Kp)	Property	Model name	Cate-gory
3-Hexadence	Absorption	Skin permeability	-2.167	Toxicity	Skin Sensitisation	Yes
Propiolactone	Absorption	Skin permeability	-3.193	Toxicity	Skin Sensitisation	No
N-(4-Tolylsulfonyl)azetidin-3-one	Absorption	Skin permeability	-2.851	Toxicity	Skin Sensitisation	No
1H-Tetrazole	Absorption	Skin permeability	-3.692	Toxicity	Skin Sensitisation	No
N-Methylene-2-phenylethanamine	Absorption	Skin permeability	-1.248	Toxicity	Skin Sensitisation	Yes
Butanenitrile	Absorption	Skin permeability	-2.391	Toxicity	Skin Sensitisation	No
Hexadecane	Absorption	Skin permeability	-2.7	Toxicity	Skin Sensitisation	Toxic
Neophytadiene	Absorption	Skin permeability	-3.28	Toxicity	Skin Sensitisation	Toxic
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	Absorption	Skin permeability	-2.629	Toxicity	Skin Sensitisation	Yes
Hexadecanoic acid, ethyl ester	Absorption	Skin permeability	-3.41	Toxicity	Skin Sensitisation	Toxic
Acetic acid	Absorption	Skin permeability	-2.54	Toxicity	Skin Sensitisation	No
2-(Benzyloxy) ethanamine	Absorption	Skin permeability	-3.31	Toxicity	Skin Sensitisation	Yes

In order to understand how the bioactive compounds contented in *Caulerpa racemosa* extract work as wound healing, ADMET study should be performed on each single compound, particularly as these were revealed through GC-MS analysis. However, due to limitations in performing our own phytochemical analysis, GC-MS data utilized in this study were derived from previously published work by Palaniyappan and coworkers (2023), who contributed elucidating the phytochemical composition of *Caulerpa racemosa* [20]. The phytochemical dataset was employed to infer potential bioactive compounds contributing to the current observed outcomes. Log Kp of all of the compounds do not exceed-5.0 cm/s and most of them were calculated greater than-3.0 cm/s, i. e., 3-hexadecane (-2.167 cm/s), N-(4-tolysulfonyl)azetidine-3-one (-2.851 cm/s), butanenitrile (-2.391 cm/s). Some compounds may indicate to trigger skin sensitization, which suggest that it may cause allergic reaction (table 3). While some compounds are considered safe, such as propiolactone, acetic acid, N-(4-tolysulfonyl)azetidine-3-one, 1H-tetrazole.

DISCUSSION

Organoleptic testing is an initial evaluation used to assess the physical appearance of the gel preparation. The results of the observation showed that the higher the concentration of sea grape ethanol extract added to the gel preparation, the greener the color and the thinner the consistency of the preparation. This preparation has a characteristic smell of sea grape, but the smell produced is not as strong as the thick extract. The homogeneity of the gel can be seen from the absence of particles that clump in the gel preparation. The homogeneity of the gel ensures that the active ingredients are evenly distributed in the base, so that the amount of active ingredients in each use is equal. The test results showed that the sea grape ethanol extract is evenly dispersed into the gel base.

The pH test is intended to ensure that the pH of the preparation is suitable for the skin pH, which is 4-8. If the pH is too high, it will cause the skin to dry out, but if the pH is too acidic, it will cause skin irritation [12]. The change in pH occurs because the pH of the sea grape ethanol extract is acidic, which affects the pH of the preparation that has a basic base pH.

The spreadability test is intended to ensure the even distribution of the gel when applied to the skin and to determine the softness of the gel preparation [13]. The spreadability of the preparation is good if it is 4-7 cm [7]. The larger the amount of sea grape extract added to the gel preparation, the thinner the preparation becomes, and the softer its consistency. This causes the spreadability of the preparation to increase. The higher the concentration of sea grape extract added, the greater the spreadability of the preparation.

The adhesion test is a test used to determine whether the preparation can adhere perfectly when applied to the skin. The preparation is declared to have good adhesion if it can adhere for more than 1 second [12]. The test results showed that the higher the addition of sea grape extract in the preparation, the smaller the adhesion produced. The change in adhesion is caused by the consistency of the gel, the addition of sea grape extract makes the gel thinner.

