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Therapeutic Potential of Marine Macroalgae in Peptic Ulcer Disease: Mechanisms, Bioactive Compounds, and Pharmaceutical Applications

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Abstract

Peptic ulcer disease is a problem that affects the stomach and intestines. It happens when there is not balance between the acid in the stomach and the stomachs defense system. The medicines that doctor usually given to people with this problem do work. They can have bad side effects if people take them for a long time. Sometimes the ulcer comes back so we need to find safer ways to treat it. Marine algae are like plants that grow in the ocean. They have many good things in them that can help the stomach. We looked at two types of algae called Gracilaria edulis and Ulva lactuca to see if they can help with peptic ulcer disease. We took these algae dried them and then used liquids to get the good stuff out of them. We tested these extracts to see what was in them. If they were safe to use. We did tests on these extracts including some that showed they have anti-ulcer properties. This means that they can help protect the stomach from ulcers. We think that this is because they have things like phenolics and flavonoids that help keep the stomach safe and reduce stress. Our study shows that Gracilaria edulis and Ulva lactuca are very good at helping with peptic ulcer disease and could be used to make medicines that are safer for people to take.

Keywords: Gracilaria edulis, Ulva lactuca, Anti-ulcer activity, Gastroprotective agents**,** Sulfated polysaccharides, Phenolic compounds, Bioactive compounds, Natural anti-ulcer agents.

1. Introduction

Ulcers in the gut often come back, causing ongoing trouble worldwide. These sores form when harsh stomach chemicals overpower the body's natural protections. Though treatments have improved, problems like internal bleeding or holes in the gut wall still happen. What keeps things difficult is how often the condition returns despite care. Damage happens mainly where acid and digestive juices act strongest - either in the stomach or upper intestine.[1] Few things spark peptic ulcers, one being too much stomach acid, another tied to long-term NSAID use. Damage often follows where H. pylori invade, stirring deeper harm. Instead of helping, some body responses

turn harmful when molecules run wild during oxidative strain. Cells falter under this assault, their walls weaken, repair slows down. Healing stalls because balance tips away from recovery.[2] NSAIDs produce ulcers because they block cyclooxygenase enzymes which decreases prostaglandin production and damages the protective abilities of gastric mucosal tissues.[3] H. pylori infection creates chronic inflammation which raises gastric acid production and stops the body from healing its mucosal tissues, making it the main cause of ulcer formation.[4] Most stomach ulcers from NSAIDs happen because these drugs block certain enzymes, which drops prostaglandin levels and leaves the gut lining less protected. On top of that, an H. pylori infection damages healing efforts by sparking long-term irritation and boosting acid production in the stomach.[5] Because of these limits, researchers began looking at natural options that are both safer and work better. Starting deep in the ocean, compounds from sea life caught interest - not just for variety in structure but also for wide-ranging effects on health.[6] The marine algae red and green seaweeds contain high levels of sulphated polysaccharides and phenolic compounds and flavonoids which provide both antioxidant and gastroprotective effects.[7] The current study selected Gracilaria edulis and Ulva lactuca because these species have been used by coastal communities for digestive treatment and scientific research shows their ability to protect gastric mucosa and decrease ulcer development..

1.1 Marine Algae as Medicinal Resources

From ocean depths come algae packed with potent natural chemicals, shaped by tough saltwater surroundings. These sea dwellers build rare defenses - not found on land - like sulfated sugars and complex tannin-like molecules. Instead of common plant traits, they form special steroids and protein fragments through adaptation. Some of these substances show strong effects in biological systems when tested. Harsh waves, shifting salinity, and constant sunlight drive this chemical creativity beneath the surface.[8] The research has studied red seaweeds, green seaweeds, and brown seaweeds because these three types of seaweed show potential to be used as treatments through their antioxidant and anti-inflammatory and antimicrobial and anticancer and gastroprotective properties.[9]

