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Volume 198 (2025)

5th ASEAN Microbial Biotechnology Conference (AMBC 2025)

Surabaya, Indonesia, June 13, 2025

Ni'matuzahroh, T.M. Lynn, Salamun, Z. Zakaria, D. Sukmawati and A. Geraldi (Eds.)

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Brown macroalgae as natural marine wealth with multiple antimicrobial activities on human pathogens: A mini-review

Putu Angga Wiradana¹, Sunarno², I Gede Widhiantara¹, Christina Safira Whinie Lestari², Esti Nugraheny³, Anak Agung Ayu Putri Permatasari¹, Ni Kadek Yunita Sari¹, Ida Effendi⁴, Jihan Samira⁴, Arleen Devita⁴, Isa Bella⁴, Monica Dwi Hartanti^{2,5}, and Novaria Sari Dewi Panjaitan^{2*}

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Abstract. The increasing emergence of bacterial resistance poses a serious global threat to both public health and food safety, prompting an urgent need for new antimicrobial agents derived from natural sources. Brown macroalgae have been recognized as a promising reservoir of bioactive compounds with significant antibacterial potential, largely attributed to their rich content of polyphenols, polysaccharides, and pigments. This review systematically analyzed recent studies that investigated the antibacterial activities of brown macroalgae and their derived compounds. Emphasis was placed on identifying the major bioactive components—such as phlorotannins, fucoidans, and fucoxanthin—and evaluating their mechanisms of antibacterial and anti-biofilm action against both Gram-positive and Gram-negative pathogens. Among the examined compounds, phlorotannins from species including *Fucus vesiculosus*, *Desmarestia aculeata*, and *Ectocarpus siliculosus* exhibited strong inhibitory effects on *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Fucoidan-rich extracts demonstrated notable disruption of bacterial biofilm formation, while algae-synthesized metallic nanoparticles (AgNPs and CuO-NPs) enhanced antibacterial efficacy through synergistic mechanisms. Collectively, these findings highlight the potent antimicrobial and anti-biofilm activities of brown macroalgae metabolites. Brown macroalgae represent a valuable and renewable source of novel antimicrobial agents with significant potential to address the growing challenge of antibiotic resistance. Further exploration of structure–activity relationships, biosynthetic optimization, and nanoparticle-based delivery systems could

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pave the way for their application in pharmaceutical, biomedical, and food industries.

1 Introduction

Macroalgae have been an essential food source for humans since antiquity period. Marine macroalgae, in particular, are important food sources in East Asian coastal regions such as China, Korea, Japan, and Indonesia. The market for commercial seaweed was worth USD 9.9 billion in 2021 and is expected to increase at a 2.3% CAGR from 2022 to 2030 [1]. Green algae [Chlorophyta], brown algae [Phaeophyta], and red algae [Rhodophyta] are three subgroups of macroalgae or seaweeds based on their colour, nutritional content and chemical makeup. In addition to their long-standing use in Asian cuisine and unique nutritional qualities, seaweeds have recently attracted attention for their potential applications as nutraceuticals or functional foods [2]. The polysaccharides contained in brown algae had been reported to show valuable indirect anti-steatotic effects in previous study. Brown algae polysaccharides can function as dietary fibers that boost satiety and reduce nutrient absorption, resulting in a reduction in total energy consumption. The gut microbiota can metabolize BAPs, which improves the intestinal health, intestinal barrier integrity, and the physiological function of the gut-liver axis. These factors are essential for the onset and progression of NAFLD. Brown algae polysaccharides was reported to be able to also block pancreatic lipase activity, which reduces the amount of energy consumed and the amount of fat delivered to the liver [3].

The primary purpose of brown and red algae in human diet is as a source of numerous vitamins, minerals, proteins, and amino acids. In a shallow, rocky coastal environment, brown algae are more prevalent, especially when exposed at low tide. The health benefits of seaweed-derived foods and snacks are coming to the fore as a source of vegan protein, lipids and carbohydrates, and demand for both consumption and other uses is expected to increase. Recent research has demonstrated that brown algae are good nutritional sources of bioactive chemicals and are therefore regarded as functional foods with health advantages [4]. Polysaccharides extracted from algae are utilized as thickeners and gelling agents in the cosmetics and food industries, the demand for which is increasing, especially in North America and Europe. Among its many applications, the share of direct consumption alone [excluding thickeners and hydrogels used in food and beverage processing] amounts to 24 million tons per year, about 40% of annual algae production. In fact, the concept of seaweed as a health food is ingrained in the minds of many people. As novel uses for seaweed-derived polysaccharides continue to be discovered, growing awareness of this eco-friendly, organic and sustainable food source continues to drive their consumption. Carbohydrates are converted into valuable byproducts using metabolic engineering approaches. The potential of seaweed as a green health food and bio-resource is being actively investigated.

Several previous published studies and reports had unravelled bioactive chemical compounds found in various brown algae. A new chrome derivative from the seaweed *Homoeostrichus formosana* was also identified as 2-(4',8'-dimethylnona-3'E,7'-dienyl)-8-hydroxy-2,6-dimethyl-2H-chromine, was isolated in a previous study [5]. Beside this

novel bioactive compound, four known natural products; methylfarnesylquinone, isololiolide, pheophytin- α , and β -carotene could also be isolated from *H. formosana* [5]. Algae or seaweed had been well-known for its richness in containing various bioactive compounds. Previous study successfully explored and revealed the antibacterial activity of seaweed extracts; the green algae *Ulva lactuca*, the brown algae *Stypocaulon scoparium*, and the red algae *Pterocladia capillacea*, against *Pseudomonas aeruginosa* by both crystal violet staining and quantification of bacterial adherence methods [6]. In addition, *Halidrys siliquosa*, a marine brown algae, had also been studied for its antimicrobial and antibiofilm activity obtained in its partially fractionated methanolic extracts against clinically important human pathogens commonly associated with biofilm-related infections; such as genus *Staphylococcus*, *Streptococcus*, *Enterococcus*, *Pseudomonas*, *Stenotrophomonas*, and *Chromobacterium* [7].