This test aims to determine the resistance of the gel preparation to flow. The viscosity of the gel preparation is good according to Nardi-ricart *et al.,* which is 1000-100000 cPs for medium to high viscosity [14]. Viscosity testing was conducted using spindle No. 64 at room temperature (± 25 °C) with a speed range of 1-20 rpm. The test results showed that the higher the concentration of sea grape ethanol extract used, the lower the viscosity of the preparation. This is caused by the pH of the sea grape ethanol extract, which tends to be acidic, so that the gel base fails to form a gel mass. The carbopol base will form a gel consistency at a pH of 6-11 [15, 16], so that the addition of acidic extract will cause a decrease in viscosity.

This study was conducted using male Wistar rats as test animals after obtaining ethical clearance with the number 52/YP-NA/KEPK/STIFAR/EC/XII/2023. Macroscopic observation was conducted to observe the changes in the wound from the initial incision to complete closure. Visual observation can be used as a reference to determine the condition of the wound. Initially, the wound was open, wide, and bleeding on the first day. Subsequently, the wound underwent a gradual healing process, characterized by drying and cessation of bleeding. As the wound edges slowly closed, a scab eventually formed. Over time, the scab decreased in size as it gradually peeled off [17].

All the doses used in this regard were determined accroding to our previous optimisation experiments. The wound healing process in the K(-) group was a natural bodily process to repair or regenerate cells without the aid of active compounds, resulting in a slower healing process. In contrast, F3 exhibited the fastest wound healing ability among all formulations, comparable to that of K(+). Statistical analysis of wound healing time revealed significant differences between the K(-) and K(+) groups, as well as between the F1, F2, and F3 groups and K(-). These findings demonstrate that sea grape ethanol extract can enhance wound healing rates.

This study used Binasol Gel as a positive control (K+) due to its utilization of secondary metabolite compounds as active ingredients, making it a suitable comparator for the sea grape extract gel. The binahong extract, as the active compound in Binasol Gel, has been

proven to accelerate wound healing due to its content of alkaloids, saponins, and flavonoids, which can function as anti-inflammatory, analgesic, and antibacterial agents. Complications arising from wounds can lead to prolonged healing times. The phytochemical content in sea grape extract influences the formation of new tissue. Saponins and steroids can accelerate the epithelialization process and facilitate collagen synthesis [18].

The flavonoid compounds present in the sea grape extract possess anti-inflammatory activity through the inhibition of cyclooxygenase and lipoxygenase enzymes [19, 20]. Flavonoids decreased IL-1β and TNF-α levels in blood serum, in addition to decreasing the transcriptional activity of NFκB in blood mononuclear cells [21]. Flavonoid were found to inhibit the release of rat mast cell histamine [22]. Inhibitory activity was associated with the following structural features: the presence of a C-4 keto group, a reduced double bond at position C-2 to C-3 in the y-pyrone ring, and an appropriate pattern of hydroxylation in the B-ring. Several flavonoids are relatively selective inhibitors of 5-lipoxygenase, which initiates the biosynthesis of leucotrienes, compounds considered to be of importance in mediator release, inflammation and immediate-type hypersensitivity reaction [23]. The tannins present in the sea grape extract can act as an astringent, thereby helping to stop bleeding. The astringent properties of tannins can form macromolecules, which can accelerate the hemostatic process. The inflammatory stage triggers a detrimental response, necessitating treatment or prevention to alleviate uncomfortable symptoms. Alkaloids can also play a role as antibacterial and anti-inflammatory agents. Antibacterial properties are necessary for preventing infection [24].

Based on the previous study that have identified the main compounds of ethanolic extract of C. racemose [25], we leveraged their findings to substantiate our investigation. While earlier studies focused solely on the compositional analysis of sea grape extract, we extended this foundation by incorporating in silico absorption, distribution, metabolism, excretion, toxicity (ADMET) analyses with our *in vivo* pharmacokinetic evaluations to assess the potential of the plant for topical formulations. This integrative approach allows us to elucidate the molecular-level mechanisms underlying the wound healing properties of sea grape, thereby reinforcing its therapeutic potency.