The research shows that sulphated polysaccharides from red and green algae enhance gastric mucosal protections by two mechanisms which include their ability to increase mucus production and their capacity to eliminate free radicals and their power to prevent acid-related mucosal damage.[10] Aforementioned polyphenols found in marine algae contribute to their marked antioxidant potency, which serves to protect gastric epithelial cells from oxidative stress-related damage.[11] From shorelines across East Asia, old healing ways often turned to seaweed when stomach troubles arose. Wounds met it too, touched by its presence through generations. Inflammation found a quiet answer there, woven into practice without fanfare. These uses were never written down in labs first - they grew instead from watching tides and bodies alike. Knowledge passed hand to hand, wave to skin. Not theory but doing gave weight to such choices. Time shaped trust in what washed up on rocks.[12] Fresh findings in sea-based science lately back up old beliefs, showing seaweed might hold new medicines for long-term gut issues - thanks to ongoing lab work and ocean exploration shaping its role naturally over time.[13]

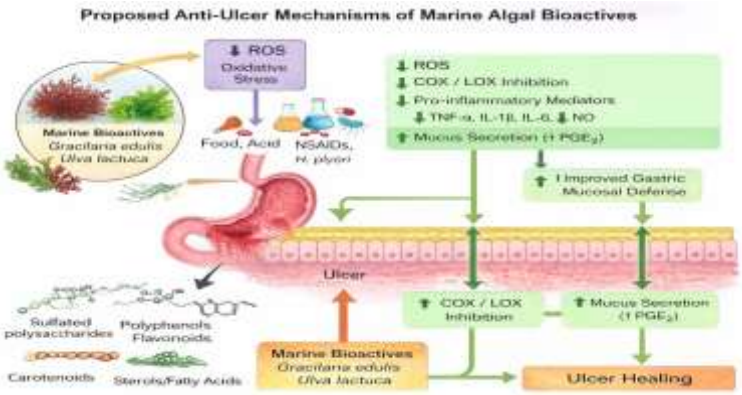
1.2 Anti-Ulcer Activity: Mechanisms and Therapeutic Relevance

Ulcers in the stomach happen when damage outweighs healing. Acid inside the gut plays a part, just like an enzyme called pepsin does. Harmful molecules known as free radicals add strain too. Painkillers such as ibuprofen tilt things off balance. Drinking alcohol makes conditions worse. Mental tension contributes more than once thought. A germ named H. pylori often shows up during flare-ups. Protection comes from slime-like barriers made by cells. Baking soda released nearby helps shield tissue. Natural body chemicals help maintain lining strength. Cells replace themselves regularly if all works well. Enzymes that fight rusting processes matter here. Blood moving steadily through gut walls keeps repair going.[14] When the stomach makes too much acid and pepsin, the gut's protective layer wears away. Oxidative stress worsens damage by breaking down fats in cell walls and

triggering cell death. Healing slows because of these combined effects.[15] The primary cause of NSAID-induced ulcers occurs when cyclooxygenase-1 (COX-1) activity becomes blocked which leads to decreased prostaglandin production that results in diminished mucosal defense through reduced mucus production and gastric blood circulation.[16] Furthermore, *H. pylori* infection induces chronic inflammation of the gastric mucosa, increases acid secretion, and interferes with normal repair processes, significantly contributing to ulcer recurrence and chronicity.[17]

Conventional anti-ulcer therapies, including proton pump inhibitors (PPIs), H2-receptor antagonists, antacids, and cytoprotective agents, aim mainly to reduce gastric acid secretion or neutralize acidity, thereby allowing ulcer healing.[18] Although these drugs are clinically effective, their prolonged use has been associated with several limitations such as nutrient malabsorption, increased susceptibility to infections, altered gut microbiota, rebound acid hypersecretion, and frequent ulcer relapse after cessation of therapy.[19] In addition, eradication therapy for *H. pylori* is often complicated by antibiotic resistance and patient non-compliance, further highlighting the need for alternative therapeutic strategies.