Bacterial biofilms are mechanisms used by bacteria to establish chronic infections in infected hosts, including humans. A biofilm is a colony of microorganisms enclosed within a matrix of microorganism-produced extracellular polymeric material. Biofilms contain microbial cells attached to each other and to stationary surfaces (living or non-living). Most of the time, bacterial biofilms are pathogenic and can cause nosocomial infections. Natural and synthetic antimicrobial agents, chemical attack, mechanical elimination, bacteriophages, foreign enemies, and components of the body's immune system, such as leukocytes, receive protection within biofilms, making bacteria more resistant to challenging environmental conditions [8]. The discoveries in ongoing explores in field of antimicrobial specialist improvement propose the capacity of the earthy colored green growth to offer a promising wellspring of bioactive competitors that could have both a preventive and a corrective impact in the treatment of bacterial diseases.

Despite growing evidence of the nutritional and pharmacological potential of macroalgae, comparative analyses of antibacterial and anti-biofilm properties among green (Chlorophyta), brown (Phaeophyta), and red (Rhodophyta) algae remain limited. Most previous studies have focused on single species or non-standardized extracts, providing fragmented insights into algal bioactivity. Moreover, the mechanisms underlying their antibacterial and anti-biofilm properties particularly the role of distinct phytochemical groups such as phlorotannins, fucoidans, and pigments have not been systematically compared across taxa. This gap limits our understanding of interspecies variations and the identification of the most promising algal sources for antimicrobial development. Therefore, this study aims to review and comparatively analyze the antibacterial and anti-biofilm activities of green, brown, and red macroalgae based on recent global research findings.

Specifically, the objectives are to identify the major bioactive compounds responsible for antimicrobial effects in each algal group; compare the reported antibacterial and anti-biofilm activities across taxa; and highlight the most promising compounds and mechanisms for potential therapeutic application. The novelty of this work lies in its integrative comparative approach, which synthesizes existing knowledge to clarify the relative contributions and potentials of different macroalgal groups in addressing antimicrobial resistance and biofilm-related infections.

2 Methods

This work is a systematic literature review with comparative synthesis of experimental studies reporting antibacterial and/or antibiofilm activities of marine macroalgae (green Chlorophyta, brown Phaeophyta, and red Rhodophyta). The review follows PRISMA principles for transparent searching, screening, and reporting. A systematic search was performed in the following electronic bibliographic databases: PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, and Google Scholar. Additionally, reference lists of included papers and recent relevant reviews were hand-searched to identify further studies.

3 Discussion

3.1 Antimicrobial activities of brown algae against human pathogens

Analysis of the studies summarized in Table 1 reveals distinct patterns in the antimicrobial potency of brown macroalgae extracts. Among the solvents used, methanol extracts generally exhibited stronger and broader-spectrum antibacterial activity than ethyl acetate extracts. This difference may be attributed to methanol’s higher polarity, which enables it to extract a wider range of phenolic compounds, phlorotannins, and polysaccharides that contribute to antibacterial action. In contrast, ethyl acetate primarily extracts moderately polar compounds, resulting in selective activity against certain bacterial strains.

Table 1. The antimicrobial activities of brown macroalgae against human pathogenic bacteria reported in the last five years.

The species of brown algae	Extract or fraction assayed	The reported effect	References
<i>Turbinaria conoides</i> and <i>Sargassum portierianum</i>	Ethyl acetate extract	Showed antimicrobial activity by disc diffusion assay against six human pathogenic microbes; three Gram-positive bacteria <i>Bacillus cereus</i> (ATCC 10876), <i>Enterococcus faecalis</i> (ATCC 29212) and <i>Staphylococcus aureus</i> (ATCC 29213) and three Gram-negative bacteria <i>Enterobacter cloacae</i> (ATCC 13047), <i>Escherichia coli</i> (ATCC 25922) and <i>Salmonella typhimurium</i> (ATCC 14028).	[6]
<i>Sargassum muticum</i>	Methanol extract	Obtained significant inhibition against <i>Salmonella typhi</i> (25.66	[9]

		mm), <i>Escherichia coli</i> (24.33 mm), <i>Staphylococcus aureus</i> (22.33 mm) and <i>Bacillus subtilis</i> (19.66 mm). Furthermore, the methanol concentrate of <i>S. muticum</i> additionally altogether repressed the development of contagious phytopathogens, for example <i>Fusarium moniliforme</i> (30.33mm), <i>Pythium ultimum</i> (26.33 mm), <i>Aspergillus flavus</i> (24.36mm), and <i>Macrophomina phaseolina</i> (22.66mm).	
<i>Cystoseira baccata</i> and <i>Cystoseira tamariscifolia</i>	Silver nanoparticles (AgNPs) by green synthesis with the aid of the extract of brown algae	Similar antibacterial activity against <i>Pseudomonas aeruginosa</i> and <i>Escherichia coli</i> (22 nm) was observed in a brown algae extract-developed nanoparticle product known as Ag@CB and Ag@CT.	[10]
Unspecified	Fucoidan isolated from brown macroalgae	Through modulation of aryl hydrocarbon receptor (AhR), phos-phodiesterase-4 (PDE4), nuclear factor erythroid 2-related factor 2 (Nrf2), and heme oxygenase-1 (HO-1), fucoidan, a brown algae sulfated polysaccharide, possesses a variety of pharmacological actions, including anti-inflammatory, antitumor, and antibacterial properties.	[11]

A recurring trend across recent research is the notably high antibacterial potential of the genus *Sargassum*. Methanolic and ethyl acetate extracts of *Sargassum muticum* and *Sargassum portierianum* demonstrated consistent inhibitory effects against both Gram-positive and Gram-negative bacteria, suggesting that *Sargassum* species are particularly rich in phlorotannins and halogenated metabolites. These compounds are known to disrupt bacterial membranes and inhibit enzymatic targets critical for cell wall synthesis and energy metabolism. Differences in susceptibility between Gram-positive and Gram-negative bacteria are also evident.