The GC-MS analyses performed by Palaniyappan *et al.* [25] showed that ethanolic extract of sea grape contained 12 compounds, namely 3-hexadecene, acetic acid, 2-(benzyloxy)ethanamine, propiolactone, N-(4-Tolysulfonyl)azetidine-3-one, 1H-tetrazole, N-methylene-2-phenylethanamine, butanenitrile, hexadecane, neophytadiene, 3,7,11,15-tetramethyl-2-hexadecen-1-ol, and hexadecanoic acid. In our study, the ethanol extract of sea grape was made into a gel preparation for anti-inflammatory treatment, which was intended for topical administration. Therefore, skin permeability (logKp) was calculated through *in silico* ADMET for each compound herein since it affects the drug/compound delivery and efficacy once being applied and penetrated the skin.

The logKp of most of the compounds were calculated greater than-3.0 cm/s, which are within the acceptable range of skin permeability [26, 27]. Indeed, for a compound to be considered successful in topical administration, these values should be in the range of-0.7659 to-5.218 cm/s [28, 29]. These compounds may be partially attributed to the effectiveness of the *in vivo* wound healing performance as observed in this study, particularly as shown from their predicted skin permeability reflected by logKp values from ADMET analyses. Compounds with higher logKp values (within that range) indicate greater potential for transdermal penetration, which is critical for delivering active agents effectively to the wound site, e. g., 3-hexadence with logKp of-2.167 and propiolactone with logKp of-3.193. The improved permeability enhances the local bioavailability of therapeutic compounds, potentially accelerating tissue repair and modulating inflammation more efficiently. Therefore, the favorable wound healing outcomes may correlate with the presence of compounds exhibiting higher logKp values, supporting their topical efficacy in the gel formulation. Further, some compounds were calculated for their possibility to trigger skin sensitization that may suggest allergic reaction. However, some components considered safe, such as propiolactone, acetic acid, N-(4-tolysulfonyl) azetidine-3-one, 1H-tetrazole. In this regard, we formulated the extract in hydrogel form, which can create a barrier between the drug and skin, thus minimizing irritation.

In addition, although tannins and flavonoids were not directly identified in the GC-MS analysis, likely due to their non-volatile nature and the absence of derivatization, the total flavonoid and tannins content are possibly to be measured through complementary assays, such as colorimetry test [25]. The GC-MS results were considered to reflect the volatile compounds profiles of the extract, which may act synergistically with non-volatile flavonoids not identified by this technique.

CONCLUSION

The results showed that increasing concentrations of ethanol extract of *C. racemosa* decreased pH, viscosity, and adhesion, while increasing spreadability. The effective concentration of sea grape ethanol extract (*C. racemosa*) in gel form that demonstrates a wound healing effect on the skin of male Wistar rats is 1.6%. Based on *in silico* ADMET studies, the ethanolic extract of sea grape is potential to be formulated in the form of gel due to potential skin permeability. This study has several limitations, notably the absence of histological analysis and a relatively small animal sample size. Future studies should focus on conducting clinical trials and in-depth mechanistic investigations to build upon these findings.

LIST OF ABBREVIATIONS

GC-MS: Gas Chromatography-Mass Spectrometry, F1: Gel ethanol extract of sea grapes 0.4%, F2: Gel ethanol extract of sea grapes 1.0%, F3: Gel ethanol extract of sea grapes 1.6%, TEA: Triethanolamine, TLC: Thin Layer Chromatography, ADMET: Absorption, Distribution, Metabolism, Excretion, and Toxicity, LC50: Lethal Concentration 50.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

