Antioxidant bioactivity of Caulerpa spp.: potential, challenges, and future research directions

Athila Zahra Ariesta Akhmad[1], Yasman Yasman[1,2]

[1]*Marine Science Study Program, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok 16424, West Java, Indonesia*

[2]*Research Group of Metabolomics and Chemical Ecology, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok, West Java, Indonesia*

Corresponding Author: Yasman Yasman
Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok 16424, West Java, Indonesia
Email yasman.si@sci.ui.ac.id

Received: May 21, 2025
Accepted: August 15, 2025
Doi: 10.21608/egyjs.2025.387686.1048

ABSTRACT: The genus *Caulerpa* is gaining attention for its significant antioxidant bioactivity, driven by the diverse array of bioactive compounds it produces, such as polyphenols and caulerpin. This review examines the integration of emerging technologies and genetic studies with interdisciplinary approaches in marine biology, pharmacology, and food science to enhance the discovery and utilization of antioxidants from *Caulerpa* spp. *In vitro* and in silico analyses of *C. racemosa* have revealed potent antioxidant, antidiabetic, and anticancer activities, emphasizing the importance of its bioactive components. Genetic insights into sulfotransferases offer opportunities for producing complex sulfated polysaccharides with pharmaceutical applications. Moreover, controlled light exposure can elevate the antioxidant levels of *C. lentillifera*, making it comparable to nutrient-rich fruits. The review also highlights the potential of advanced molecular techniques, such as DNA barcoding, for accurately identifying species and their bioactive compounds. Furthermore, the local utilization of *C. lentillifera* in Indonesia showcases its role as a nutraceutical resource. Collectively, these findings underscore the need for further research to fully exploit the antioxidant capabilities of *Caulerpa*, contributing to human health and environmental sustainability.

Keywords: Antioxidants, Bioactive Compounds, *Caulerpa* spp., Nutraceuticals, Marine Biotechnology

INTRODUCTION

Caulerpa is a genus of green macroalgae with significant diversity and distribution in the Caribbean Sea, the Indo-Malay islands, and southern Australia. It belongs to the Caulerpaceae family in the order Bryopsidales, comprising over 100 recognized species worldwide (Zubia *et al*., 2020; Lagourgue *et al*., 2024). *Caulerpa* has a unique structure consisting of single and multinucleated siphonous cells, contributing to its invasive potential and adaptability across various marine environments (Landi *et al*., 2022). Previously, the taxonomic classification of *Caulerpa* species was challenging due to their phenotypic plasticity, which complicated identification. However, recent phylogenetic studies have clarified species distinctions, such as the recovery of *C. pickeringii* in French Polynesia (Lagourgue *et al*., 2024).

Biologically, *Caulerpa* plays a vital role in marine ecosystems, often dominating habitats such as seagrass beds and coral reefs, where it can significantly impact biodiversity by outcompeting native species and altering community structures (Raza'I *et al*., 2023). Its invasive nature is partly due to the production of toxic secondary metabolites, such as caulerpenyne, which deters herbivores and affects other marine organisms. However, *Caulerpa* also contributes to the aquatic food web and provides habitats for various marine species (Mehra *et al*., 2019).

Despite its invasive tendencies, *Caulerpa* offers ecological benefits, including bioremediation potential through the absorption of pollutants like zinc and nitrogen, thereby improving water quality (Landi *et al*., 2022). In the context of climate change, *Caulerpa* interactions with coral species such as *Acropora hyacinthus* highlight its role in modulating physiological responses to heat stress, potentially mitigating some of the negative impacts of ocean warming on coral reefs (Fu *et al*., 2022).

This genus is also a promising candidate for sustainable aquaculture, offering both economic and environmental benefits through its use in functional foods and as a blue carbon sink (Zubia *et al*., 2020). *Caulerpa* contains not only high nutritional value but also has significant pharmaceutical potential, with compounds such as sulfated polysaccharides and caulerpin exhibiting medicinal properties, including anticancer, antibacterial, and anti-inflammatory activities (Mehra *et al*., 2019).

Overall, *Caulerpa*'s taxonomic complexity and biological significance highlight its dual role as both a potential threat and a valuable resource in marine ecosystems. This requires careful management and further research to maximize its benefits while mitigating its invasive impacts. This article aims to review *Caulerpa*'s potential as a functional food, particularly as a source of antioxidants.

MATERIALS AND METHODS

This review was conducted to systematically assess the recent scientific literature on the antioxidant bioactivity of *Caulerpa* species, focusing on environmental influences, cultivation conditions, and biochemical responses. The primary aim was to highlight recent trends, current findings, and research gaps within the field.

To identify relevant studies, a comprehensive literature search was performed using databases such as ScienceDirect, SpringerLink, PubMed, and Google Scholar. The search covered articles published between January 2018 and March 2024. Keywords used in various combinations included "*Caulerpa*," "antioxidant activity," "bioactive compounds," "secondary metabolites," "environmental stressors," and "climate change." Boolean operators such as AND and OR were employed to refine the search results, and filters were applied to include only peer-reviewed articles published in English.

The inclusion criteria consisted of original research and review articles that specifically focused on *Caulerpa* spp. and their antioxidant activities. Studies examining environmental stressors, such as light intensity, nutrient levels, or pollution, and their influence on antioxidant compounds in *Caulerpa* were also included. Articles employing phytochemical, chemical, or metabolomic analysis methods were selected. On the other hand, non-peer-reviewed publications, non-English articles, and those that did not address *Caulerpa* or antioxidant properties were excluded from the review.

Data extracted from the selected articles included the publication year, *Caulerpa* species studied, research objectives, experimental approaches, types of antioxidant compounds identified, environmental conditions investigated, and analytical methods used (such as DPPH, FRAP, HPLC, or LC-MS). The data were synthesized to reveal common research themes, highlight recent advancements, and identify existing gaps in knowledge and methodology.

Analysis

A total of 83 relevant articles were included in this review. The majority of these, 60 articles or approximately 72.3%, were published between 2022 and 2024. This indicates a strong increase in research interest and activity in recent years, particularly regarding *Caulerpa*'s antioxidant potential and the development of analytical technologies.

Only four articles (approximately 4.8%) were published before 2020, specifically two in 2018 and two in 2019. These earlier publications were retained in the review due to their foundational significance or because they provided context or methodology that was still referenced in more recent studies.

Most of the reviewed articles focused on species such as *Caulerpa racemosa*, *C. lentillifera*, *C. taxifolia*, and *C. sertularioides*. A noticeable number of recent studies have employed advanced analytical techniques, including LC-MS, GC-MS, and NMR, particularly those published since 2023. Common research themes included the influence of environmental stressors—such as ultraviolet radiation, salinity variation, temperature shifts, and eutrophication—on the production of antioxidant compounds in *Caulerpa*.

An emerging trend is the integration of metabolomic profiling with sustainable cultivation approaches to enhance the production of antioxidant-rich *Caulerpa* biomass for nutraceutical and pharmaceutical applications. Overall, this review reflects the rapidly evolving research landscape, with the most significant contributions published in the last two years, underscoring both the urgency and innovation surrounding the study of *Caulerpa*'s antioxidant bioactivity in changing environmental contexts.

DISCUSSION

Exploring *Caulerpa*'s antioxidant potential in mitigating oxidative stress

Oxidative stress, primarily caused by an imbalance between the production of free radicals, such as reactive oxygen species (ROS), and the body's ability to counteract their harmful effects with antioxidants, plays a crucial role in the pathogenesis of various human diseases. This imbalance leads to oxidative damage of critical biomolecules, including DNA, proteins, and lipids, contributing to the development and progression of chronic conditions like cardiovascular diseases, neurodegenerative disorders, cancer, diabetes, and inflammatory diseases (Petrucci *et al*., 2022; Jomova *et al*., 2023; Ashraf *et al*., 2024; Blagov *et al*., 2024; Houldsworth 2024; Muro *et al*., 2024). In neurodegenerative diseases such as Alzheimer's and Parkinson's, oxidative stress is associated with neuroinflammation and nerve damage, which worsen disease progression (Bhandari *et al*., 2024; Houldsworth, 2024). Similarly, in cardiovascular diseases, oxidative stress accelerates atherosclerosis by promoting lipid oxidation and endothelial dysfunction (Petrucci *et al*., 2022). Inflammatory conditions, such as inflammatory bowel disease, are also exacerbat by oxidative stress, which damages the intestinal lining and activates inflammatory pathways (Muro *et al*., 2024).

Against this backdrop, *Caulerpa* species are gaining recognition as a promising source of natural antioxidants. These seaweeds produce bioactive compounds that can neutralize reactive oxygen species (ROS), reduce cellular damage, and potentially slow disease progression associated with oxidative stress (Jomova *et al.*, 2023; Bhandari *et al.*, 2024; Muscolo *et al.*, 2024). Extracts from *Caulerpa* species—particularly *C. lentillifera*, *C. racemosa*, and *C. sertularioides*—exhibit significant antioxidant activity (Aroyehun *et al.*, 2020; Saberivand *et al.*, 2022; Palaniyappan *et al.*, 2023; Tesvichian *et al.*, 2024). These extracts are rich in bioactive components, including sulfated and unsulfated polysaccharides, phenolics, flavonoids, terpenes, and tannins (Table 1), which contribute to their radical scavenging capacity in DPPH and ABTS assays. The presence of these compounds (Figure 1) reflects the increasing global interest in marine-derived antioxidants for promoting health and combating oxidative stress (Ashraf *et al.*, 2024; Muscolo *et al.*, 2024). Furthermore, *Caulerpa* species have shown promising applications in the fields of health, nutrition, and cosmetics (Iveša *et al.*, 2024).

Beyond radical scavenging, *Caulerpa* extracts exhibit dual bioactivities, combining antioxidant properties with anti-inflammatory or anticancer effects. For instance, studies have shown that *Caulerpa* extracts can suppress pro-inflammatory mediators such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), cyclooxygenase-2 (COX-2), prostaglandin E2 (PGE2), and nitric oxide (NO) in LPS-stimulated RAW 264.7 macrophages, demonstrating a synergistic antioxidant and anti-inflammatory response (Yoojam *et al.*, 2021).

In cancer-related research, metabolites such as caulerpin and monomethyl caulerpinate from *Caulerpa* inhibit enzymes in the pentose phosphate pathway—a key metabolic route that supports cancer cell growth—indicating potential antioxidant-linked anticancer properties (Mert-Ozupek *et al.*, 2022). Some compounds also exhibit inhibitory effects on Human Epidermal Growth Factor Receptor 2 (HER2) protein, a target in breast cancer therapy, suggesting chemopreventive roles (Sanger *et al.*, 2023).

Mechanistically, *Caulerpa* species act through multiple antioxidant pathways. For example, squalene from *Caulerpa* reduces intracellular reactive oxygen species (ROS), thereby protecting cells from oxidative damage (Anjali *et al.*, 2022). In contrast, clionasterol-rich fractions have been shown to reduce both intracellular and mitochondrial ROS, thereby preventing apoptosis, particularly in skin cells (Liyanage *et al.*, 2022). Extracts from *C. sertularioides* enhance sperm antioxidant defenses by increasing the activities of key enzymes such as superoxide dismutase and glutathione peroxidase (Saberivand *et al.*, 2022).