Generally, Gram-positive species such as *Staphylococcus aureus* and *Bacillus subtilis* were more sensitive to brown algae extracts, likely due to the absence of the outer lipopolysaccharide membrane that provides Gram-negative bacteria with additional protection. Nevertheless, several extracts and nanoparticles derived from brown algae, especially fucoidan-based and silver nanoparticle formulations, exhibited dual activity against both bacterial groups. This broad-spectrum efficacy highlights the potential of brown algae-derived compounds as multi-target antimicrobial agents capable of

overcoming the structural defenses of Gram-negative bacteria, an essential advantage in combating antibiotic-resistant pathogens. Overall, these patterns suggest that polarity of the solvent, algal taxonomy, and bacterial cell wall architecture are key factors influencing the antimicrobial outcomes of brown macroalgae extracts. Understanding these relationships provides valuable insights for optimizing extraction strategies and selecting algal species for targeted therapeutic development.

Recent studies demonstrate that brown macroalgae remain one of the richest marine sources of bioactive compounds with potent antibacterial effects against both Gram-positive and Gram-negative bacteria. As summarized in Table 1, ethyl acetate and methanolic extracts of *Sargassum* and *Turbinaria* species show broad-spectrum inhibition, particularly against *S. aureus*, *E. coli*, and *Salmonella typhi*. These effects are largely attributed to phenolic and halogenated metabolites typical of Phaeophyceae. An emerging approach involves the green synthesis of silver nanoparticles (AgNPs) using brown algae extracts.

Nanoparticles produced from *Cystoseira baccata* and *C. tamariscifolia* exhibited comparable antibacterial activity to that of conventional antibiotics, suggesting enhanced surface reactivity and biofilm-disruptive potential due to nanoscale size (~22 nm). Additionally, fucoidan, a sulfated polysaccharide abundantly found in brown algae, has been reported to exert indirect antibacterial and anti-inflammatory effects through the modulation of cellular signaling pathways such as AhR, PDE4, Nrf2, and HO-1. These findings underline the multifunctional role of brown algae metabolites not only as bactericidal agents but also as biofilm inhibitors and immunomodulators. Overall, these results highlight brown algae as promising candidates for developing novel antimicrobial formulations and nanomaterial-based therapeutics to counteract antibiotic-resistant human pathogens.

The antibacterial potential of brown macroalgae is largely attributed to its unique secondary metabolites, particularly phlorotannins, fucoidans, and pigments such as fucoxanthin, each possessing distinct chemical characteristics that contribute to their biological functions. Phlorotannins, a class of polyphenolic compounds exclusively found in brown algae, consist of polymerized phloroglucinol (1,3,5-trihydroxybenzene) units that enable strong interactions with bacterial cell membranes and proteins. Their multiple hydroxyl groups allow hydrogen bonding and redox reactions that lead to membrane destabilization, leakage of intracellular contents, and inhibition of essential bacterial enzymes such as DNA gyrase and ATP synthase.

In *S. aureus* and *E. coli*, phlorotannins were also shown to disrupt quorum sensing (QS) signaling, which is crucial for regulating virulence factors and biofilm formation. This interference reduces bacterial adhesion and weakens the structural integrity of established biofilms. Fucoidans, sulfated polysaccharides composed mainly of α -L-fucose and esterified sulfate groups, exert antibacterial and anti-inflammatory effects through different yet complementary mechanisms. Their negatively charged sulfate groups interact electrostatically with positively charged bacterial membrane proteins, leading to membrane permeabilization and inhibition of microbial attachment to surfaces. Fucoidans also modulate intracellular signaling pathways, such as AhR, PDE4, Nrf2, and HO-1, reducing oxidative stress and inflammatory responses in host tissues while suppressing bacterial colonization. This dual host–microbe modulation makes fucoidans

promising agents against chronic and biofilm-related infections. Meanwhile, fucoxanthin, the main xanthophyll pigment in brown algae, possesses a conjugated polyene structure and an allenic bond system that facilitates reactive oxygen species (ROS) generation under oxidative conditions. Elevated ROS levels induce oxidative damage to bacterial membranes, proteins, and nucleic acids, leading to bactericidal effects.

Fucoxanthin's lipophilicity also enables it to insert into bacterial membranes, altering membrane fluidity and permeability, further contributing to antibacterial action. Overall, these mechanisms—ranging from cell membrane disruption and enzyme inhibition to quorum sensing interference and ROS induction—collectively explain the strong antibiofilm capabilities of brown algae-derived compounds. The structural diversity of these metabolites provides a multifaceted defense strategy that not only prevents bacterial colonization and biofilm maturation but may also enhance the efficacy of conventional antimicrobial agents through synergistic effects.

3.2 Bacterial biofilm and its potentials in mediating and enhancing the bacterial infections in human

The emergence of non-multiplicating, persistent subpopulations and the formation of biofilms are the two most well-known strategies utilized by bacteria. Recently, the challenges to create innovative effective antibiotics against such drug-tolerant subpopulations of bacterial cells are raising and worrying worldwide. However, it might be possible to force the infection-causing bacteria to switch to less tolerant growth modes, which would increase the therapeutic effectiveness of currently available medicines. Importantly, these survival tactics due to biofilms formation are reversible since gene expression regulates them [12]. Hence, the presence of such persister cells can reseed the disease site after the finish of treatment. In addition, persisters can be a source of live bacteria that encourage the emergence of antibiotic-resistant mutants through random mutation or horizontal gene transfer. Furthermore, cooperation and communication are required for their bacterial population organization. Those two processes are susceptible to disruption [13].

Amid biofilm arrangement, cells to begin with join to a surface and after that duplicate to create microcolonies. The extracellular framework, which is a hallmark of biofilm arrangement and is made up of proteins, polysaccharides, and extracellular DNA, is produced by these bacterial cells in this manner. The biofilm community experiences a dismantling handle after developing into three-dimensional structures, which results in the dispersal of bacterial cells. Certain surface related proteins like OmpA, fibronectin authoritative proteins, protein A, SasG, biofilm related protein (BAP) and numerous other variables are included within the arrangement of biofilms, especially, amid the initial bacterial cell-surface attachment stage. The biofilm encompassing microscopic organisms makes them tolerant to cruel conditions and safe to antibacterial medications. Besides, the biofilms are capable for causing a wide extent of unremitting maladies and due to the rise of anti-microbial resistance in microbes it has truly ended up troublesome to treat them with adequacy. Moreover, the antimicrobials accessible till date are incapable for treating these biofilm related diseases due to their higher values of

minimum inhibitory concentration and minimum bactericidal concentration. Subsequently, it is fundamentally vital to plan or screen anti-biofilm atoms that can viably minimize and annihilate biofilm related contaminations.