Sri Haryanti: Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Athika Darumas Putri: Validation, Methodology, Writing-Review and Editing, Data curation. Mutmainah: Validation, Methodology, Formal analysis, Conceptualization. Monica Cahyani: Validation, Methodology, Investigation, Formal analysis, Data curation, Writing-Original Draft.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Nefai MS, Emmanuel MH, TJG. Wound healing and antifungal evaluations of some surveyed plants of Gwadabawa/Illela communities of sokoto state Nigeria. Int J Pharm Pharm Sci. 2023 Feb 1;15(2):18-24. doi: 10.22159/ijpps.2023v15i2.45973.
2. Kumar JG, Umamaheswari S, Kavimani S, Ilavarasan R. Pharmacological potential of green algae *Caulerpa*: a review. IJPSR. 2019;10(3):1014-24.
3. De Souza ET, De Lira DP, De Queiroz AC, Da Silva DJ, De Aquino AB, Mella EA. The antinociceptive and anti-inflammatory activities of caulerpin a bisindole alkaloid isolated from seaweeds of the genus *Caulerpa*. Mar Drugs. 2009 Dec 1;7(4):689-704. doi: 10.3390/md7040689, PMID 20098607.
4. Chowdhury KR, Alim MA, Zaman NR, Nayem A, Audri EM, Mondal P. Screening of anti-inflammatory and analgesic activities of *Caulerpa racemosa* from the bay of Bengal, Bangladesh. Biores Commun. 2023 Jun 20;9(2):1330-9. doi: 10.3329/brc.v9i2.67090.
5. Giwo E, Ti Ha N, Wirawan IG, Wijaya IN, Suada IK. Identification of phytochemical compounds of ethyl acetate extract of bulung Anggur (Caulerpa sp.) by GC-MS and toxicity test on artemia Salina Leach shrimp larvae. Int J Biosci Biotech. 2023 Apr 21;10(2):33. doi: 10.24843/IJBB.2023.v10.i02.p05.