Caulerpa species have also shown efficacy in managing metabolic and inflammatory disorders. For example, *C. okamurae* extract improves insulin sensitivity and suppresses NO production in obese mouse models (Manandhar *et al.*, 2020). Similarly, a combination of *C. racemosa* and *Eleutherine americana* sulfated polysaccharides has been shown to enhance macrophage function and nitric oxide production, underscoring its immunomodulatory and antioxidant effects (Pakki *et al.*, 2020). Additionally, caulerpin has demonstrated anti-inflammatory effects in murine colitis by downregulating the Nuclear Factor kappa-light-chain-enhancer of activated B cells (NFκB) and increasing IL-10 expression, highlighting its therapeutic potential in inflammation-associated oxidative stress (Lucena *et al.*, 2018).

Collectively, these studies confirm the rich and diverse phytochemical profile of *Caulerpa*, supporting its potential for development in pharmaceutical and nutraceutical applications. The integration of *Caulerpa*-derived compounds into functional foods, supplements, and therapeutic formulations presents a promising strategy for managing oxidative stress-related conditions (Crupi *et al*., 2023; Jomova *et al*., 2023).

In summary, *Caulerpa* species mitigate oxidative stress through various mechanisms, including ROS scavenging, enhancement of endogenous antioxidant enzymes, inhibition of pro-inflammatory mediators, and regulation of redox-sensitive pathways. The synergistic actions of these bioactive compounds underscore their potential as candidates for innovative therapies targeting oxidative stress-associated diseases.

Table 1. Radical scavenging capacity in DPPH and ABTS assays.

Compound	*Caulerpa* Species	Activity Type	Extraction Method	Reference(s)
Polyphenols	*C.racemosa*, *C.lentillifera*	Antioxidant, Antidiabetic	Methanol, Ethanol	Palaniyappan *et al.*, 2023
Terpenoids: Carotenoids (β-Carotene and canthaxanthin)	*C. racemosa*	antidiabetic, anti-obesity, antioxidant, and anti-inflammatory	Ethanol	Kurniawan *et al.*, 2023
β-1,3-xylooligosaccharides (XOS-3)	*C.lentillifera*	Antioxidant, anti-inflammatory	--	Cai *et al.*, 2024
sulfated polysaccharides (glucose, galacturonic acid, xylose, mannose, sulfates, and β-d-galactan)	*C.lentillifera, C. racemosa, C. sertularioides*	Antioxidant, immunostimulant,	-	Pakki *et al*., 2020; Anjali *et al.*, 2022; Mayulu *et al.*, 2023; Tesyichian *et al.*, 2024
Flavonoids, tannins	*C. racemosa*	Antioxidant	-	Palaniyappan *et al.*, 2023
Terpenoids: squalen	*C. racemosa*	Antioxidant	-	Anjali *et al.*, 2022
Terpenoids: clionasterol	*C. racemosa*	protects skin damage	-	Liyanage *et al.*, 2022
Extract	*C. sertularioides*	Antioxidant	ethanol	Saberiyand *et al.*, 2022
Remorin-like protein	*C. sertularioides*	Anti-inflamatory	-	Sanniyasi *et al*., 2023
Extract	*C. lentillifera*	suppresses pro-inflammatory, antioxidant	-	Yoojam *et al.*, 2021; Nurkholis *et al.*, 2023
Bisindol alkaloid (Caulerpin dan monomethyl caulerpinate)	*Caulerpa* sp.	Anticancer, anti-imflammatory	-	Lucena *et al.*, 2018; Mert-Ozupek *et al.*, 2022
Extract	*C. okamurae*	to alleviate obesity-related inflammation and improve glucose metabolism	-	Manandhar *et al.*, 2020
Terpenoid: 3,7,11,15-tetramethyl-2-hexadecen-1-ol	*C. racemosa*	Antimicrobial, antioxidant, anticancer, antimutagenic	-	Palaniyappan *et al.*, 2023
Extract	*C. racemosa*	Antioxidant, antibacterial	methanol	Palaniyappan *et. al.*, 2023

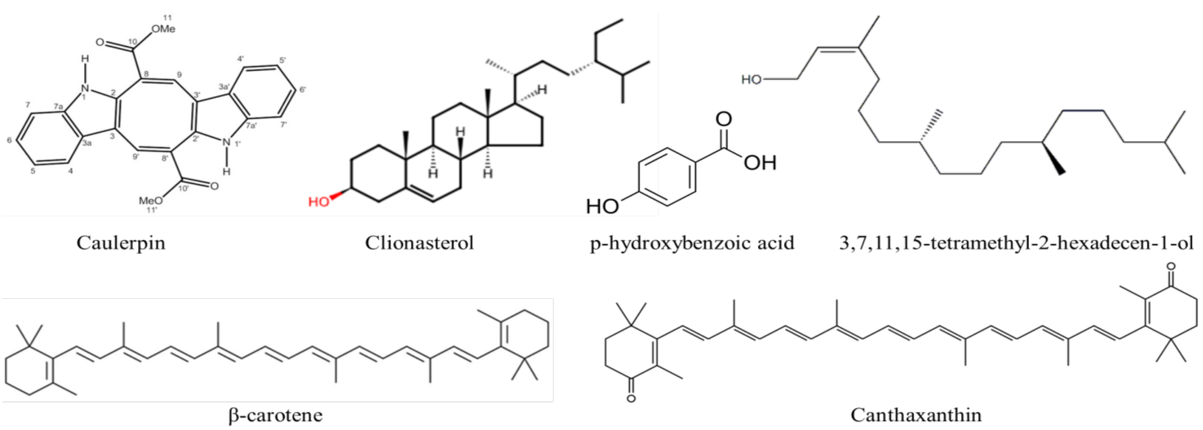


Figure 1. Representative Bioactive Compounds Derived from *Caulerpa* spp. (Lucena et al., 2018; Mert-Ozupek *et al*., 2022; Liyanage *et al*., 2022; Kurniawan *et al*., 2023; Palaniyappan *et al*., 2023)

Analyzing the antioxidant potential and bioactive compound profile of *Caulerpa*

Metabolite profiling in *Caulerpa* species has employed a variety of advanced methodologies. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) is a prominent technique for identifyingand quantifying phenolic compounds in seaweeds, including *Caulerpa* spp., enabling detailed metabolite profiling. Studies using liquid chromatography-tandem mass spectrometry (LC-MS) have identified notable metabolites, including malvidin, kaempferol, cyanidin, quercetin, apigenin, lutein, and myristicin,n *Caulerpa* (Tanna *et al*., 2018). High-performance liquid chromatography-photodiode array (HPLC-PDA) quantification has also been utilized to determine the abundance of specific phenolic compounds, such as p-hydroxybenzoic acid, in *Caulerpa* spp. (Cai *et al*., 2024). Nuclear magnetic resonance (NMR) spectroscopy, including ^{1}H and ^{13}C NMR, has been employed to characterize the structure of polysaccharides extracted from *Caulerpa*, thereby linking their composition to antioxidant activity (Tesvichian *et al*., 2024).

Similarly, gas chromatography-mass spectrometry (GC-MS) has been applied to analyze the ethyl acetate fraction of *C. racemosa*, revealing key compounds such as n-hexadecanoic acid and hexadecanoic acid methyl ester that contribute to its antioxidant properties (Dissanayake *et al*., 2022). High-performance thin-layer chromatography (HPTLC) has been utilized to analyze caulerpin, a secondary metabolite in *Caulerpa*, which is recognized for its significant anticancer activity and antioxidant potential (Mert-Ozupek *et al*., 2022).

To evaluate the antioxidant capacity of *Caulerpa* extracts, researchers commonly use standard tests such as ABTS, DPPH, and ferric reducing antioxidant power (FRAP) assays (Rumpf *et al*., 2023). Among these, the DPPH assay is popular due to its simplicity and cost-effectiveness. However, it is sensitive to experimental conditions, such as reaction time and concentration, which are not always standardized (Yamauchi *et al*., 2024). The Folin-Ciocalteu (FC) test, used for measuring total phenolic content (TPC) as an indirect measure of antioxidant activity, can be influenced by non-phenolic compounds, potentially leading to inaccuracies (Torres *et al*., 2024).

The FRAP test is another common method, valued for its simplicity and affordability, although it is traditionally time-consuming. Modifications, such as sequential injection analysis, have improved its speed and accuracy (Jiménez-Morales and Cañizares-Macias,2024). The Oxygen Radical Absorbance Capacity (ORAC) test assesses the scavenging ability of antioxidants, with the ORAC Fluorescein (ORAC-FL) method proving useful for evaluating mixtures. However, it may not precisely characterize individual metabolites (Pozo-Martínez *et al*., 2022). The ORAC Pyranine (ORAC-PYR) method provides a high-throughput approach, focusing on the chemical reactivity and stoichiometry of antioxidants (Gregório *et al*., 2020).

The 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) test, although not specifically applied to *Caulerpa*, exhibits a good correlation with the FRAP and FC tests and can be used to measure antioxidant capacity (Rumpf *et al*., 2023). Emerging techniques, such as potentiometric methods using $DPPH^{-}$ as an oxidant, offer versatility and can accommodate samples of various colors without the limitations of spectrophotometry.

These diverse assays provide a comprehensive toolkit for assessing the antioxidant capacity of *Caulerpa* species, each offering unique insights into its antioxidant properties. The selection of the appropriate assay depends on the research objectives, such as the need for high-throughput analysis or sensitivity to specific antioxidant compounds. Despite individual limitations, combining these methods offers a more holistic view of *Caulerpa*'s antioxidant potential.

Integrating *in vitro* and silico analyses further expands understanding of *Caulerpa*'s therapeutic properties, including antioxidant, antidiabetic, and anticancer activities. Molecular docking studies, for example, have shown high binding affinities between caulerpin and target enzymes, highlighting its potential as a therapeutic agent (Dissanayake *et al*., 2022). Together, these methods form a comprehensive framework for isolating and characterizing the antioxidant compounds in *Caulerpa*, underscoring its potential applications in functional foods, pharmaceuticals, and nutraceuticals.

Extraction and Isolation Methods

The extraction and isolation of antioxidant compounds from *Caulerpa* species are central to maximizing the yield and quality of their secondary metabolites, particularly phenolics, flavonoids, and other bioactive constituents. Various solvent-based methods have been employed, with methanol and ethanol being the most used solvents for recovering antioxidant-rich fractions. For instance, methanolic extracts of *C. racemosa* have been shown to yield high concentrations of phenolic, flavonoid, and tannin compounds, which correlate strongly with the presence of key constituents such as 3,7,11,15-tetramethyl-2-hexadecen-1-ol and phthalic acid (Palaniyappan *et al*., 2023). Similarly, ethanolic extraction of *Caulerpa* species from Indonesia has successfully isolated a diverse set of bioactive compounds, demonstrating the effectiveness of this solvent in capturing a broad antioxidant profile (Wirawan *et al*., 2022).