In this context, alternative therapies derived from natural sources have gained considerable attention due to their multi-targeted mode of action and better safety profiles. Natural products exert anti-ulcer effects not only by suppressing gastric acid secretion but also by enhancing mucosal defense mechanisms, scavenging free radicals, reducing inflammation, and promoting tissue regeneration.[20] Marine-derived natural compounds, particularly those obtained from algae, are of special interest because of their unique chemical composition and broad pharmacological potential. Bioactive constituents such as sulphated polysaccharides, flavonoids, and phenolic compounds present in marine algae have been reported to exhibit antioxidant, anti-inflammatory, and cytoprotective properties, which play a crucial role in ulcer prevention and healing.[21] These compounds strengthen the gastric mucosal **Figure 1.** Proposed mechanism of anti-ulcer activity of marine macroalgae (*Gracilaria edulis*



and *Ulva lactuca*) in gastric mucosal protection.

barrier, inhibit oxidative damage, and modulate inflammatory pathways, thereby offering a holistic approach to ulcer management. Hence, marine algae represent a promising and sustainable source of novel anti-ulcer agents with significant therapeutic relevance.

2. Gracilaria edulis: Profile and Bioactive Compounds

Gracilaria edulis is a red marine macroalga of the family Gracilariaceae that is abundantly distributed along tropical and subtropical coastal regions, particularly along the southeast and west coasts of India, Sri Lanka, and

other parts of the Indian Ocean. The alga typically inhabits intertidal and shallow subtidal zones, growing attached to rocks, coral fragments, or sandy substrates, where it is subjected to fluctuating environmental conditions such as variations in salinity, temperature, light intensity, and tidal exposure.[22] These environmental stresses play a crucial role in stimulating the biosynthesis of structurally diverse secondary metabolites with significant biological activities. Due to its ecological abundance and economic importance, *G. edulis* has been widely explored for both industrial and medicinal applications. Extraction of bioactive compounds from *G. edulis* is commonly carried out using aqueous methods to isolate sulphated polysaccharides and agar-type galactans, which are the major constituents of the algal cell wall, while organic solvent extraction using ethanol, methanol, acetone, or hydroalcoholic mixtures is employed to recover phenolic compounds, flavonoids, sterols, and other low-molecular-weight metabolites.[23]

Aqueous extracts are particularly rich in sulphated galactans, which have been reported to exhibit strong cytoprotective and gastroprotective properties by enhancing mucus secretion, strengthening epithelial barriers, and modulating inflammatory responses.[24] Phytochemical investigations have confirmed the presence of sulphated polysaccharides, phenolics, flavonoids, sterols, proteins, vitamins, and essential minerals in *G. edulis*, all of which contribute synergistically to its pharmacological profile.[25] Phenolic compounds and flavonoids present in the algal extracts are known to exert potent antioxidant activity by scavenging reactive oxygen species, chelating metal ions, and inhibiting lipid peroxidation, thereby protecting gastric epithelial cells from oxidative damage, which is a key factor in ulcer pathogenesis.[26]

In vitro antioxidant studies using assays such as DPPH, ABTS, and ferric reducing antioxidant power (FRAP) have demonstrated significant free radical scavenging activity of *G. edulis* extracts, comparable to standard antioxidants.[27] Furthermore, cytoprotective assays have revealed that *G. edulis* extracts stabilize cell membranes and reduce chemically induced cellular injury, indicating their potential to preserve gastric mucosal integrity.

These antioxidants and cytoprotective effects collectively contribute to the anti-ulcer activity of *G. edulis* by reducing oxidative stress, enhancing mucosal defense mechanisms, and promoting tissue repair (Table 1). Consequently, *G. edulis* represents a promising marine-derived natural resource for the development of safer and more effective anti-ulcer therapeutic agents.