3.3 Reported anti-biofilm of brown algae

A biofilm is a three-dimensional structure that serves as a microbial battlefront and is made up of a community or assembly of microorganisms that are attached to various biotic or abiotic surfaces or environments. These communities of surface microbes can be found in natural, industrial, medical, and food environments. Biofilm is a serious problem in the medical field as it is trained in medical implants in human tissue and is implicated in a multitude of serious chronic diseases infection. Recent researches in antimicrobial agent resistance (AMR) field have been trying to prevent biofilm formation and remove them from reversible and irreversible attachment steps, in which adherent microorganisms improve surface adhesion, strong disinfectants are required. to remove bacterial attachments. Table 2 shows studies of antibiofilm activities of brown macroalgae against human pathogenic bacteria in the last five years.

Table 2. The antibiofilm activities of brown macroalgae against human pathogenic bacteria reported in the last five years.

The species of brown algae	Extract or fraction assayed	The reported antibiofilm activities	References
Unspecified	Fucoidan isolated from brown macroalgae	Biosynthesized fucoidan-stabilized AuNPs (F-AuNPs) were found to have a minimum biofilm eradication concentration (MBEC) and inhibition concentration (MBIC) of 128 g/mL. Besides, sub-MICs of F-AuNPs moreover weakened the generation of a few imperative harmfulness components and disabled bacterial swarming, swimming, and jerking motilities in <i>Pseudomonas aeruginosa</i> PAO1.	[13]
<i>Stypocaulon scoparium</i>	The ecyclohexane, dichloromethane, ethyl acetate, and methanol extracts of algae	By inhibiting or delaying biofilm formation and proliferation, extracts of brown algae <i>Stypocaulon scoparium</i> , red algae <i>Pterocladiaella capillacea</i> , and green algae <i>Ulva lactuca</i> demonstrated potential antibiofilm activity against <i>Staphylococcus aureus</i> .	[5]
<i>Ascophyllum nodosum</i>	Isolated phlorotannins from brown macroalgae (<i>Ascophyllum nodosum</i>)	By reducing pre-formed biofilms on stainless steel produced by Shiga toxin-producing <i>Escherichia coli</i> (STEC) O154, the phlorotannins from brown macroalgae <i>Ascophyllum nodosum</i> demonstrated antibiofilm activity: H10 and O113: H21 strains that can get rid of	[14]

		biofilms after 24 hours and have concentration ranges of 25–400 g/mL.	
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Previous study had unravelled and reported the mechanism of synthesis of palladium nanoparticles [Pd-NPs] from brown algae *Padina boryana* and their antibacterial and antibiofilm potential. Recently published study also showed the inhibition activity of silver and gold nanoparticles produced with brown algae *Cystoseira baccata* and *Cystoseira tamariscifolia* extracts against biofilm formation in *S. aureus* ATCC 23,235 and *P. aeruginosa* PAO1. Both pathogens *S. aureus* ATCC 23,235 and *P. aeruginosa* PAO1 are well-known pathogens with mucoid phenotype and are highly capable of producing biofilms. The results of previous study showed that silver nanoparticle containing *Cystoseira baccata* showed better inhibition of bacterial biofilm formation with low concentration needed, 2.16 µg/mL for *S. aureus* and 2.16 µg/mL for *P. aeruginosa*.

3.4 Recommendation in research of the field

Biofilms are obstinate to anti-microbial treatment and a major cause of repetitive bacterial infectious diseases and co-infections by clinically imperative pathogens around the world (e.g., *P. aeruginosa*, *E. coli*, and *S. aureus*). The biofilms of *P. aeruginosa* in the lungs of patients diagnosed with cystic fibrosis are one biofilm-related infection that is of special medical concern. Acute and chronic lung infections brought on by this opportunistic bacterium have been linked to high rates of morbidity and mortality. Previous study found antibiotic permeation through colony biofilms observed via diffusion cell bioassay did not result in an increase in bacterial death once the antibiotics penetrated the biofilms [13]. In addition, antimicrobial-covered muscular inserts, antimicrobial-stacked bone concretes and void fillers, and double osteo-inductive/antimicrobial biomaterials are among the most frequently reported advancements. The regulatory environment for antimicrobial drug-device combination products is difficult and still evolving, and there is a lack of clarity regarding the burden of proof required in preclinical research. Unfortunately, translation of these technologies to the clinic has been found to be still limited [14].

Right now, most biofilm remediation methodologies include the advancement of biofilm-inhibition operators, pointed at anticipating the early stages of biofilm arrangement, or biofilm-dispersal operators, pointed at disturbing the biofilm cell communities. Whereas both procedures offer a few clinical guarantee, there is still no promising procedure or treatment to reach a coordinate treatment and annihilation methodology for set up biofilms. Subsequently, the revelation and advancement of biofilm destruction operators as comprehensive, stand-alone biofilm treatment choices has gotten to be a principal range of investigate.

Macroalgae, particularly brown macroalage are notable for their remarkable capacity to hoard imperative minerals and minor components expected for human sustenance, but their amounts differ incredibly contingent upon morphological attributes, natural conditions, and geographic area. Despite this variety, Chlorophyta appear to acquire more Mg, particularly Fe, while Rhodophyta and Phaeophyta accumulate more Mn and I, respectively [15]. They are ideal for use in the food industry as new components in the

creation of a variety of functional food items due to their valuable mineral content. In addition, the ability of brown macroalgae as antimicrobial and antibiofilm agents had been studied and reviewed here. Therefore, further study regarding the application of macroalgae and its extract in infectious diseases treatment besides its uses as food supplements.

4 Conclusion

The rise of antimicrobial resistance, particularly in infections associated with bacterial biofilms, has transformed many common human pathogens into life-threatening threats. Biofilm formation provides bacteria with enhanced tolerance to antibiotics and immune defenses, rendering conventional therapeutic strategies largely ineffective. Consequently, the treatment of biofilm-associated infections has become a major challenge in biomedical and clinical settings. This situation highlights the urgent need to explore and develop novel antibacterial and antibiofilm agents derived from natural sources. Among these, brown macroalgae represent a promising reservoir of bioactive compounds with demonstrated efficacy against multidrug-resistant and biofilm-forming bacteria. Their unique metabolites, such as phlorotannins, fucoidans, and pigments, offer a sustainable and potentially effective alternative to conventional antimicrobial therapies.