Fractionation techniques, such as solvent partitioning, have also been used to enhance compound specificity. Ethyl acetate fractions from crude polyphenolic extracts of *C. racemosa* have yielded concentrated antioxidant components, indicating that selective solvent-based isolation can improve compound purity and enhance functional profiling (Dissanayake *et al*., 2022). In addition to polar solvents, lipid-based extractions have been employed for recovering antioxidant-rich fatty acids from *C. lentillifera* waste biomass, particularly palmitic acid, through conventional lipid extraction procedures (Srinorasing *et al*., 2021).

Recent advancements in extraction technology have further improved the efficiency, selectivity, and sustainability of antioxidant recovery from marine algae such as *Caulerpa*. Green extraction techniques—such as supercritical fluid extraction (SFE) and subcritical water extraction (SWE) have gained attention for eliminating toxic solvents while preserving thermolabile compounds. These methods utilize supercritical CO_2 or pressurized water as the extraction medium, offering high selectivity and reduced degradation of bioactive compounds (Zhang *et al*., 2020).

Non-thermal extraction technologies are particularly promising for maintaining the integrity of delicate antioxidant compounds. Microwave-assisted extraction (MAE) accelerates solvent penetration and compound release through dielectric heating, thereby reducing extraction time and solvent usage. Ultrasonic-assisted extraction (UAE), on the other hand, utilizes high-frequency sound waves to disrupt cell walls and enhance mass transfer, thereby yielding higher extraction yields (Bagade and Patil, 2021; Shen *et al*., 2023).

Emerging methods such as pulsed electric field (PEF) extraction further offer advantages in cell membrane permeabilization, facilitating the release of intracellular compounds with minimal thermal input. PEF has been successfully applied to extract pigments and polyphenols from other algal sources, such as *Tetraselmis chuii* and *Phaeodactylum tricornutum*, and holds promise for adaptation to *Caulerpa* (Kokkali *et al*., 2020). Enzymatic-assisted extraction (EAE) and fermentation-assisted extraction (FAE) are also being increasingly explored for their ability to liberate bound phenolic compounds and modify their structure through enzymatic biotransformation, thereby enhancing extraction efficiency and compound stability (Vilas-Franquesa *et al*., 2023).

Moreover, the integration of green solvents—such as natural deep eutectic solvents (NADESs) and other bio-based alternatives—complements these advanced extraction techniques. These solvents offer a low-toxicity, biodegradable option that aligns with sustainable processing goals while maintaining or improving extraction yields of phenolics and flavonoids (Hashemi *et al*., 2022).

In combination with standardized antioxidant assays such as DPPH and ABTS, these extraction innovations provide robust tools for assessing extract quality and guiding optimization. As noted by Leo and Ong (2023), coupling modern extraction methods with reliable bioactivity screening facilitates the development of reproducible and scalable protocols suitable for industrial applications.

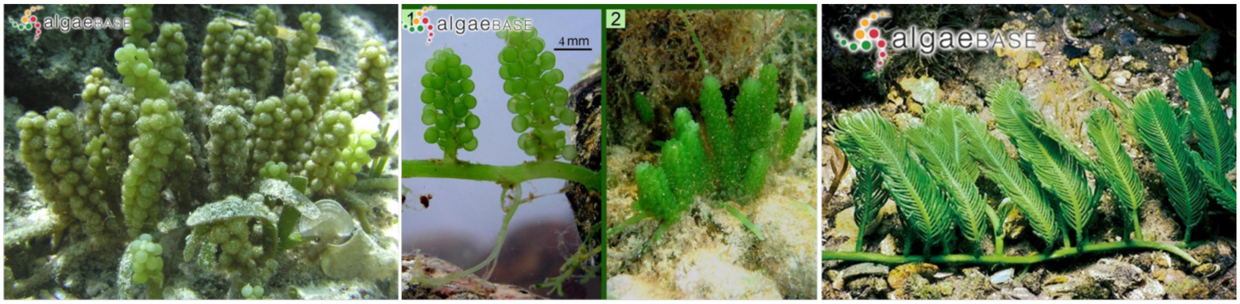
Overall, these advancements in extraction and isolation represent a pivotal step toward unlocking the full antioxidant potential of *Caulerpa* species. The adoption of selective, green, and high-efficiency extraction technologies ensures the better preservation of bioactive compounds while supporting the sustainable utilization of these compounds in functional foods, nutraceuticals, and beyond.

Variation in antioxidant bioactivity among different *Caulerpa* species

Extracts of *Caulerpa* have demonstrated antioxidant activity comparable to the standard antioxidant Trolox, highlighting their potential for therapeutic applications (Nurkolis *et al.*, 2023). However, the antioxidant bioactivity among *Caulerpa* species varies significantly, primarily due to differences in the composition and concentration of their secondary metabolites. Among the most extensively studied species—*C. racemosa*, *C. lentillifera*, and *C. sertularioides* (Figure 2) each exhibit a distinct antioxidant profile.

For instance, *C. racemosa* has demonstrated a remarkable antioxidant capacity, with an IC_{50} value of 5.58 µg/mL in hydroxyl radical scavenging assays, indicating its potent ability to neutralize free radicals (Honey *et al.*, 2024). Further supporting its biochemical complexity, *C. racemosa* contains compounds such as 3,7,11,15-tetramethyl-2-hexadecen-1-ol and phthalic acid, both of which are known for their antioxidant and pharmacological effects (Palaniyappan *et al.*, 2023). Moreover, its polyphenol-rich ethyl acetate fraction has shown potent antioxidant, antidiabetic, and anticancer activities in both *in vitro* and in silico analyses, attributed to its high phenolic content (Dissanayake *et al.*, 2022).

In contrast, *C. lentillifera* is especially noted for its abundance of sulfated polysaccharides, which have demonstrated strong scavenging activity against DPPH, ABTS, and nitric oxide radicals (Tesvichian *et al.*, 2024). These findings position *C. lentillifera* as a promising candidate for antioxidant-based interventions. Meanwhile, *C. sertularioides* is primarily recognized for the antioxidant efficacy of its sulfated polysaccharides (Cs-SPs), which are rich in total sugars and sulfate groups. These compounds contribute not only to robust in vitro antioxidant activity but also to the enhancement of both enzymatic and non-enzymatic antioxidant defenses in vivo, suggesting broader physiological benefits (Anjali *et al.*, 2022).



C. racemosa C. lentillifera C. sertularioides

Figure 2. Selected Representatives of Three Distinct *Caulerpa* Species (source: https://www.algaebase.org).

The chemical diversity observed among these *Caulerpa* species reflects species-specific biochemical strategies for mitigating oxidative stress. This intra-genus variation underscores the importance of targeted, species-level investigations to fully unlock the antioxidant potential of *Caulerpa* as a natural therapeutic resource.

Unique antioxidant features of *Caulerpa* relative to other marine algal species

Caulerpa species, particularly *C. racemosa* and *C. lentillifera*, exhibit distinctive and often superior antioxidant profiles compared to other marine macroalgae such as *Ulva*, *Gracilaria*, and *Sargassum*. These enhanced capacities are largely attributed to their high phenolic and flavonoid content, which result in low IC_{50} values in DPPH and hydroxyl radical scavenging assays (Palaniyappan *et al*., 2023; Honey *et al*., 2024). Methanolic extracts of *C. racemosa* show strong activity in both DPPH and ABTS assays (Palaniyappan *et al*., 2023), while sulfated polysaccharides from *C. lentillifera* demonstrate EC_{50} values comparable to the standard antioxidant Trolox (Nurkolis *et al*., 2023).

Other algae also display antioxidant properties—*Ulva lactuca* through its polyphenols and flavonoids (Ouahabi *et al*., 2024), *Ulva rigida* via ulvan polysaccharides (Nova *et al*., 2023), and *Sargassum muticum* with its potent phenolic content (Bouzenad *et al*., 2024)—*Caulerpa* stands out due to its broader and more potent bioactive profile. *Gracilaria gracilis*, despite its high nutritional value, exhibits relatively weaker antioxidant activity (Nova *et al.*, 2023), and red algae like *Colaconema formosanum* rely primarily on protein hydrolysates for their antioxidant effects (Windarto *et al.*, 2024). In contrast, *Caulerpa* species not only excel in radical scavenging capacity but also exhibit multifunctional bioactivity, including anti-obesity and anticancer properties linked to their sulfated polysaccharides (Nurkolis *et al.*, 2023).

A defining feature of *Caulerpa*, especially *C. racemosa*, is the presence of unique antioxidant compounds not commonly found in other macroalgae. One such compound is caulerpin, a secondary metabolite with demonstrated high binding affinities in molecular docking studies, highlighting its potential in the development of antidiabetic and anticancer drugs (Dissanayake *et al*., 2022). Additionally, *C. racemosa* contains an extensive range of carotenoids—particularly xanthophylls such as fucoxanthin, lutein, astaxanthin, canthaxanthin, zeaxanthin, β-carotene, and β-cryptoxanthin—with β-carotene and canthaxanthin being especially abundant. These pigments contribute to diverse biological activities, including anti-inflammatory, anti-obesity, and antidiabetic effects (Kurniawan *et al*., 2023).

Moreover, a bioactive peptide—Glu-Leu-Trp-Lys-Thr-Phe (ELWKTF)—isolated from *C. racemosa* enhances its antioxidant profile and holds promise as a functional food ingredient (Nurkolis *et al*., 2022). Supporting this, ethanolic extracts rich in phenolics, flavonoids, and tannins have shown substantial antioxidant activity (Gazali *et al*., 2022). Metabolomic profiling further reveals a diverse array of antioxidant-related compounds contributing to both antioxidant and cytotoxic functions in *Caulerpa* extracts (Nurkolis *et al*., 2022).

Altogether, these bioactive features distinguish *Caulerpa*, especially *C. racemosa*, as a uniquely potent source of marine antioxidants. Its combination of high phenolic content, specialized metabolites like caulerpin and peptides, and multifunctional carotenoids positions it beyond the capabilities of many other macroalgae. This makes *Caulerpa* an exceptional candidate for the development of novel nutraceuticals and therapeutics targeting oxidative stress-related conditions, underscoring its significance in future health and functional food innovations.

The benefits, bioavailability, and efficacy of bioactive compounds from *Caulerpa* in biological systems

Antioxidants derived from *Caulerpa* species have demonstrated promising potential in preventing or reducing diseases associated with oxidative stress, as shown in various biological systems. An aqueous extract of *C. racemosa* has been reported to improve cardiometabolic syndrome in mice by modulating oxidative stress and inflammation, as well as improving blood lipid and glucose levels—factors central to cardiovascular health (Nurkolis *et al*., 2023). Additionally, *C. racemosa* extracts have been shown to influence the gut microbiome, which plays a crucial role in systemic health, including cardiovascular and metabolic regulation. Other studies have emphasized its therapeutic relevance in protecting against skin damage, where a clionasterol-rich fraction of *C. racemosa* has been shown to inhibit oxidative stress and apoptosis-related signalling pathways in response to environmental pollutants, supporting its use in the prevention of chronic diseases (Liyanage *et al*., 2022). Furthermore, the antioxidant mechanisms of *Caulerpa* compounds, such as the regulation of reactive oxygen species (ROS) and enhancement of endogenous defenses, have implications for managing neurodegenerative diseases, cardiovascular conditions, and cancer (Bhandari et al., 2024; Blagov *et al*., 2024; Houldsworth, 2024; Muscolo *et al*., 2024).