6. Nikam V, Maniyar S. Formulation development and evaluation of niosomal gel of collective anti-fungal agents. Asian J Pharm Clin Res. 2022;15(2):64-74. doi: 10.22159/ajpcr.2022.v15i2.43484.
7. Rudra A, Shoeb A. Development formulation and evaluation of aloe vera tooth gel: an antimicrobial study. Int J Pharm Pharm Sci. 2023 Oct 1:15(10):6-12. doi: 10.22159/ijpps.2023v15i10.48765.
8. Wayal V, NV T. Assessment of wound healing activity of potent herbal extracts gel in albino Wistar rat. Asian J Pharm Clin Res. 2022 Aug 7;15(8):109-13. doi: 10.22159/ajpcr.2022.v15i8.44914.
9. Bhattacharya S, Paul B, Biswas GR. Development and evaluation of hydrogel of an anti-fungal drug. Int J Pharm Pharm Sci. 2023 Oct 1;15(10):29-33. doi: 10.22159/ijpps.2023v15i10.48728.
10. Khan AA, Kumar V, Singh BK, Singh R. Evaluation of wound healing property of terminalia catappa on excision wound models in Wistar rats. Drug Res (Stuttg). 2014 May;64(5):225-8. doi: 10.1055/s-0033-1357203, PMID 24132703.
11. Sherley HNPE, Agustin M. The effect of extraction methods on total phenolics and antioxidant activities in *Caulerpa racemosa* (Forsskal) J. Agardh extracts. Natural Products. 2023 May 8;30(2). doi: 10.17533/udea.vitae.v30n2a349405.
12. Parvez Baig R, Wais M. Formulation and development of proniosomal gel for topical delivery of amphotericin. Int J Pharm Pharm Sci. 2022 Jan 1;14(1):37-49. doi: 10.22159/ijpps.2022v14i1.43237.
13. Sarfaraz MSZ, Doddayya H. Preparation and characterization of fluconazole topical nanosponge hydrogel. Int J Pharm Pharm Sci. 2024 Apr 1:16(4):18-26. doi: 10.22159/ijpps.2024v16i4.50589.
14. Nardi Ricart A, Linares MJ, Villca Pozo F, Perez Lozano P, Sune Negre JM, Bachs De Miquel L. A new design for the review and appraisal of semi-solid dosage forms: semi-solid control diagram (SSCD). PLOS One. 2018 Sep 7;13(9):e0201643. doi: 10.1371/journal.pone.0201643, PMID 30192759.
15. Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. 6th ed. London: Pharmaceutical Press London; 2009.
16. Sheskey PJ, Hancock B, Moss G, Goldfarb D. Handbook of pharmaceutical excipients. 9th ed. London: Pharmaceutical Press; 2020.
17. Pandey R, Kumar Gupta R. Models of rat skin wound healing: an overview. Asian J Pharm Clin Res. 2023 Mar 7;16(3):1-5. doi: 10.22159/ajpcr.2023.v16i3.46339.
18. Irfan F, Jameel F, Khan I, Aslam R, Faizi S, Salim A. Role of quercetin and rutin in enhancing the therapeutic potential of mesenchymal stem cells for cold-induced burn wound. Regen Ther. 2022 Aug 23;21:225-38. doi: 10.1016/j.reth.2022.07.011, PMID 36092499.
19. Komala I, Betha OS, Muliati F, Ni Mah M. Antioxidant and anti-inflammatory activity of the Indonesian ferns, *Nephrolepis falcata* and *Pyrrosia lanceolata*. International Journal of Pharmacy and Pharmaceutical Sciences. 2015;7(12):162-5.
20. Fristiohady A, Wahyuni W, Malik F, La Ode Muhammad, Purnama J, Sadarun B. Anti-inflammatory activity of marine sponge Callyspongia Sp. and its acute toxicity. Asian J Pharm Clin Res. 2019 Oct 23;12(12):97-100. doi: 10.22159/ajpcr.2019.v12i12.34737.
21. Chekalina N, Burmak Y, Petrov Y, Borisova Z, Manusha Y, Kazakov Y. Quercetin reduces the transcriptional activity of NF-kB in stable coronary artery disease. Indian Heart J. 2018 Sep 1;70(5):593-7. doi: 10.1016/j.ihj.2018.04.006, PMID 30392493.
22. Basumatary H, Bordoloi P, Deka D. Evaluation of anti-inflammatory activity of aqueous extract of mimosa pudica on swiss albino mouse. Int J Pharm Pharm Sci. 2024 Aug 1;16(8):12-6. doi: 10.22159/ijpps.2024v16i8.51414.
23. Harborne JB. The flavonoids. London: Champmanand Hall; 1986.
24. Tiwari A, Tiwari A, Sharma S. Wound healing potential of acacia catechu in excision wound model using *in vitro* and *in vivo* approach. Int J Pharm Pharm Sci. 2023 Dec 1;15(12):27-36. doi: 10.22159/ijpps.2023v15i12.49539.
25. Palaniyappan S, Sridhar A, Kari ZA, Tellez Isaias G, Ramasamy T. Evaluation of phytochemical screening, pigment content *in vitro* antioxidant antibacterial potential and GC-MS metabolite profiling of green seaweed Caulerpa racemosa. Mar Drugs. 2023;21(5):278. doi: 10.3390/md21050278, PMID 37233472.
26. Aonsri C, Kuljarusnont S, Tungmunnithum D. Discovering skin anti-aging potentials of the most abundant flavone phytochemical compound reported in Siam violet pearl a medicinal plant from Thailand by in silico and *in vitro* assessments. Antioxidants (Basel). 2025;14(3):272. doi: 10.3390/antiox14030272, PMID 40227229.
27. Chen CP, Chen CC, Huang CW, Chang YC. Evaluating molecular properties involved in transport of small molecules in stratum corneum: a quantitative structure activity relationship for skin permeability. Molecules. 2018;23(4):911. doi: 10.3390/molecules23040911, PMID 29662033.
28. Alves VM, Muratov E, Fourches D, Strickland J, Kleinstreuer N, Andrade CH. Predicting chemically induced skin reactions. Part II: QSAR models of skin permeability and the relationships between skin permeability and skin sensitization. Toxicol Appl Pharmacol. 2015;284(2):273-80. doi: 10.1016/j.taap.2014.12.013, PMID 25560673.
29. Arshad U, Shafiq N, Parveen S, Rashid M. Discovery of novel dihydro-pyrimidine hybrids: insight into the design, synthesis, biological evaluation and absorption, distribution metabolism and excretion studies. Future Med Chem. 2024;16(19):1949-69. doi: 10.1080/17568919.2024.2389767, PMID 39263831.