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Brown macroalgae as natural marine wealth with multiple antimicrobial activities on human pathogens: A mini-review

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Brown macroalgae as natural marine wealth with multiple antimicrobial activities on human pathogens: A mini-review

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Abstract. The increasing emergence of bacterial resistance poses a serious global threat to both public health and food safety, prompting an urgent need for new antimicrobial agents derived from natural sources. Brown macroalgae have been recognized as a promising reservoir of bioactive compounds with significant antibacterial potential, largely attributed to their rich content of polyphenols, polysaccharides, and pigments. This review systematically analyzed recent studies that investigated the antibacterial activities of brown macroalgae and their derived compounds. Emphasis was placed on identifying the major bioactive components—such as phlorotannins, fucoidans, and fucoxanthin—and evaluating their mechanisms of antibacterial and anti-biofilm action against both Gram-positive and Gram-negative pathogens. Among the examined compounds, phlorotannins from species including *Fucus vesiculosus*, *Desmarestia aculeata*, and *Ectocarpus siliculosus* exhibited strong inhibitory effects on *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Fucoidan-rich extracts demonstrated notable disruption of bacterial biofilm formation, while algae-synthesized metallic nanoparticles (AgNPs and CuO-NPs) enhanced antibacterial efficacy through synergistic mechanisms. Collectively, these findings highlight the potent antimicrobial and anti-biofilm activities of brown macroalgae metabolites. Brown macroalgae represent a valuable and renewable source of novel antimicrobial agents with significant potential to address the growing challenge of antibiotic resistance. Further exploration of structure–activity relationships, biosynthetic optimization, and nanoparticle-based delivery systems could

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pave the way for their application in pharmaceutical, biomedical, and food industries.

1 Introduction

Macroalgae have been an essential food source for humans since antiquity period. Marine macroalgae, in particular, are important food sources in East Asian coastal regions such as China, Korea, Japan, and Indonesia. The market for commercial seaweed was worth USD 9.9 billion in 2021 and is expected to increase at a 2.3% CAGR from 2022 to 2030 [1]. Green algae [Chlorophyta], brown algae [Phaeophyta], and red algae [Rhodophyta] are three subgroups of macroalgae or seaweeds based on their colour, nutritional content and chemical makeup. In addition to their long-standing use in Asian cuisine and unique nutritional qualities, seaweeds have recently attracted attention for their potential applications as nutraceuticals or functional foods [2]. The polysaccharides contained in brown algae had been reported to show valuable indirect anti-steatotic effects in previous study. Brown algae polysaccharides can function as dietary fibers that boost satiety and reduce nutrient absorption, resulting in a reduction in total energy consumption. The gut microbiota can metabolize BAPs, which improves the intestinal health, intestinal barrier integrity, and the physiological function of the gut-liver axis. These factors are essential for the onset and progression of NAFLD. Brown algae polysaccharides was reported to be able to also block pancreatic lipase activity, which reduces the amount of energy consumed and the amount of fat delivered to the liver [3].

The primary purpose of brown and red algae in human diet is as a source of numerous vitamins, minerals, proteins, and amino acids. In a shallow, rocky coastal environment, brown algae are more prevalent, especially when exposed at low tide. The health benefits of seaweed-derived foods and snacks are coming to the fore as a source of vegan protein, lipids and carbohydrates, and demand for both consumption and other uses is expected to increase. Recent research has demonstrated that brown algae are good nutritional sources of bioactive chemicals and are therefore regarded as functional foods with health advantages [4]. Polysaccharides extracted from algae are utilized as thickeners and gelling agents in the cosmetics and food industries, the demand for which is increasing, especially in North America and Europe. Among its many applications, the share of direct consumption alone [excluding thickeners and hydrogels used in food and beverage processing] amounts to 24 million tons per year, about 40% of annual algae production. In fact, the concept of seaweed as a health food is ingrained in the minds of many people. As novel uses for seaweed-derived polysaccharides continue to be discovered, growing awareness of this eco-friendly, organic and sustainable food source continues to drive their consumption. Carbohydrates are converted into valuable byproducts using metabolic engineering approaches. The potential of seaweed as a green health food and bio-resource is being actively investigated.

Several previous published studies and reports had unravelled bioactive chemical compounds found in various brown algae. A new chrome derivative from the seaweed *Homoeostrichus formosana* was also identified as 2-(4',8'-dimethylnona-3'E,7'-dienyl)-8-hydroxy-2,6-dimethyl-2H-chromine, was isolated in a previous study [5]. Beside this

novel bioactive compound, ²⁷ four known natural products; methylfarnesylquinone, isololiolide, pheophytin- α , and β -carotene could also be isolated from *H. formosana* [5]. Algae or seaweed had been well-known for its richness in containing various bioactive compounds. Previous study successfully explored and revealed the antibacterial activity of seaweed extracts; the green algae *Ulva lactuca*, the brown algae *Stypocaulon scoparium*, and the red algae *Pterocladia capillacea*, against *Pseudomonas aeruginosa* by both crystal violet staining and quantification of bacterial adherence methods [6]. In addition, *Halidrys siliquosa*, a marine brown algae, had also been studied for its antimicrobial and antibiofilm activity obtained in its partially fractionated methanolic extracts against clinically important human pathogens commonly associated with biofilm-related infections; such as genus *Staphylococcus*, *Streptococcus*, *Enterococcus*, *Pseudomonas*, *Stenotrophomonas*, and *Chromobacterium* [7].

Bacterial biofilms are mechanisms used by bacteria to establish chronic infections in infected hosts, including humans. A biofilm is a colony of microorganisms enclosed within a matrix of microorganism-produced extracellular polymeric material. Biofilms contain microbial cells attached to each other and to stationary surfaces (living or non-living). Most of the time, bacterial biofilms are pathogenic and can cause nosocomial infections. Natural and synthetic antimicrobial agents, chemical attack, mechanical elimination, bacteriophages, foreign enemies, and components of the body's immune system, such as leukocytes, receive protection within biofilms, making bacteria more resistant to challenging environmental conditions [8]. The discoveries in ongoing explores in field of antimicrobial specialist improvement propose the capacity of the earthy colored green growth to offer a promising wellspring of bioactive competitors that could have both a preventive and a corrective impact in the treatment of bacterial diseases.