The growing body of evidence supporting *Caulerpa*'s ability to scavenge free radicals and repair damaged cells suggests that these antioxidants can reduce the risk of oxidative stress-related diseases (Akbari *et al*., 2022). The antioxidant efficacy of *Caulerpa* has been confirmed by both *in vitro* and *in vivo* studies. Methanolic extracts of *C. racemosa* demonstrated strong radical scavenging activity against DPPH and ABTS, attributed to high phenolic, flavonoid, and tannin content (Nurkolis *et al*., 2023; Palaniyappan *et al.*, 2023). GC-MS analysis identified bioactive constituents responsible for these effects, while carotenoids, such as fucoxanthin and β-carotene, further contributed to antioxidant, anti-inflammatory, and antidiabetic activities (Kurniawan *et al*., 2023). *In vivo* studies confirm systemic effects, including the regulation of oxidative stress and inflammation, as well as modulation of the microbiome (Nurkolis *et al.*, 2023). Integrated *in vitro* and in silico research also demonstrated *C. racemosa*'s antidiabetic and anticancer potential, revealing high binding affinities of certain compounds to disease-relevant molecular targets (Dissanayake *et al.*, 2022). Additionally, XOS-3 from *C. lentillifera* improved cell viability and modulated inflammatory markers *in vitro*, highlighting potential applications in treating osteoarthritis (Cai *et al*., 2024).

These findings collectively underscore the significant bioavailability and biological efficacy of *Caulerpa*-derived compounds in reducing oxidative stress-related pathologies. Understanding the mechanisms behind these effects is crucial for integrating them into functional foods and therapeutic agents (Yan *et al*., 2023; Ghosh *et al*., 2024). However, to transition from research to application, key challenges must be addressed. These include ensuring compound stability during processing, optimizing extraction methods, and conducting clinical trials to validate safety and efficacy in humans (Oliverio *et al*., 2022). Furthermore, navigating regulatory frameworks and promoting cross-sector collaboration will be crucial to support the development of *Caulerpa*-based nutraceuticals and pharmaceuticals.

Environmental Influences and Stressors Impacting Antioxidant Bioactivity in *Caulerpa* spp.

The antioxidant profile of *Caulerpa* species is shaped by a variety of environmental and biological factors, including light exposure, nutrient availability, habitat conditions, and possibly the harvest season. Among these, light plays a particularly critical role. Moderate high-intensity light has been shown to enhance total phenolic content in *C. lentillifera*, whereas overexposure may lead to chlorophyll degradation and bleaching (Stuthmann *et al*., 2020). A comparable trend is observed in *Agarophyton vermiculophyllum*, which exhibits increased antioxidant activity under elevated light conditions, highlighting the critical need to optimize light regimes in macroalgal cultivation systems (Tretiak *et al*., 2021).

Environmental disturbances such as pollution and climate change also influence antioxidant responses in *Caulerpa*. For instance, *C. racemosa* has demonstrated bioremediation potential by effectively removing zinc—a pollutant commonly derived from plastic leachates—indicating an upregulated antioxidant response under stress (Landi *et al.*, 2022). Polyphenolic extracts from *C. racemosa* exhibit dose-dependent antioxidant activity in polluted environments, underscoring the relationship between environmental stress and the biosynthesis of defensive bioactive compounds (Dissanayake *et al.*, 2022).

Nutrient availability, particularly nitrogen, is another significant factor influencing growth and metabolism. Variations in nitrate concentrations affect protein expression and biochemical pathways in *C. lentillifera*, thereby modulating antioxidant-related metabolic activity (Hsu *et al*., 2023). Similarly, habitat conditions such as salinity and temperature play critical roles; for example, increased salinity has been associated with elevated antioxidant activity, likely as part of a stress-induced defensive mechanism (Tretiak *et al*., 2021).

Microbial communities associated with *Caulerpa* further contribute to its antioxidant capacity. These microbial consortia exhibit varying degrees of resilience and resistance to environmental changes, such as nutrient enrichment and temperature shifts. Endomicrobiota are characterized by high resistance but low resilience, and their dynamic interactions with the host may influence oxidative stress responses and the production of bioactive compounds (Morrissey *et al.*, 2021).

Additionally, specific secondary metabolites produced by *Caulerpa*, such as caulerpin—a known Peroxisome Proliferator-Activated Receptor (PPAR) agonist—are involved in detoxification and modulation of oxidative stress, especially in the presence of environmental contaminants like caffeine (Russo *et al.*, 2024). The species' ecological interactions further reflect its antioxidant roles; for example, *C. taxifolia* has been reported to reduce oxidative stress in corals during thermal events, suggesting ecological benefits beyond the algal cells themselves (Fu *et al.*, 2022). Furthermore, genetic diversity and site-specific adaptation, as demonstrated in phylogenetic studies of *Caulerpa* from French Polynesia, underscore the species' varied responses to environmental pressures (Lagourgue *et al.*, 2024).

The relationship between environmental stress and antioxidant production is not unique to *Caulerpa*. Similar adaptive strategies have been observed in other organisms. In microalgae, antioxidant capacity often correlates with the growth phase and is closely tied to the synthesis of carotenoids and phenolic compounds (Rahman *et al.*, 2020). In fungi, exposure to UV radiation has been shown to increase phenolic acid production and antioxidant activity, as seen in *Trametes versicolor* and *Flammulina velutipes* (Krsmanović *et al.*, 2023). Likewise, callus cultures of *Barleria prionitis* L. have demonstrated higher flavonoid and phenolic content compared to the parent plant, resulting in enhanced antioxidant capacity (Ranade and Kudale, 2023). Marine fungi also display this trend, producing diverse antioxidant-rich secondary metabolites in response to stress (Vitale *et al.*, 2020)

In *Caulerpa*, these responses reflect a complex interplay of abiotic stressors, metabolic regulation, and microbial interactions. Bioactive compounds such as phenolics, flavonoids, and carotenoids are highly sensitive to fluctuations in light intensity, nutrient concentrations, salinity, and temperature (Kurniawan *et al*., 2023). However, natural marine environments are inherently variable, which poses a challenge to maintain consistent antioxidant yield. This reinforces the importance of controlled cultivation strategies aimed at stabilizing key environmental parameters. Controlled aquaculture systems, particularly those using artificial seawater—offer a promising approach to precisely manipulate growth conditions and consistently optimize antioxidant content in *Caulerpa* (Tretiak *et al*., 2021).

Ultimately, the antioxidant capacity of *Caulerpa* is the outcome of multifactorial interactions involving environmental variables, species-specific traits, symbiotic relationships, and cultivation practices. Strategic optimization of these factors is essential for maximizing the nutritional, pharmaceutical, and ecological potential of *Caulerpa*-derived antioxidants.

In conclusion, *Caulerpa* species exhibit dynamic and multifaceted antioxidant responses to diverse environmental stressors. These responses are shaped not only by abiotic influences—such as light, salinity, nutrients, and pollutants—but also by biotic factors, including microbial symbionts and interspecies interactions. A deeper understanding of these influences is crucial for advancing sustainable cultivation and fully harnessing *Caulerpa*'s antioxidant potential for applications in food, medicine, and environmental resilience.

Toxicological Considerations and Potential Risks of *Caulerpa* for Human Consumption

Given that the genus *Caulerpa* has demonstrated considerable potential for bioremediation—particularly in effectively removing heavy metals such as zinc (Zn) from aquatic environments (Landi *et al*., 2022) this raises critical concerns regarding the toxicological and safety aspects of consuming *Caulerpa*. While the metal uptake ability of *Caulerpa* is advantageous for environmental clean-up, it also presents a double-edged sword when considering these macroalgae for food or nutraceutical use. A study by Rajaram *et al.* (2020) found that ten commonly consumed seaweed species had metal concentrations exceeding World Health Organization (WHO) safety standards, with *C. racemosa* and *C. scalpelliformis* ranking among the top three in terms of heavy metal accumulation. Similarly, Rahhou *et al.* (2024) highlighted the remarkable bioaccumulation capacities of *C. prolifera*, underscoring their utility in heavy metal remediation but simultaneously drawing attention to the implications of this trait for public health, especially in regions where wild-harvested seaweeds are consumed without stringent quality controls.

Given these findings, ensuring the safe consumption of algae products, including *Caulerpa*, requires a multi-pronged approach involving rigorous toxicological assessments (Salehipour-Bavarsad *et al.*, 2024). Future research should prioritize evaluating metal uptake under various environmental conditions, including different salinity levels, pollution levels, and water temperatures, which can influence bioaccumulation rates. Toxicological studies should incorporate standardized protocols for heavy metal testing, particularly for elements like cadmium, lead, arsenic, and mercury, which pose significant health risks even at low concentrations. Additionally, human dietary exposure models should be used to assess long-term consumption risks. At the same time, decontamination methods—such as pre-treatment washing, blanching, or fermentation—should be further developed and validated to mitigate contamination in harvested biomass (Akomea-Frempong *et al.*, 2021; Patria *et al.*, 2023). These assessments will be crucial for shaping regulatory frameworks that guide the safe use of *Caulerpa* in food, pharmaceuticals, and cosmetics.

Challenges, Limitations, and Research Gaps in the Study of *Caulerpa* Antioxidants

Research on *Caulerpa* antioxidants, like other antioxidant studies, faces methodological challenges that may impact the reliability and comparability of the results. One significant issue is the variability in sample composition, a common obstacle in nutritional and antioxidant research. The chemical makeup of foods, including marine sources like *Caulerpa*, is complex and influenced by environmental conditions and processing methods, leading to potential bias if not adequately controlled, as demonstrated in food composition and nutrient intake studies (Ottaviani *et al*., 2024). Furthermore, the lack of standardization in antioxidant measurement methods complicates the research landscape. Various assays, including spectrophotometry, chromatography, and electrochemical techniques, are used to measure antioxidant activity, each with its strengths and limitations. For instance, spectrophotometric methods are widely used due to their sensitivity and cost-effectiveness; however, they may not accurately reflect antioxidant capacity because of potential interference and sample preparation that can alter the biological matrix (Christodoulou *et al*., 2022).

Emerging techniques, such as electrochemical methods, provide alternatives to conventional approaches by addressing issues like the use of hazardous solvents and the need for extensive sample pretreatment. However, these methods are still under development and require further validation (Alam *et al*., 2022). Additionally, inconsistencies in using different assays and the lack of universally accepted standards for measuring antioxidant capacity hinder the comparability of studies. This challenge is further compounded by the inherent limitations of conventional assays, such as DPPH, which require the separation of hydrophilic and lipophilic fractions—an approach that may introduce artifacts and compromise the accuracy of the results (Finotti *et al*., 2024). To address these issues, innovative techniques such as the OXEFIN unit have been developed, aiming to streamline antioxidant capacity measurements by eliminating the need for extensive sample preparation. OXEFIN® is designed to assess the antioxidant capacity of both individual compounds and complex, opaque matrices—such as food samples—without relying on target molecules, optical detection instruments like spectrophotometers, or any sample pre-treatment. However, despite its potential, this method has yet to gain widespread adoption (Finotti *et al*., 2024).