Figure 2. Morphological appearance of Gracilaria edulis

Table – 1: Analysis of Anti-Ulcer Mechanisms

Protective Strategy	Action of Algal Bioactive	Therapeutic Relevance
Physical Shielding	Sulfated polysaccharides form a gel-like viscous barrier over the gastric epithelium.	Protects against direct chemical injury from alcohol or NSAIDs.
Mucosal Defense	Stimulates mucin secretion and increases prostaglandin synthesis.	Improves local blood flow and bicarbonate secretion.
Oxidative Control	Scavenges ROS and enhances enzymes like Superoxide Dismutase and Catalase.	Limits DNA damage and lipid peroxidation in stomach cells.
Regeneration	Supports epithelial cell migration and proliferation.	Accelerates the closing and healing of mucosal lesions.

3. Ulva lactuca: Profile and Bioactive Constituents

Ulva lactuca, commonly known as sea lettuce, is a green marine macroalga belonging to the family Ulvaceae and is widely distributed along temperate and tropical coastlines worldwide, including the Indian, Atlantic, and Pacific Oceans. It predominantly grows in intertidal and shallow subtidal regions, attaching to rocks, coral rubble, and other hard substrates, where it is exposed to environmental stresses such as salinity fluctuations, ultraviolet radiation, and oxidative conditions.[28]

These harsh ecological conditions stimulate the synthesis of a wide range of bioactive metabolites that play protective roles for the alga and impart significant pharmacological potential. Owing to its rapid growth, ecological abundance, and long history of dietary use, *U. lactuca* has attracted considerable interest as a sustainable marine resource for nutraceutical and pharmaceutical applications.[29]

Chemically, *U. lactuca* is rich in a diverse array of primary and secondary metabolites, among which sulphated polysaccharides, particularly ulvan, represent the major bioactive fraction. Ulvan is a complex heteropolysaccharide composed mainly of rhamnose, glucuronic acid, iduronic acid, xylose, and sulphate groups, which contribute to its biological activity.[30] In addition to ulvan, *U. lactuca* contains essential fatty acids such as linoleic acid, α-linolenic acid, palmitic acid, and oleic acid, which are known to modulate inflammatory pathways and maintain membrane integrity.[31] Phytochemical analyses have further identified flavonoids, phenolic acids, sterols, terpenoids, vitamins (A, C, and E), and trace minerals, all of which synergistically contribute to its antioxidant and cytoprotective properties.[32] Organic solvent extracts (methanol, ethanol, and hydroalcoholic mixtures) are particularly effective in isolating phenolics and flavonoids, whereas aqueous extraction yields polysaccharide-rich fractions with pronounced gastro-protective effects.[33]

Extensive bioactivity studies have demonstrated that *U. lactuca* exhibits strong antioxidant, anti-inflammatory, and cytoprotective properties. In vitro antioxidant assays such as DPPH, ABTS, superoxide radical scavenging, and ferric reducing antioxidant power (FRAP) have shown significant free radical scavenging activity of *U. lactuca* extracts, which is attributed mainly to its phenolic and sulphated polysaccharide content.[34]

These antioxidant effects are particularly relevant in the context of gastric ulceration, as oxidative stress plays a central role in gastric mucosal injury by promoting lipid peroxidation, DNA damage, and epithelial cell apoptosis. Additionally, anti-inflammatory studies have reported that *U. lactuca* extracts inhibit the production of pro-

inflammatory mediators such as nitric oxide, prostaglandins, and cytokines (TNF-α, IL-1β, IL-6), thereby reducing inflammation-induced gastric damage.[35]

Experimental evidence supporting the anti-ulcer potential of *U. lactuca* has been reported in both in vitro and in vivo models. Polysaccharide-rich extracts have shown the ability to protect gastric epithelial cells from ethanol- and NSAID-induced injury by enhancing mucus secretion, stabilizing cell membranes, and reducing acid-mediated damage.[36]

Animal studies using ulcer induction models such as ethanol-induced, pylorus ligation-induced, and indomethacin-induced gastric ulcers have demonstrated significant reductions in ulcer index, gastric acidity, and mucosal lesions following treatment with *U. lactuca* extracts.[37] Histopathological examinations further confirmed preservation of gastric mucosal architecture, reduced inflammatory cell infiltration, and enhanced regeneration of epithelial tissues, supporting the gastro-protective role of the alga.