Despite growing evidence of the nutritional and pharmacological potential of macroalgae, comparative analyses of antibacterial and anti-biofilm properties among green (Chlorophyta), brown (Phaeophyta), and red (Rhodophyta) algae remain limited. Most previous studies have focused on single species or non-standardized extracts, providing fragmented insights into algal bioactivity. Moreover, the mechanisms underlying their antibacterial and anti-biofilm properties particularly the role of distinct phytochemical groups such as phlorotannins, fucoidans, and pigments have not been systematically compared across taxa. This gap limits our understanding of interspecies variations and the identification of the most promising algal sources for antimicrobial development. Therefore, this study aims to review and comparatively analyze the antibacterial and anti-biofilm activities of green, brown, and red macroalgae based on recent global research findings. ¹⁸

Specifically, the objectives are to identify the major bioactive compounds responsible for antimicrobial effects in each algal group; compare the reported antibacterial and anti-biofilm activities across taxa; and highlight the most promising compounds and mechanisms for potential therapeutic application. The novelty of this work lies in its integrative comparative approach, which synthesizes existing knowledge to clarify the relative contributions and potentials of different macroalgal groups in addressing antimicrobial resistance and biofilm-related infections.

2 Methods

This work is a systematic literature review with comparative synthesis of experimental studies reporting antibacterial and/or antibiofilm activities of marine macroalgae (green Chlorophyta, brown Phaeophyta, and red Rhodophyta). The review follows PRISMA principles for transparent searching, screening, and reporting. A systematic search was performed in the following electronic bibliographic databases: PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, and Google Scholar. Additionally, reference lists of included papers and recent relevant reviews were hand-searched to identify further studies.

3 Discussion

3.1 Antimicrobial activities of brown algae against human pathogens

Analysis of the studies summarized in Table 1 reveals distinct patterns in the antimicrobial potency of brown macroalgae extracts. Among the solvents used, methanol extracts generally exhibited stronger and broader-spectrum antibacterial activity than ethyl acetate extracts. This difference may be attributed to methanol's higher polarity, which enables it to extract a wider range of phenolic compounds, phlorotannins, and polysaccharides that contribute to antibacterial action. In contrast, ethyl acetate primarily extracts moderately polar compounds, resulting in selective activity against certain bacterial strains.

Table 1. The antimicrobial activities of brown macroalgae against human pathogenic bacteria reported in the last five years.

The species of brown algae	Extract or fraction assayed	The reported effect	References
Turbinaria conoides and Sargassum portierianum	Ethyl acetate extract	Shown antimicrobial activity by disc diffusion assay against six human pathogenic microbes; three Gram-positive bacteria <i>Bacillus cereus</i> (ATCC 10876), <i>Enterococcus faecalis</i> (ATCC 29212) and <i>Staphylococcus aureus</i> (ATCC 29213) and three Gram-negative bacteria <i>Enterobacter cloacae</i> (ATCC 13047), <i>Escherichia coli</i> (ATCC 25922) and <i>Salmonella typhimurium</i> (ATCC 14028).	[6]
Sargassum muticum	Methanol extract	Obtained significant inhibition against <i>Salmonella typhi</i> (25.66	[9]

		mm), <i>Escherichia coli</i> (24.33 mm), <i>Staphylococcus aureus</i> (22.33 mm) and <i>Bacillus subtilis</i> (19.66 mm). Furthermore, the methanol concentrate of <i>S. muticum</i> additionally altogether repressed the development of contagious phytopathogens, for example <i>Fusarium moniliforme</i> (30.33mm), <i>Pythium ultimum</i> (26.33 mm), <i>Aspergillus flavus</i> (24.36mm), and <i>Macrophomina phaseolina</i> (22.66mm).	
<i>Cystoseira baccata</i> and <i>Cystoseira tamariscifolia</i>	Silver nanoparticles (AgNPs) by green synthesis with the aid of the extract of brown algae	Similar antibacterial activity against <i>Pseudomonas aeruginosa</i> and <i>Escherichia coli</i> (22 nm) was observed in a brown algae extract-developed nanoparticle product known as Ag@CB and Ag@CT.	[10]
Unspecified	Fucoidan isolated from brown macroalgae	Through modulation of aryl hydrocarbon receptor (AhR), phosphodiesterase-4 (PDE4), nuclear factor erythroid 2-related factor 2 (Nrf2), and heme oxygenase-1 (HO-1), fucoidan, a brown algae sulfated polysaccharide, possesses a variety of pharmacological actions, including anti-inflammatory, antitumor, and antibacterial properties.	[11]

A recurring trend across recent research is the notably high antibacterial potential of the genus *Sargassum*. Methanolic and ethyl acetate extracts of *Sargassum muticum* and *Sargassum portierianum* demonstrated consistent inhibitory effects against both Gram-positive and Gram-negative bacteria, suggesting that *Sargassum* species are particularly rich in phlorotannins and halogenated metabolites. These compounds are known to disrupt bacterial membranes and inhibit enzymatic targets critical for cell wall synthesis and energy metabolism. Differences in susceptibility between Gram-positive and Gram-negative bacteria are also evident.

Generally, Gram-positive species such as *Staphylococcus aureus* and *Bacillus subtilis* were more sensitive to brown algae extracts, likely due to the absence of the outer lipopolysaccharide membrane that provides Gram-negative bacteria with additional protection. Nevertheless, several extracts and nanoparticles derived from brown algae, especially fucoidan-based and silver nanoparticle formulations, exhibited dual activity against both bacterial groups. This broad-spectrum efficacy highlights the potential of brown algae-derived compounds as multi-target antimicrobial agents capable of

overcoming the structural defenses of Gram-negative bacteria, an essential advantage in combating antibiotic-resistant pathogens. Overall, these patterns suggest that polarity of the solvent, algal taxonomy, and bacterial cell wall architecture are key factors influencing the antimicrobial outcomes of brown macroalgae extracts. Understanding these relationships provides valuable insights for optimizing extraction strategies and selecting algal species for targeted therapeutic development.