Additionally, concerns remain regarding the precision and comparability of antioxidant assays in general, as reaction kinetics and thermodynamic variables often complicate the interpretation of results. Using green-synthesized nanoparticles for antioxidant measurements is promising for environmental sustainability and accuracy, but it also requires additional validation and standardization (Beğiç *et al*., 2021). Overall, research on *Caulerpa* antioxidants is challenged by sample variability, methodological inconsistency, and the need for improved analytical techniques to ensure reliable and comparable outcomes across studies.

Research on *Caulerpa* antioxidant bioactivity has remained largely focused on general compound identification without a specific analysis of antioxidant chemical compositions, which vary according to environmental conditions and cultivation practices (Stuthmann *et al*., 2022). Few studies have examined the impact of environmental factors, such as sunlight intensity, on specific antioxidants in *Caulerpa* species. Since over 80% of *Caulerpa* production in Southeast Asia occurs in open waters affected by nutrient and light variability, understanding *Caulerpa*'s biochemical responses to these changes is crucial. Existing research has not isolated the effects of nutrient dosage on antioxidant activity in *C. lentillifera* cultivated in open waters under consistent sunlight exposure. Most studies have assessed nutrients under varying environmental conditions, creating a gap in understanding the isolated effects of nutrients separate from other factors, such as light intensity. Similarly, the impact of reduced sunlight on the production of specific antioxidants in *C. lentillifera* remains understudied. Current research generally explores antioxidant activity in response to changing light conditions alongside other variables, indicating a need for studies that explicitly isolate the effects of sunlight limitation in open-water cultivation scenarios.

Exploration of *C. racemosa* as an antioxidant source for food and pharmaceutical applications highlights several knowledge gaps regarding the long-term stability and safety of its bioactive compounds. While *C. racemosa* exhibits promising antidiabetic, anticancer, and antioxidant properties, studies often overlook the stability of these compounds during processing, storage, and digestion, as observed in broader research bioactive food compounds (Giaconia *et al*., 2020; Dissanayake *et al*., 2022). The stability of phenolic antioxidants is influenced by factors like pH and atmosphere, with alkaline conditions promoting oxidation and degradation (Pasquet *et al*., 2024). This suggests that similar challenges may affect *Caulerpa*-derived antioxidants, necessitating further investigation into optimal preservation conditions. Incorporating bioactive compounds into nanostructures has been suggested to enhance stability and bioactivity; however, this approach requires careful material selection and method optimization, which still warrants further exploration (Giaconia *et al*., 2020). Although the use of natural antioxidants from plants in food systems is growing as a sustainable alternative to synthetic options, *Caulerpa*-based antioxidants have not yet been thoroughly tested in this context (Gharby *et al*., 2022). Techniques such as encapsulation, as seen with puerarin, enhance stability and solubility, indicating potential for *Caulerpa* compounds; however, further studies are needed to validate these methods (Zheng *et al*., 2022).

Additionally, the safety of these compounds, particularly regarding their interactions with other food components and behavior under various storage conditions, remains unexplored. Antioxidant stability in various formulations, such as nano-micelles, shows potential for both food and pharmaceutical applications; however, specific studies on *Caulerpa* antioxidants are lacking (Janik-Zabrotowicz *et al*., 2020). The relationship between antioxidant capacity and health benefits remains complex, requiring further research into the health impacts of *Caulerpa* antioxidants (Pellegrini *et al*., 2020). Natural antioxidants, such as carnosic acid, can outperform synthetic options under specific conditions, suggesting that *Caulerpa* antioxidants may offer similar benefits; however, empirical validation is needed (Wei *et al*., 2023). While *C. racemosa* has demonstrated pharmacological potential, comprehensive studies on its long-term stability, safety, and efficacy in food and pharmaceutical applications are crucial for fully realizing its benefits and ensuring consumer safety.

Another critical challenge lies in the lack of methodological uniformity across studies investigating *Caulerpa* antioxidants, which undermines the comparability and translatability of findings. Firstly, the variability of antioxidant assays remains a major limitation. Different studies employ diverse methods—such as DPPH, ABTS, FRAP, and ORAC—each with distinct principles, sensitivities, and reaction conditions. This inconsistency complicates cross-study comparisons and may yield contradictory results for the same extract (Christodoulou *et al.*, 2022; Finotti *et al.*, 2024). Secondly, extraction protocols for *Caulerpa* metabolites vary significantly in terms of solvent type, polarity, duration, and temperature, all of which impact the yield and profile of bioactive compounds. The absence of standardized extraction procedures often results in incomparable antioxidant values, which are further compounded by the underreporting of critical methodological parameters, such as solvent ratios, sample-to-solvent volume, and pre-treatment steps. These inconsistencies may explain divergent IC_{50} values or differing compound identification across similar species (Giaconia *et al.*, 2020; Dissanayake *et al.*, 2022). Lastly, a persistent translation gap exists between *in vitro* findings and real-world applications. Most antioxidant studies on *Caulerpa* remain confined to cell-free assays, with a limited investigation into *in vivo* bioavailability, metabolism, or physiological relevance. The efficacy of these antioxidants in biological systems, particularly in digestion, systemic absorption, and interactions with human enzymes or microbiota, remains poorly understood. Bridging this gap will require multidisciplinary approaches, including pharmacokinetics, clinical trials, and food formulation studies, to evaluate the health implications of *Caulerpa*-based antioxidants beyond the laboratory setting.

Commercializing *Caulerpa*-based antioxidants involves considering regulatory and ethical aspects, with a focus on safety, efficacy, and sustainability. New products, especially therapeutic ones, must undergo extensive testing to ensure safety and efficacy. This includes in vitro and in vivo studies to evaluate antioxidant, antidiabetic, and anticancer activities, as demonstrated *C. racemosa* research (Dissanayake *et al*., 2022; Nurkolis *et al*., 2023). Extracting bioactive compounds from marine sources, such as *Caulerpa*, must also comply with environmental regulations to avoid overharvesting and promote sustainable use. Circular economy approaches, such as lipid extraction from *C. lentillifera* waste, highlight the importance of efficiently using materials to align with sustainability goals (Srinorasing *et al*., 2021). Ethical considerations are essential to ensure benefits are accessible and do not harm local communities or ecosystems. The potential of *Caulerpa* spp. in antidiabetic and anticancer drugs underscores the need for ethical sourcing and equitable resource distribution (Dissanayake *et al*., 2022; Mert-Ozupek *et al*., 2022). In silico studies of *Caulerpa* secondary metabolites aid in predicting interactions and side effects, thereby supporting regulatory compliance and ethical transparency in product development (Mert-Ozupek *et al*., 2022). The proven antioxidant properties of *Caulerpa*-based products suggest their potential applications in pharmaceuticals, food, and cosmetics; however, these products must comply with industry regulations to ensure safety. Ethical implications related to marine resources necessitate a balance between innovation and conservation to prevent biodiversity loss. Techniques like *in vitro* cultivation can increase metabolite production sustainably, serving as a model for *Caulerpa* commercialization practices. Overall, the successful commercialization of *Caulerpa*-based antioxidants depends on navigating regulatory and ethical landscapes to ensure products are safe, effective, and sustainably sourced while considering broader environmental and social impacts.

Research Trends on Antioxidant Bioactive Compounds in *Caulerpa*

Emerging technologies and genetic studies of *Caulerpa* can be effectively integrated with interdisciplinary efforts in marine biology, pharmacology, and food science to enhance the discovery and utilization of antioxidants from this genus. The combination of *in vitro* and in silico analyses has demonstrated the potential of *C. racemosa* in antioxidant, antidiabetic, and anticancer activities, highlighting bioactive compounds such as polyphenols and caulerpin, which exhibit high binding affinity in molecular docking studies (Dissanayake *et al*., 2022). Furthermore, metabolomics profiling and identification of bioactive peptides in *C. racemosa* reveal its potential as a functional food with antioxidant and cytotoxic properties that make it promising for nutraceutical applications (Nurkolis *et al*., 2022).

Genetic studies of sulfotransferases in *Caulerpa* have revealed unique genome features that can be harnessed for producing complex sulfated polysaccharides, which hold value for pharmaceutical and nutraceutical applications (Landi and Esposito, 2020). The antioxidant potential of *C. lentillifera*, for example, can be enhanced through controlled light exposure, yielding antioxidant levels comparable to those of nutrient-rich fruits, such as pomegranates, and serving as a post-cultivation treatment to boost the nutritional value of sea grapes (Sommer *et al*., 2022). The bioactive components of *C. lentillifera*, including phenolic compounds, polysaccharides, and siphonaxanthin, demonstrate significant antioxidants, immunomodulatory, and cancer-preventive properties, supporting its use in health-related industries (Chen *et al*., 2019).

The interdisciplinary approach also involves advanced molecular identification techniques, such as DNA barcoding, to accurately identify *Caulerpa* species and analyze their bioactive components, which is crucial for developing algae-based products with antioxidant, antibacterial, anticancer, and anti-inflammatory properties (Wirawan *et al*., 2022). Additionally, the exploration of sea cucumber peptides, which share the same marine habitat as *Caulerpa*, has revealed promising anti-neurodegenerative properties, suggesting that similar cryptic peptides in *Caulerpa* could be investigated for their health benefits. The isolation and characterization of bioactive compounds from other seaweeds, like *Dyctyosphaeria* sp., further illustrates the potential of marine algae as natural antioxidant sources, which can be applied to *Caulerpa* research (Loupatty *et al*., 2023).

Moreover, the local use of *C. lentillifera* in Indonesia as a food source, along with its rich fatty acid content, highlights its potential as a nutraceutical resource, underscoring the need for further research to exploit its antioxidant properties fully. By combining emerging technologies and genetic insights with interdisciplinary efforts, *Caulerpa*'s full potential as a source of antioxidants can be realized, benefiting various industries and contributing to human health and environmental sustainability.

CONCLUSION

In conclusion, *Caulerpa* spp. offers significant potential as a source of antioxidant bioactive compounds, which hold promise for applications in pharmaceuticals, food, and nutraceuticals. Despite the promising antioxidant properties highlighted in studies, several research gaps remain, particularly concerning the effects of environmental factors such as light intensity and nutrient availability on the antioxidant composition and activity of *Caulerpa*. Advances in emerging technologies and interdisciplinary research, including genetic studies, metabolomics, and *in vitro*/in silico assays, have begun to uncover the complex bioactive profiles of *Caulerpa* species, such as *C. racemosa* and *C. lentillifera*, showcasing their antioxidant, antidiabetic, and anticancer potential. To fully harness the antioxidant capabilities of *Caulerpa*, future research should prioritize the standardization of antioxidant measurement techniques and address the stability and efficacy of its bioactive compounds in various applications. By refining these methodologies and understanding the influence of environmental and cultivation factors, *Caulerpa* could become a reliable and sustainable source of natural antioxidants for enhancing human health.

REFERENCES

Akbari, B.; Baghaei-Yazdi, N.; Bahmaie, M. and Abhari, F. M. (2022). The role of plant-derived natural antioxidants in reduction of oxidative stress. *BioFactors*. 48(3):611-633. doi:10.1002/biof.1831.