At the molecular level, the gastro-protective and anti-ulcer effects of *U. lactuca* are mediated through multiple mechanisms. Ulvan and associated bioactive compounds exert antioxidant action by scavenging reactive oxygen species and enhancing endogenous antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase.[38] Anti-inflammatory effects are mediated through inhibition of cyclooxygenase-2 (COX-2), down-regulation of nuclear factor-κB (NF-κB) signalling, and suppression of pro-inflammatory cytokine expression. Furthermore, *U. lactuca* polysaccharides enhance gastric mucosal defense by stimulating mucus and bicarbonate secretion, improving microcirculation, and promoting epithelial cell proliferation and repair.[39]

These multifactorial molecular actions collectively contribute to reduced gastric acid injury, improved mucosal integrity, and accelerated healing of ulcers, highlighting *U. lactuca* as a promising marine-derived candidate for the development of safer natural anti-ulcer therapeutics.

Figure 3. Morphological appearance of Ulva lactuca

4. Comparative Analysis between *Gracilaria edulis* and *Ulva lactuca*

Marine algae have been widely recognized as promising natural sources of bioactive compounds with diverse therapeutic applications, including gastro-protection and anti-ulcer activity. Among the various marine macroalgae investigated, *Gracilaria edulis* (a red alga) and *Ulva lactuca* (a green alga) have attracted considerable scientific attention due to their wide availability, ease of collection, and pharmacologically relevant phytochemical profiles. Although both species occupy similar coastal habitats and are traditionally consumed in several cultures, they differ markedly in their biochemical composition and biological activities, particularly with respect to mechanisms involved in ulcer prevention and healing (Table 2).

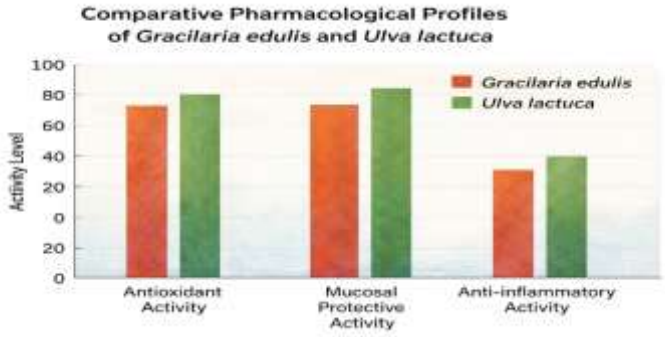


Figure 4. Microscopic observation showing the structural morphology of marine algal sample used in the study.

Table - 2: Comparative Profile of Gracilaria edulis and Ulva lactuca

Feature	**Gracilaria edulis (Red Algae)**	**Ulva lactuca (Green Algae)**
Primary Bioactive Compound	Sulphated Galactans (Agar-type)	Ulvan (Sulphated Heteropolysaccharide)
Secondary Metabolites	Phenolics, Flavonoids, Sterols, Proteins	Essential Fatty Acids, Vitamins (A, C, E), Trace Minerals
Main Anti-Ulcer Mechanism	Direct Mucosal Protection: Forms a physical gel-like barrier to shield the stomach lining	Antioxidant & Anti-inflammatory: Scavenges free radicals and inhibits pro-inflammatory cytokines
Extraction Methods	Aqueous (polysaccharides) and Organic solvents (phenolics)	Ultrasonic assisted (UAE) is particularly effective for ulvan recovery
Industrial Role	Major commercial source of Agar	Widely used in functional foods and nutraceuticals

4.1 Quantity and Types of Bioactive Compounds

The pharmacological potential of marine algae is largely determined by the nature and abundance of their bioactive constituents. *Gracilaria edulis* is rich in sulphated polysaccharides, mainly agar-type galactans, which constitute a major structural component of its cell wall and play an important role in its biological activity.[40] These sulphated polysaccharides are known to exhibit muco-protective and cytoprotective effects by strengthening gastric mucosal defenses and reducing epithelial damage. In addition to polysaccharides, extracts of *G. edulis* contain moderate levels of phenolic compounds, flavonoids, sterols, and proteins, which collectively contribute to antioxidant activity and cellular stabilization.[41]