Recent studies demonstrate that brown macroalgae remain one of the richest marine sources of bioactive compounds with potent antibacterial effects against both Gram-positive and Gram-negative bacteria. As summarized in Table 1, ethyl acetate and methanolic extracts of *Sargassum* and *Turbinaria* species show broad-spectrum inhibition, particularly against *S. aureus*, *E. coli*, and *Salmonella typhi*. These effects are largely attributed to phenolic and halogenated metabolites typical of Phaeophyceae. An emerging approach involves the green synthesis of silver nanoparticles (AgNPs) using brown algae extracts.

Nanoparticles produced from *Cystoseira baccata* and *C. tamariscifolia* exhibited comparable antibacterial activity to that of conventional antibiotics, suggesting enhanced surface reactivity and biofilm-disruptive potential due to nanoscale size (~22 nm). Additionally, fucoidan, a sulfated polysaccharide abundantly found in brown algae, has been reported to exert indirect antibacterial and anti-inflammatory effects through the modulation of cellular signaling pathways such as AhR, PDE4, Nrf2, and HO-1. These findings underline the multifunctional role of brown algae metabolites not only as bactericidal agents but also as biofilm inhibitors and immunomodulators. Overall, these results highlight brown algae as promising candidates for developing novel antimicrobial formulations and nanomaterial-based therapeutics to counteract antibiotic-resistant human pathogens.

The antibacterial potential of brown macroalgae is largely attributed to its unique secondary metabolites, particularly phlorotannins, fucoidans, and pigments such as fucoxanthin, each possessing distinct chemical characteristics that contribute to their biological functions. Phlorotannins, a class of polyphenolic compounds exclusively found in brown algae, consist of polymerized phloroglucinol (1,3,5-trihydroxybenzene) units that enable strong interactions with bacterial cell membranes and proteins. Their multiple hydroxyl groups allow hydrogen bonding and redox reactions that lead to membrane destabilization, leakage of intracellular contents, and inhibition of essential bacterial enzymes such as DNA gyrase and ATP synthase.

In *S. aureus* and *E. coli*, phlorotannins were also shown to disrupt quorum sensing (QS) signaling, which is crucial for regulating virulence factors and biofilm formation. This interference reduces bacterial adhesion and weakens the structural integrity of established biofilms. Fucoidans, sulfated polysaccharides composed mainly of α -L-fucose and esterified sulfate groups, exert antibacterial and anti-inflammatory effects through different yet complementary mechanisms. Their negatively charged sulfate groups interact electrostatically with positively charged bacterial membrane proteins, leading to membrane permeabilization and inhibition of microbial attachment to surfaces. Fucoidans also modulate intracellular signaling pathways, such as AhR, PDE4, Nrf2, and HO-1, reducing oxidative stress and inflammatory responses in host tissues while suppressing bacterial colonization. This dual host-microbe modulation makes fucoidans

promising agents against chronic and biofilm-related infections. Meanwhile, fucoxanthin, the main xanthophyll pigment in brown algae, possesses a conjugated polyene structure and an allenic bond system that facilitates reactive oxygen species (ROS) generation under oxidative conditions. Elevated ROS levels induce oxidative damage to bacterial membranes, proteins, and nucleic acids, leading to bactericidal effects.

Fucoxanthin's lipophilicity also enables it to insert into bacterial membranes, altering membrane fluidity and permeability, further contributing to antibacterial action. Overall, these mechanisms—ranging from cell membrane disruption and enzyme inhibition to quorum sensing interference and ROS induction—collectively explain the strong antibiofilm capabilities of brown algae-derived compounds. The structural diversity of these metabolites provides a multifaceted defense strategy that not only prevents bacterial colonization and biofilm maturation but may also enhance the efficacy of conventional antimicrobial agents through synergistic effects.

3.2 Bacterial biofilm and its potentials in mediating and enhancing the bacterial infections in human

The emergence of non-multiplicating, persistent subpopulations and the formation of biofilms are the two most well-known strategies utilized by bacteria. Recently, the challenges to create innovative effective antibiotics against such drug-tolerant subpopulations of bacterial cells are raising and worrying worldwide. However, it might be possible to force the infection-causing bacteria to switch to less tolerant growth modes, which would increase the therapeutic effectiveness of currently available medicines. Importantly, these survival tactics due to biofilms formation are reversible since gene expression regulates them [12]. Hence, the presence of such persister cells can reseed the disease site after the finish of treatment. In addition, persisters can be a source of live bacteria that encourage the emergence of antibiotic-resistant mutants through random mutation or horizontal gene transfer. Furthermore, cooperation and communication are required for their bacterial population organization. Those two processes are susceptible to disruption [13].

Amid biofilm arrangement, cells to begin with join to a surface and after that duplicate to create microcolonies. The extracellular framework, which is a hallmark of biofilm arrangement and is made up of proteins, polysaccharides, and extracellular DNA, is produced by these bacterial cells in this manner. The biofilm community experiences a dismantling handle after developing into three-dimensional structures, which results in the dispersal of bacterial cells. Certain surface related proteins like OmpA, fibronectin authoritative proteins, protein A, SasG, biofilm related protein (BAP) and numerous other variables are included within the arrangement of biofilms, especially, amid the initial bacterial cell-surface attachment stage. The biofilm encompassing microscopic organisms makes them tolerant to cruel conditions and safe to antibacterial medications. Besides, the biofilms are capable for causing a wide extent of unremitting maladies and due to the rise of anti-microbial resistance in microbes it has truly ended up troublesome to treat them with adequacy. Moreover, the antimicrobials accessible till date are incapable for treating these biofilm related diseases due to their higher values of

minimum inhibitory concentration and minimum bactericidal concentration. Subsequently, it is fundamentally vital to plan or screen anti-biofilm atoms that can viably minimize and annihilate biofilm related contaminations.