Akomea-Frempong, S.; Skonberg, D. I.; Camire, M. E. and Perry, J. J. (2021). Impact of blanching, freezing, and fermentation on physicochemical, microbial, and sensory quality of sugar kelp (*Saccharina latissima*). *Foods*. 10(10):2258. https://doi.org/10.3390/foods10102258.

Alam, M. W.; Najeeb, J.; Naeem, S.; Usman, S. M.; Nahvi, I.; Alismail, F.; Abuzir, A.; Farhan, M. and Nawaz, A. (2022). Electrochemical methodologies for investigating the antioxidant potential of plant and fruit extracts: A review. *Antioxidants*. 11(6):1205. doi:10.3390/antiox11061205.

Anjali, R.; Palanisamy, S.; Vinosha, M.; Selvi, A. M.; Manikandakrishnan, M.; Sathiyaraj, G.; Marudhupandi, T.; You, S. G. and Prabhu, N. M. (2022). Sulfated polysaccharides from *Caulerpa sertularioides*: extraction and evaluation of antioxidant, antibacterial, and immunological properties. *Industrial Crops and Products*. 188(Part B):115671. doi:10.1016/j.indcrop.2022.115671.

Aroyehun, A. Q. B.; Razak, S. A.; Palaniveloo, K.; Nagappan, T.; Rahmah, N. S. N.; Jin, G. W.; Chellappan, D. K.; Chellian, J. and Kunnath, A. P. (2020). Bioprospecting cultivated tropical green algae, *Caulerpa racemosa*: a perspective on nutritional properties, antioxidative capacity and antidiabetic potential. *Foods*. 9(9):1313. doi:10.3390/foods9091313.

Ashraf, M. V.; Khan, S.; Misri, S.; Gaira, K. S.; Rawat, S.; Rawat, B.; Khan, M. A. H.; Shah, A. A.; Asgher, M. and Ahmad, S. (2024). High-altitude medicinal plants as promising source of phytochemical antioxidants to combat lifestyle-associated oxidative stress-induced disorders. *Pharmaceuticals*. 17(8):975. doi:10.3390/ph17080975.

Bagade, S. B. and Patil, M. (2021). Recent advances in microwave assisted extraction of bioactive compounds from complex herbal samples: A review. *Critical Reviews in Analytical Chemistry*. 51(2):138-149. doi:10.1080/10408347.2019.1686966.

Beğiç, N.; Bener, M. and Apak, R. (2021). Development of a green synthesized silver nanoparticle-based antioxidant capacity method using carob extract. *Journal of Nanostructure in Chemistry*. 11(3):381–394. doi:10.1007/s40097-020-00374-6.

Bhandari, U. R.; Danish, S. M.; Ahmad, S.; Ikram, M.; Nadaf, A.; Hasan, N.; Kesharwani, P. and Ahmad, F. J. (2024). New opportunities for antioxidants in amelioration of neurodegenerative diseases. *Mechanisms of Ageing and Development*. 221:111961. doi:10.1016/j.mad.2024.111961.

Blagov, A. V.; Summerhill, V. I.; Sukhorukov, V. N.; Zhigmitova, E. B.; Postnov, A. Y. and Orekhov, A. N. (2024). Potential use of antioxidants for the treatment of chronic inflammatory diseases. *Frontiers in Pharmacology*. 15:1378335. doi:10.3389/fphar.2024.1378335.

Bouzenad, N.; Ammouchi, N.; Chaib, N.; Messaoudi, M.; Bousabaa, W.; Bensouici, C.; Sawicka, B.; Atanassova, M.; Ahmad, S. F. and Zahnit, W. (2024). Exploring bioactive components and assessing antioxidant and antibacterial activities in five seaweed extracts from the Northeastern Coast of Algeria. *Marine Drugs*. 22(6):273. doi:10.3390/md22060273.

Cai, L.; Zheng, J.; Liu, L.; Chen, X. and Wang, H. (2024). Unlocking the potential of β-1,3-Xylooligosaccharides from *Caulerpa lentillifera*: Structural characterization, antioxidative and anti-osteoarthritis applications. *Chemical and Biological Technologies in Agriculture*. 11:54. doi:10.1186/s40538-024-00581-1.

Chen, X.; Sun, Y.; Liu, H.; Liu, S.; Qin, Y. and Li, P. (2019). Advances in cultivation, wastewater treatment application, bioactive components of *Caulerpa lentillifera* and their biotechnological applications. *PeerJ*. 7:e6118. doi:10.7717/peerj.6118.

Christodoulou, M. C.; Palacios, J. C. O.; Hesami, G.; Jafarzadeh, S.; Lorenzo, J. M.; Domínguez, R.; Moreno, A. and Hadidi, M. (2022). Spectrophotometric methods for measurement of antioxidant activity in food and pharmaceuticals. *Antioxidants*. 11(11):2213. doi:10.3390/antiox11112213.

Crupi, P.; Faienza, M. F.; Naeem, M. Y.; Corbo, F.; Clodoveo, M. L. and Muraglia, M. (2023). Overview of the potential beneficial effects of carotenoids on consumer health and well-being. *Antioxidants*. 12(5):1069. doi:10.3390/antiox12051069.

Dissanayake, I. H.; Bandaranayake, U.; Keerthirathna, L. R.; Manawadu, C.; Silva, R. M.; Mohamed, B.; Rizwan, A. and Peiris, D. C. (2022). Integration of *in vitro* and in-silico analysis of *Caulerpa racemosa* against antioxidant, antidiabetic, and anticancer activities. *Scientific Reports*. 12:20848. doi:10.1038/s41598-022-24021-y.

Finotti, E.; Gezzi, R.; Crudeli, M. L. and Remediani, E. (2024). A preliminary study on a new approach for measurement of the antioxidant capacity of single molecules in food. *Journal of Food Composition and Analysis*. 128:106023. doi:10.1016/j.jfca.2024.106023.

Fu, J. R.; Zhou, J.; Zhang, Y. P. and Liu, L. (2022). Effects of *Caulerpa taxifolia* on physiological processes and gene expression of *Acropora hyacinthus* during thermal stress. *Biology*. 11(12):1792. doi:10.3390/biology11121792.

Gazali, M.; Nurjanah; Zamani, N. P.; Zuriat, Suriani, M.; Alfitrah, R.; Syafitri, R.; Hanum, Z.; Zurba, N. and Febrina, C. D. (2022). Antioxidant activity of green seaweed *Caulerpa racemosa* (Försskal) J. Agardh from Balai island water, Aceh. In *IOP Conference Series: Earth and Environmental Science*. 1033:1-8. doi:10.1088/1755-1315/1033/1/012052.

Gharby, S.; Oubannin, S.; Bouzid, H. A.; Bijla, L.; Ibourki, M.; Gagour, J.; Koubachi, J.; Sakar, E. H.; Majourhat, K. and Lee, L. H. (2022). An overview on the use of extracts from medicinal and aromatic plants to improve nutritional value and oxidative stability of vegetable oils. *Foods*. 11(20):3258. doi:10.3390/foods11203258.

Ghosh, S.; Kumar, V.; Mukherjee, H.; Saini, S.; Gupta, S.; Chauhan, S.; Kushwaha, K.; Lahiri, D.; Sircar, D. and Roy, P. (2024). Assessment of the mechanistic role of an Indian traditionally used ayurvedic herb *Bacopa monnieri* (L.)Wettst. for ameliorating oxidative stress in neuronal cells. *Journal of Ethnopharmacology*. 328:117899. doi:10.1016/j.jep.2024.117899.

Giaconia, M. A.; Ramos, S. D. P.; Pereira, C. F.; Lemes, A. C.; Rosso, V. V. D. and Braga, A. R. C. (2020). Overcoming restrictions of bioactive compounds biological effects in food using nanometer-sized structures. *Food Hydrocolloids*. 107:105939. doi:10.1016/j.foodhyd.2020.105939.

Gregório, B. J. R.; Ramos, L I. I.; Magalhães, M.; Silva, E. M. P.; Reis, S. and Segundo, M. A. (2020). Microplate ORAC-Pyranine spectrophotometric assay for high-throughput assessment of antioxidant capacity. *Microchemical Journal*. 158:105156. doi:10.1016/j.microc.2020.105156.

Hashemi, B.; Shiri, F.; Švec, F. and Nováková, L. (2022). Green solvents and approaches recently applied for extraction of natural bioactive compounds. *TrAC - Trends in Analytical Chemistry*. 157:116732. doi:10.1016/j.trac.2022.116732.

Honey, O.; Nihad, S. A. I.; Rahman, M. A.; Rahman, M. M.; Islam, M. and Chowdhury, M. Z. R. (2024). Exploring the antioxidant and antimicrobial potential of three common seaweeds of Saint Martin’s Island of Bangladesh. *Heliyon*. 10(4):e26096. doi:10.1016/j.heliyon.2024.e26096.

Houldsworth, A. (2024). Role of oxidative stress in neurodegenerative disorders: a review of reactive oxygen species and prevention by antioxidants. *Brain Communications*. 6(1):fcad356. doi:10.1093/braincomms/fcad356.

Hsu, P. H.; Kang, L. K.; Lim, W. T. and Hwang, P. A. (2023). Proteomics analysis reveals the mechanism of growth retardation under a specific nitrogen environment for *Caulerpa lentillifera*. *Algal Research*. 69:102953. doi:10.1016/j.algal.2022.102953.

Iveša, N.; Burić, P.; Buršić, M.; Kovačić, I.; Paliaga, P.; Pustijanac, E.; Šegulja, S.; Modrušan, A.; Bilić, J.; Millotti, G. (2024). A review on nutrients, phytochemicals, health benefits and applications of the green seaweed *Caulerpa racemosa* (Forsskål) J. Agardh. *Journal of Applied Phycology*. 36:3451-3473. doi: 10.1007/s10811-024-03341-8.

Janik-Zabrotowicz, E.; Arczewska, M.; Prochniewicz, P.; Świetlicka, I. and Terpiłowski, K. (2020). Stability of chlorophyll a monomer incorporated into cremophor EL Nano-Micelles under dark and moderate light conditions. *Molecules*. 25(21), 5059. doi:10.3390/molecules25215059.

Jiménez-Morales, W. A. and Cañizares-Macias, M. D. P. (2024). Fast FRAP-SIA method to determine antioxidant capacity. *Talanta*. 273:125813. doi:10.1016/j.talanta.2024.125813.

Jomova, K.; Raptova, R.; Alomar, S. Y.; Alwasel, S. H.; Nepovimova, E.; Kuca, K. and Valko, M. (2023). Reactive oxygen species, toxicity, oxidative stress, and antioxidants: Chronic diseases and aging. *Archives of Toxicology.* 97:2499-2574. doi:10.1007/s00204-023-03562-9.

Kokkali, M.; Martí-Quijal, F. J.; Taroncher, M.; Ruiz, M. J.; Kousoulaki, K. and Barba, F. J. (2020). Improved extraction efficiency of antioxidant bioactive compounds from *Tetraselmis chuii* and *Phaedoactylum tricornutum* using pulsed electric fields. *Molecules*. 25(17):3921. doi:10.3390/molecules25173921.