In contrast, *Ulva lactuca* is characterized by the presence of ulvan, a distinctive sulphated heteropolysaccharide composed mainly of rhamnose, glucuronic acid, iduronic acid, xylose, and sulphate groups.[42] Ulvan and its derivatives have been reported to possess strong antioxidant, anti-inflammatory, and immunomodulatory properties. Beyond ulvan, *U. lactuca* contains appreciable quantities of essential fatty acids such as linoleic acid, α-linolenic acid, palmitic acid, and oleic acid, which are present in lower amounts in *G. edulis*.[43] Furthermore, *U.*

lactuca is a rich source of flavonoids, phenolic acids, carotenoids, vitamins (A, C, and E), and trace minerals that enhance its overall antioxidant capacity and support cellular repair processes.[44]

Comparatively, *U. lactuca* exhibits a broader spectrum of low-molecular-weight antioxidants and micronutrients, which may result in stronger free-radical scavenging activity. Conversely, *G. edulis* tends to contain higher levels of structural polysaccharides that provide direct mucosal protection. This difference suggests complementary therapeutic roles, where *U. lactuca* may be more effective in counteracting oxidative and inflammatory damage, while *G. edulis* may be particularly efficient in reinforcing gastric mucosal barriers.

4.2 Relative Anti-Ulcer Effectiveness

Anti-ulcer activity is a multifactorial process influenced by antioxidant potential, cytoprotective mechanisms, anti-inflammatory effects, and regulation of gastric secretions. Both *G. edulis* and *U. lactuca* have demonstrated significant anti-ulcer activity in experimental models, although the dominant mechanisms appear to differ due to variations in phytochemical composition.

Oxidative stress plays a central role in the pathogenesis of gastric and peptic ulcers, as excessive generation of reactive oxygen species damages the gastric mucosa and delays ulcer healing. In vitro antioxidant studies, including DPPH, ABTS, and ferric reducing antioxidant power (FRAP) assays, have consistently shown that *U. lactuca* extracts possess strong free-radical scavenging activity, largely attributed to their high ulvan, phenolic, and flavonoid content.[45] This potent antioxidant capacity suggests that *U. lactuca* may be particularly effective in protecting gastric epithelial cells from oxidative injury.

In contrast, *G. edulis* demonstrates pronounced cytoprotective effects, mainly due to its high content of sulphated polysaccharides, which may enhance mucus secretion, stabilize epithelial cell membranes, and protect the gastric lining against acid-induced injury.[46] In various experimental ulcer models, including ethanol-, NSAID-, and pylorus ligation-induced ulcers, both algae have shown reductions in ulcer index, gastric acidity, and mucosal damage. Although direct comparative studies using identical experimental conditions are limited, available evidence suggests that *U. lactuca* may exert stronger systemic antioxidant and anti-inflammatory effects, whereas *G. edulis* may be more effective in strengthening local mucosal defense mechanisms. This observation highlights the potential benefit of developing combined or synergistic formulations.

4.3 Strengths and Limitations of Current Research

Current research on *G. edulis* and *U. lactuca* presents several strengths, including consistent evidence of antioxidant, anti-inflammatory, and cytoprotective activities in both in vitro and in vivo models. These effects are supported by well-documented phytochemical profiles and favorable preclinical safety data, reinforcing their potential as natural anti-ulcer agents.[47]

However, significant limitations remain. A lack of standardized extraction methods and experimental protocols complicates direct comparison between studies and affects reproducibility. Direct comparative studies using identical models and dosages are scarce, making it difficult to conclusively establish relative efficacy. Moreover, mechanistic insights at the molecular level are limited, and human clinical trials are largely absent. Seasonal and environmental variations affecting algal phytochemistry are also insufficiently addressed, highlighting the need for more controlled and translational research.[48]