3.3 Reported anti-biofilm of brown algae

A biofilm is a three-dimensional structure that serves as a microbial battlefield and is made up of a community or assembly of microorganisms that are attached to various biotic or abiotic surfaces or environments. These communities of surface microbes can be found in natural, industrial, medical, and food environments. Biofilm is a serious problem in the medical field as it is trained in medical implants in human tissue and is implicated in a multitude of serious chronic diseases infection. Recent researches in antimicrobial agent resistance (AMR) field have been trying to prevent biofilm formation and remove them from reversible and irreversible attachment steps, in which adherent microorganisms improve surface adhesion, strong disinfectants are required. to remove bacterial attachments. Table 2 shows studies of antibiofilm activities of brown macroalgae against human pathogenic bacteria in the last five years.

Table 2. The antibiofilm activities of brown macroalgae against human pathogenic bacteria reported in the last five years.

The species of brown algae	Extract or fraction assayed	The reported antibiofilm activities	References
Unspecified	Fucoidan isolated from brown macroalgae	Biosynthesized fucoidan-stabilized AuNPs (F-AuNPs) were found to have a minimum biofilm eradication concentration (MBEC) and inhibition concentration (MBIC) of 128 g/mL. Besides, sub-MICs of F-AuNPs moreover weakened the generation of a few imperative harmfulness components and disabled bacterial swarming, swimming, and jerking motilities in <i>Pseudomonas aeruginosa</i> PAO1.	[13]
<i>Stypocaulon scoparium</i>	The ecyclohexane, dichloromethane, ethylacetate, and methanol extracts of algae	By inhibiting or delaying biofilm formation and proliferation, extracts of brown algae <i>Stypocaulon scoparium</i> , red algae <i>Pterocladia capillacea</i> , and green algae <i>Ulva lactuca</i> demonstrated potential antibiofilm activity against <i>Staphylococcus aureus</i> .	[5]
<i>Ascophyllum nodosum</i>	Isolated phlorotannins from brown macroalgae (<i>Ascophyllum nodosum</i>)	By reducing pre-formed biofilms on stainless steel produced by Shiga toxin-producing <i>Escherichia coli</i> (STEC) O154, the phlorotannins from brown macroalgae <i>Ascophyllum nodosum</i> demonstrated antibiofilm activity: H10 and O113: H21 strains that can get rid of	[14]

		biofilms after 24 hours and have concentration ranges of 25–400 g/mL.	
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Previous study had unravelled and reported the mechanism of synthesis of palladium nanoparticles [Pd-NPs] from brown algae *Padina boryana* and their antibacterial and antibiofilm potential. Recently published study also showed the inhibition activity of silver and gold nanoparticles produced with brown algae *Cystoseira baccata* and *Cystoseira tamariscifolia* extracts against biofilm formation in *S. aureus* ATCC 23,235 and *P. aeruginosa* PAO1. Both pathogens *S. aureus* ATCC 23,235 and *P. aeruginosa* PAO1 are well-known pathogens with mucoid phenotype and are highly capable of producing biofilms. The results of previous study showed that silver nanoparticle containing *Cystoseira baccata* showed better inhibition of bacterial biofilm formation with low concentration needed, 2.16 µg/mL for *S. aureus* and 2.16 µg/mL for *P. aeruginosa*.

3.4 Recommendation in research of the field

Biofilms are obstinate to anti-microbial treatment and a major cause of repetitive bacterial infectious diseases and co-infections by clinically imperative pathogens around the world (e.g., *P. aeruginosa*, *E. coli*, and *S. aureus*). The biofilms of *P. aeruginosa* in the lungs of patients diagnosed with cystic fibrosis are one biofilm-related infection that is of special medical concern. Acute and chronic lung infections brought on by this opportunistic bacterium have been linked to high rates of morbidity and mortality. Previous study found antibiotic permeation through colony biofilms observed via diffusion cell bioassay did not result in an increase in bacterial death once the antibiotics penetrated the biofilms [13]. In addition, antimicrobial-covered muscular inserts, antimicrobial-stacked bone concretes and void fillers, and double osteo-inductive/antimicrobial biomaterials are among the most frequently reported advancements. The regulatory environment for antimicrobial drug-device combination products is difficult and still evolving, and there is a lack of clarity regarding the burden of proof required in preclinical research. Unfortunately, translation of these technologies to the clinic has been found to be still limited [14].

Right now, most biofilm remediation methodologies include the advancement of biofilm-inhibition operators, pointed at anticipating the early stages of biofilm arrangement, or biofilm-dispersal operators, pointed at disturbing the biofilm cell communities. Whereas both procedures offer a few clinical guarantee, there is still no promising procedure or treatment to reach a coordinate treatment and annihilation methodology for set up biofilms. Subsequently, the revelation and advancement of biofilm destruction operators as comprehensive, stand-alone biofilm treatment choices has gotten to be a principal range of investigate.

Macroalgae, particularly brown macroalage are notable for their remarkable capacity to hoard imperative minerals and minor components expected for human sustenance, but their amounts differ incredibly contingent upon morphological attributes, natural conditions, and geographic area. Despite this variety, Chlorophyta appear to acquire more Mg, particularly Fe, while Rhodophyta and Phaeophyta accumulate more Mn and I, respectively [15]. They are ideal for use in the food industry as new components in the

creation of a variety of functional food items due to their valuable mineral content. In addition, the ability of brown macroalgae as antimicrobial and antibiofilm agents had been studied and reviewed here. Therefore, further study regarding the application of macroalgae and its extract in infectious diseases treatment besides its uses as food supplements.

4 Conclusion

The rise of antimicrobial resistance, particularly in infections associated with bacterial biofilms, has transformed many common human pathogens into life-threatening threats. Biofilm formation provides bacteria with enhanced tolerance to antibiotics and immune defenses, rendering conventional therapeutic strategies largely ineffective. Consequently, the treatment of biofilm-associated infections has become a major challenge in biomedical and clinical settings. This situation highlights the urgent need to explore and develop novel antibacterial and antibiofilm agents derived from natural sources. Among these, brown macroalgae represent a promising reservoir of bioactive compounds with demonstrated efficacy against multidrug-resistant and biofilm-forming bacteria. Their unique metabolites, such as phlorotannins, fucoidans, and pigments, offer a sustainable and potentially effective alternative to conventional antimicrobial therapies.

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Brown macroalgae as natural marine wealth with multiple antimicrobial activities on human pathogens: A mini-review

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