Krsmanović, N.; Rašeta, M.; Mišković, J.; Bekvalac, K.; Bogavac, M.; Karaman, M. and Isikhuemhen, O. S. (2023). Effects of UV stress in promoting antioxidant activities in fungal species *Trametes versicolor* (L.) Lloyd and *Flammulina velutipes (*Curtis) Singer. *Antioxidants*. 12(2):302. doi:10.3390/antiox12020302.

Kurniawan, R.; Nurkolis, F.; Taslim, N. A.; Subali, D.; Surya, R.; Gunawan, W. B.; Alisaputra, D.; Mayulu, N.; Salindeho, N. and Kim, B. (2023). Carotenoids composition of green algae *Caulerpa racemosa* and their antidiabetic, anti-obesity, antioxidant, and anti-inflammatory properties. *Molecules*. 28(7):3267. doi:10.3390/molecules28073267.

Lagourgue, L.; Sauvage, T.; Zubia, M.; Draisma, S. G. A.; Vieira, C.; Engelen, A. and Payri, C. E. (2024). Taxonomic insights into *Caulerpa* (Bryopsidales, Chlorophyta) species in French Polynesia: Confirmation of 13 species and reinstatement of *C. Pickeringii* Harvey & Bailey. *Diversity*. 16(4):243. doi:10.3390/d16040243.

Landi, S. and Esposito, S. (2020). Bioinformatic characterization of sulfotransferase provides new insights for the exploitation of sulfated polysaccharides in *Caulerpa*. *International Journal of Molecular Sciences*. 21(18):6681. doi:10.3390/ijms21186681.

Landi, S.; Santini, G.; Vitale, E.; Natale, G. D.; Maisto, G.; Arena, C. and Esposito, S. (2022). Photosynthetic, molecular and ultrastructural characterization of toxic effects of zinc in *Caulerpa racemosa* indicate promising bioremediation potentiality. *Plants*. 11(21):2868. doi:10.3390/plants11212868.

Leo, C. H. and Ong, E. S. (2023). Recent advances in the combination of organic solvent-free extraction, chemical standardization, antioxidant assay, and cell culture metabolomics for functional food and its by-product. *Critical Reviews in Food Science and Nutrition*. 64(32):11919-11933. doi:10.1080/10408398.2023.2245040.

Liyanage, N. M.; Nagahawatta, D. P.; Jayawardena, T. U.; Jayawardhana, H. H. A. C. K.; Lee, H. G.; Kim, Y. S.Y. and Jeon, J. (2022). Clionasterol-rich fraction of *Caulerpa racemosa* against particulate matter-induced skin damage via inhibition of oxidative stress and apoptosis-related signaling pathway. *Antioxidants (Basel)*. 1(10):1941. doi: 10.3390/antiox11101941.

Loupatty, V. D.; Dompeipen, E. J.; Radiena, M. S. Y. and Kolanus, J. P. M. (2023). Antioxidant activity and isolation of bioactive compounds from seaweed of *Silpau* (*Dyctyosphaeria* sp.). *Journal of Advanced Zoology*. 44(5):214-223. https://jazindia.com/index.php/jaz/article/view/2771/2213.

Lucena, A. M. M.; Souza, C. R. M.; Jales, J. T.; Guedes, P. M. M.; de Miranda, G. E. C.; de Moura, A. M. A.; Araújo-Júnior, J. X.; Nascimento, G. J.; Scortecci, K. C.; Santos, B. V. O. and Souto, J. T. (2018). The bisindole alkaloid caulerpin, from seaweeds of the genus *Caulerpa*, attenuated colon damage in murine colitis model. *Marine Drugs*. 16(9):318. doi: 10.3390/md16090318.

Mayulu, N.; Gunawan, W. B.; Park, M. N.; Chung, S.; Suh, J. Y.; Song, H.; Kusuma, R. J.; Taslim, N. A.; Kurniawan, R.; Kartawidjajaputra, F.; Nurkolis, F. and Kim, B. (2023). Sulfated polysaccharide from *Caulerpa racemosa* attenuates the obesity-induced cardiometabolic syndrome via regulating the PRMT1-DDAH-ADMA with mTOR-SIRT1-AMPK pathways and gut microbiota modulation. *Antioxidants (Basel)*. 12(8):1555. doi: 10.3390/antiox12081555.

Manandhar, B.; Kim, H. J. and Rhyu, D. Y. (2020). *Caulerpa okamurae* extract attenuates inflammatory interaction, regulates glucose metabolism and increases insulin sensitivity in 3T3-L1 adipocytes and RAW 264.7 macrophages. *Journal of Integrative Medicine*. 18(3):253-264. doi:10.1016/j.joim.2020.02.001.

Mehra, R.; Bhushan, S.; Bast, F. and Singh, S. (2019). Marine macroalga *Caulerpa*: role of its metabolites in modulating cancer signaling. *Molecular Biology Reports*. 46(3):3545-3555. doi:10.1007/s11033-019-04743-5.

Mert-Ozupek, N.; Calibasi-Kocal, G.; Olgun, N.; Basbinar, Y.; Cavas, L. and Ellidokuz, H. (2022). An efficient and quick analytical method for the quantification of an algal alkaloid caulerpin showed *In-Vitro* anticancer activity against colorectal cancer. *Marine Drugs*. 20(12):757. doi:10.3390/md20120757.

Morrissey, K. L.; Iveša, L.; Delva, S.; D'Hondt, S.; Willems, A. and Clerck, O. D. (2021). Impacts of environmental stress on resistance and resilience of algal-associated bacterial communities. *Ecology and Evolution*. 11(21):15004-15019. doi:10.1002/ece3.8184.

Muro, P.; Li, Z., Li, S.; Zhao, Z.; Jin, T.; Mao, F. and Mao, Z. (2024). The emerging role of oxidative stress in inflammatory bowel disease. *Frontiers in Endocrinology*. 15:1390351. doi:10.3389/fendo.2024.1390351.

Muscolo, A.; Mariateresa, O.; Giulio, T. and Mariateresa, R. (2024). Oxidative stress: the role of antioxidant phytochemicals in the prevention and treatment of diseases. *International Journal of Molecular Sciences*. 25(6):3264. doi:10.3390/ijms25063264.

Nova, P.; Pimenta-Martins, A.; Maricato, E.; Nunes, C.; Abreu, H.; Coimbra, M. A.; Freitas, A. C. and Gomes, A. M. (2023). Chemical composition and antioxidant potential of five algae cultivated in fully controlled closed systems. *Molecules*. 28(12):4588. doi:10.3390/molecules28124588.

Nurkolis, F.; Yusuf, V. M.; Yusuf, M.; Kusuma, R. J.; Gunawan, W. B.; Hendra, I. W.; Radu, S.; Taslim, N. A.; Mayulu, N.; Sabrina, N.; Tsopmo, A.; Kurniawan, R.; Theodorea, C. F.; Idrus, E. and Tallei, T. E. (2022). Metabolomic proling, *in vitro* antioxidant and cytotoxicity properties of *Caulerpa racemosa* : functional food of the future from algae. *Research Square*. pages 1-25. doi:10.21203/rs.3.rs-2158307/v1.

Nurkolis, F.; Taslim, N. A.; Qhabibi, F. R.; Kang, S.; Moon, M.; Choi, J.; Choi, M.; Park, M. N.; Mayulu, N. and Kim, B. (2023). Ulvophyte green algae *Caulerpa lentillifera*: metabolites profile and antioxidant, anticancer, anti-obesity, and *in vitro* cytotoxicity properties. *Molecules*. 28(3):1365. doi:10.3390/molecules28031365.

Oliverio, M.; Bulotta, S. and Duarte, N. (2022). Editorial: nature inspired protective agents against oxidative stress. *Frontiers in Pharmacology*. 13:859549. doi:10.3389/fphar.2022.859549.

Ottaviani, J. I.; Sagi-Kiss, V.; Schroeter, H. and Kuhnle, G. G. C. (2024). Reliance on self-reports and estimated food composition data in nutrition research introduces significant bias that can only be addressed with biomarkers. *ELife*. 13:RP92941. doi:10.7554/eLife.92941.

Ouahabi, S.; Daoudi, N. E.; Loukili, E. H.; Asmae, H.; Merzouki, M.; Bnouham, M.; Challioui, A.; Hammouti, B.; Fauconnier, M. L.; Rhazi, L.; Gotor, A. A.; Depeint F. and Ramdani, M. (2024). Investigation into the phytochemical composition, antioxidant properties, and in-vitro antidiabetic efficacy of *Ulva lactuca* extracts. *Marine Drugs*. 22(6):240. doi:10.3390/md22060240.

Pakki, E.; Tayeb, R.; Usmar, U.; Ridwan, I. A. and Muslimin, L. (2020). Effect of orally administered combination of *Caulerpa racemosa* and *Eleutherine americana* (Aubl) Merr extracts on phagocytic activity of macrophage. *Research in Pharmaceutical Sciences*. 15(4):401-409. DOI: 10.4103/1735-5362.293518.

Palaniyappan, S.; Sridhar, A.; Kari, Z. A.; Téllez-Isaías, G. and Ramasamy, T. (2023). Evaluation of phytochemical screening, pigment content, *in vitro* antioxidant, antibacterial potential and GC-MS metabolite profiling of green seaweed *Caulerpa racemosa*. *Marine Drugs*. 21(5):278. doi:10.3390/md21050278.

Pasquet, P. L.; Julien-David, D.; Zhao, M.; Villain-Gambier, M. and Trébouet, D. (2024). Stability and preservation of phenolic compounds and related antioxidant capacity from agro-food matrix: effect of pH and atmosphere. *Food Bioscience*. 57:103586. doi:10.1016/j.fbio.2024.103586.

Patria, M. P.; Kholis, N.; Anggreini, D. and Buyong, F. (2023). Abundance and distribution of microplastics in seawater, sediment, and macroalgae sea grapes *Caulerpa racemosa* from Semak Daun Island, Jakarta Bay, Indonesia. *Biodiversitas*. 24(6):3424-3430. DOI: 10.13057/biodiv/d240638.

Pellegrini, N.; Vitaglione, P.; Granato, D. and Fogliano, V. (2020). Twenty-five years of total antioxidant capacity measurement of foods and biological fluids: merits and limitations. *Journal of the Science of Food and Agriculture*. 100(14):5064-5078. doi:10.1002/jsfa.9550.

Petrucci, G.; Rizzi, A.; Hatem, D.; Tosti, G.; Rocca, B. and Pitocco, D. (2022). Role of oxidative stress in the pathogenesis of atherothrombotic diseases. *Antioxidants*. 11(7):1408. doi:10.3390/antiox11071408.

Pozo-Martínez, J.; Vázquez-Rodríguez, S.; Olea-Azar, C. and Moncada-Basualto, M. (2022). Evaluation of ORAC methodologies in determination of antioxidant capacity of binary combinations of quercetin and 3-(3,4,5-Trihydroxybenzoyl) coumarin derivatives. *Arabian Journal of Chemistry*. 15(11):104298. doi:10.1016/j.arabjc.2022.104298.

Rahman, N. A.; Katayama, T.; Wahid, M. E. A.; Kasan, N. A.; Khatoon, H.; Yamada, Y. and Takahashi, K. (2020). Taxon- and growth phase-specific antioxidant production by Chlorophyte, Bacillariophyte, and Haptophyte strains isolated from tropical waters. *Frontiers in Bioengineering and Biotechnology.* 8:581628. doi:10.3389/fbioe.2020.581628.

Rahhou, A.;, Layachi, M.; Aknaf, A.; Riouchi, O.; Ngadi, H.; Skalli, A.; Loukili, H.; Choukri, R.; El Haddaji, H.; EL Ouamari, N. and Mourad Baghour, M. (2024). Bioaccumulation of heavy metals in the green algae *Caulerpa prolifera* (Chlorophyta) from the Marchica lagoon, of Morocco: Spatio-temporal variations. *E3S Web of Conferences*. 527:02004. https://doi.org/10.1051/e3sconf/202452702004.

Rajaram, R.; Rameshkumar, S. and Anandkumar A. (2020). Health risk assessment and potentiality of green seaweeds on bioaccumulation of trace elements along the Palk Bay coast, Southeastern India. *Marine Pollution*

Bulletin. 154:111069. https://doi.org/10.1016/j.marpolbul.2020.111069.

Ranade, R., N. J. and Kudale, S. (2023). Comparative secondary metabolite expression in Callus Cultures and Mother Plant in *Barleria prionitis* L. *Plant Cell, Tissue and Organ Culture*. 155(3):653-663.doi:10.1007/s11240-023-02585-5.

Raza'I, T. S.; Putra, I. P.; Febrianto, T.; Amrifo, V. and Yanti, M. D. (2023). Distribution and potential of *Caulerpa* sp. around the Seribu Islands Waters, Jakarta. In *IOP Conference Series: Earth and Environmental Science*. 1148:1-7. doi:10.1088/1755-1315/1148/1/012023.

Rumpf, J.; Burger, R. and Schulze, M. (2023). Statistical evaluation of DPPH, ABTS, FRAP, and folin-ciocalteu assays to assess the antioxidant capacity of lignins. *International Journal of Biological Macromolecules*. 233:123470. doi:10.1016/j.ijbiomac.2023.123470.

Russo, T.; Coppola, F.; Paris, D.; Marchi, L. D.; Meucci, V.; Motta, A.; Carbone, M.; Cosmo, A. D.; Soares, A. M. V. M.; Pretti, C.; Mollo, E.; Freitas, R. and Polese, G. (2024). Exploring toxicological interactions in a changing sea: the case of the alkaloids caffeine and caulerpin. *Science of the Total Environment*. 912:169190. doi:10.1016/j.scitotenv.2023.169190.

Saberivand, A.; Sarvarzadeh, F.; Peighambarzadeh, S. Z.; Saberivand, M.; Pakizehvand, H.; Rashidi, S.; Rahbar, M. and Khoshniyat, M. (2022). The effect of *Caulerpa sertularioides* extract on bull sperm freezablity and subsequent embryo development. *Theriogenology*. 189:167-176. https://doi.org/10.1016/j.theriogenology.2022.06.017.

Salehipour-Bavarsad, F.; Nematollahi, M. A.; Pistocchi, R. and Pezzolesi, L. (2024). Algal food safety: Possible contaminations, challenges of harmonized quality assessments, and suggested recommendations for the nascent industry of microalgae-based products. *Algal Research*. 81:103579. https://doi.org/10.1016/j.algal.2024.103579.

Sanger, G. D. W.; Taher, N.; Dotulong, V.; Setiawan, A. A.; Permatasari, H. K.; Maulana, S.; Nurkolis, F.; Tsopmo, A. and Kim, B. (2023). Green seaweed *Caulerpa racemosa* - chemical constituents, cytotoxicity in breast cancer cells and molecular docking simulation. *Journal of Agriculture and Food Research*. 12:100621. doi:10.1016/j.jafr.2023.100621.

Sanniyasi, E.; Gopal, R. K.; Raj, P. P. and Shanmugavel, A. K. (2023). Anti-inflammatory, remorin-like protein from green marine macroalga *Caulerpa sertularioides* (S.G.Gmel.) M.Howe. *Heliyon*. 9(8): e19239. doi:10.1016/j.heliyon.2023.e19239.

Shen, L.; Pang, S.; Zhong, M.; Sun, Y.; Qayum, A.; Liu, Y.; Rashid, A.; Xu, B.; Liang, Q.; Ma, H. and Ren, X. (2023). Components: Principles, advantages, equipment, and combined technologies. *Ultrasonics Sonochemistry*. 101:106646. doi:10.1016/j.ultsonch.2023.106646.

Sommer, J.; Kunzmann, A.; Stuthmann, L. E. and Springer, K. (2022). The antioxidative potential of sea grapes (*Caulerpa lentillifera*, Chlorophyta) can be triggered by light to reach comparable values of pomegranate and other highly nutritious fruits. *Plant Physiology Reports*. 27:186-191. doi:10.1007/s40502-021-00637-6.

Srinorasing, T.; Chirasuwan, N.; Bunnag, B. and Chaiklahan, R. (2021). Lipid extracts from *Caulerpa lentillifera* waste: An alternative product in a circular economy. *Sustainability (Switzerland)*. 13(8):4491. doi:10.3390/su13084491.

Stuthmann, L. E. R. A.; Pribbernow, M.; Du, H. T.; Springer, K. and Kunzmann, A. (2022). Improving the nutritional value of edible *Caulerpa lentillifera* (Chlorophyta) using high light intensities. a realistic tool for sea grape farmers. *Algal Research*. 66:102785. doi:10.1016/j.algal.2022.102785.

Stuthmann, L. E.; Springer, K. and Kunzmann, A. (2020). Cultured and packed sea grapes (*Caulerpa lentillifera*): effect of different irradiances on photosynthesis. *Journal of Applied Phycology*. 33:1125-1136. doi:10.1007/s10811-020-02322-x/Published.

Tanna, B.; Choudhary, B. and Mishra, A. (2018). Metabolite profiling, antioxidant, scavenging and anti-proliferative activities of selected tropical green seaweeds reveal the nutraceutical potential of *Caulerpa* sp*. Algal Research*. 36:96-105. doi:10.1016/j.algal.2018.10.019.

Tesvichian, S.; Sangtanoo, P.; Srimongkol, P.; Saisavoey, T.; Buakeaw, A.; Puthong, S.; Thitiprasert, S.; Mekboonsonglarp, W.; Liangsakul, J.; Sopon, A.; Prawatborisut, M.; Reamtong, O, and Karnchanatat, A. (2024). Sulfated polysaccharides from *Caulerpa lentillifera*: optimizing the process of extraction, structural characteristics, antioxidant capabilities, and anti-glycation properties. *Heliyon.* 10(2):e24444. doi:10.1016/j.heliyon.2024.e24444.

Torres, P.; Osaki, S.; Silveira, E.; dos Santos, D. Y. A. C. and Chow, F. (2024). Comprehensive evaluation of folin-ciocalteu assay for total phenolic quantification in algae (Chlorophyta, Phaeophyceae, and Rhodophyta). *Algal Research*. 80:103503. doi:10.1016/j.algal.2024.103503.

Tretiak, S.; Schwoerbel, J.; Bosse, R.; Buck, B. H.; Enders, I.; Henjes, J.; Hoffmann, D.; Reimold, F. and Hofmann, L. C. (2021). Optimizing antioxidant activity in *Agarophyton vermiculophyllum* for functional packaging. *Algal Research*. 54:102232. doi:10.1016/j.algal.2021.102232.

Vilas-Franquesa, A.; Casertano, M.; Tresserra-Rimbau, A.; Vallverdú-Queralt, A. and Torres-León, C. (2023). Recent advances in bio-based extraction processes for the recovery of bound phenolics from agro-industrial by-products and their biological activity. *Critical Reviews in Food Science and Nutrition*. 64(29):10643-10667. doi:10.1080/10408398.2023.2227261.

Vitale, G. A.; Coppola, D.; Esposito, F. P.; Buonocore, C.; Ausuri, J.; Tortorella, E. and de Pascale, D. (2020). Antioxidant molecules from marine fungi: methodologies and perspectives. *Antioxidants*. 9(12):1183. doi:10.3390/antiox9121183.

Wei, W.; Han, Y. and Zhou, Y. (2023). Nutrients and sea surface temperature drive harmful algal blooms in China's coastal waters over the past decades.

Environmental Research Letters. 18(9):094068. doi:10.1088/1748-9326/acf0d7.

Windarto, S.; Hsu, J. L. and Lee, M. C. (2024). First report of antioxidant potential of peptide fraction derived from *Colaconema formosanum* (Rhodophyta) protein hydrolysates. *Biocatalysis and Agricultural Biotechnology*. 58:103232. doi:10.1016/j.bcab.2024.103232.

Wirawan, I. G. P.; Dewi, N. K. E. S.; Sasadara, M. M. V.; Sunyamurthi, I. G. N. A.; Jawi, I. M.; Wijaya, I. N.; Darmawati, I. A. P.; Suada, I. K. and Krisnandika, A. A. K. (2022). Phytochemical analysis and molecular identification of green macroalgae *Caulerpa* spp. from Bali, Indonesia. *Molecules*. 27(15):4879. doi:10.3390/molecules27154879.

Yamauchi, M.; Kitamura, U.; Nagano, H.; Kawatsu, J. and Gotoh, H. (2024). DPPH measurements and structure—activity relationship studies on the antioxidant capacity of phenols. *Antioxidants*. 13(3):309. doi:10.3390/antiox13030309.

Yan, Q.; Liu, S.; Sun, Y.; Chen, C.; Yang, S.; Lin, M.; Long, J.; Yao, J.; Lin, Y.; Yi, F.; Lei Meng, Yong Tan, Ai, Q.; Chen, N. and Yang, Y. (2023). Targeting oxidative stress as a preventive and therapeutic approach for cardiovascular disease. *Journal of Translational Medicine*. 21:519. doi:10.1186/s12967-023-04361-7.

Yoojam, S.; Ontawong, A.; Lailerd, N.; Mengamphan, K. and Amornlerdpison, D. (2021). The enhancing immune response and anti-inflammatory effects of *Caulerpa lentillifera* extract in raw 264.7 Cells. *Molecules*. 26(19):5734. doi:10.3390/molecules26195734.

Zhang, J.; Wen, C.; Zhang, H.; Duan, Y. and Ma, H. (2020). Recent advances in the extraction of bioactive compounds with subcritical water: A review. *Trends in Food Science and Technology*. 95:183-195. doi:10.1016/j.tifs.2019.11.018.

Zheng, L.; Xu, H.; Hu, H.; Ruan, J.; Shi, C.; Cao, J. and Zhang, X. (2022). Preparation, characterization and antioxidant activity of inclusion complex loaded with puerarin and corn peptide. *Food Bioscience.* 49:101886. doi:10.1016/j.fbio.2022.101886.

Zubia, M.; Draisma, S. G. A.; Morrissey, K. L.; Varela-Álvarez, E. and Clerck, O. D. (2020). Concise review of the genus *Caulerpa* J.V. Lamouroux. *Journal of Applied Phycology*. 32:23-39. doi:10.1007/s10811-019-01868-9.