5. Other Bioactivities of *Gracilaria edulis* and *Ulva lactuca*

Marine macroalgae are increasingly recognized not only for their nutritional value but also for their wide range of pharmacological properties. Among them, *Gracilaria edulis* and *Ulva lactuca* have emerged as important

sources of biologically active compounds with diverse therapeutic effects. Beyond their gastroprotective and anti-ulcer potential, these algae exhibit antimicrobial, antiviral, anticancer, immunomodulatory, antidiabetic, and cardioprotective activities, which collectively support their application as functional foods and nutraceuticals (Table 3).[49]

Table – 3: Diverse Pharmacological Activities of G. edulis and U. Lactuca

Activity	**Biological Mechanism**	**Species Highlight**
Anticancer	Induces apoptosis, disrupts mitochondrial membrane, and activates caspases.	Both; *U. lactuca* ulvan induces cell cycle arrest.
Immunomodulatory	Enhances macrophage phagocytosis and activates Natural Killer (NK) cells.	Both; stimulates cytokine production (TNF-α, interleukins).
Antidiabetic	Inhibits α-amylase and α-glucosidase enzymes to delay glucose absorption.	Both; protects pancreatic β-cells from oxidative damage.
Cardioprotective	Lowers serum cholesterol and triglycerides; inhibits lipid peroxidation.	*U. lactuca* is particularly rich in polyunsaturated fatty acids.
Antimicrobial	Inhibits growth of various pathogenic bacteria and viruses.	Both species exhibit broad-spectrum activity.

5.1 Anticancer and Immunomodulatory Effects

Recent research has increasingly highlighted marine algae as promising sources of anticancer and immunomodulatory agents, largely due to their rich content of sulfated polysaccharides, phenolic compounds, sterols, and antioxidants. Both *Gracilaria edulis* and *Ulva lactuca* have demonstrated notable anticancer activity in various in vitro studies, where their extracts inhibited the proliferation of cancer cell lines such as colon, breast, and liver cancer cells.[50] These effects are primarily attributed to their ability to induce apoptosis, disrupt mitochondrial membrane potential, and activate caspase-dependent cell death pathways. Sulfated polysaccharides from *G. edulis* have been shown to suppress tumor cell growth by modulating oxidative stress and inhibiting DNA damage, while ulvan from *U. lactuca* can induce cell cycle arrest and reduce metastatic potential.[51]

In addition to their direct anticancer properties, both algae exhibit significant immunomodulatory effects, which play an important role in cancer prevention and immune homeostasis. Polysaccharides isolated from *Gracilaria* and *Ulva* have been reported to enhance macrophage phagocytic activity, stimulate cytokine production such as interleukins and tumor necrosis factor-α, and activate natural killer (NK) cells.[52] These immune-enhancing effects help strengthen host defense mechanisms against abnormal cell proliferation and infections. The combined anticancer and immunostimulatory actions of these marine algae suggest that they may function not only as cytotoxic agents but also as immune-supportive therapeutics, making them attractive candidates for adjunct cancer therapy.

5.2 Antidiabetic and Cardioprotective Activities

Metabolic disorders, including diabetes mellitus and cardiovascular diseases, are closely linked to oxidative stress, chronic inflammation, and lipid abnormalities. Extracts of *Gracilaria edulis* and *Ulva lactuca* have shown promising antidiabetic activity in experimental models by reducing blood glucose levels and improving insulin sensitivity.[53] These effects are largely mediated through the inhibition of carbohydrate-digesting enzymes such as α-amylase and α-glucosidase, which delays glucose absorption and prevents postprandial hyperglycemia. Additionally, the antioxidant properties of algal polysaccharides help protect pancreatic β-cells from oxidative damage, thereby preserving insulin secretion.[54]

Cardioprotective effects of these algae are also well documented. *Ulva lactuca* is particularly rich in polyunsaturated fatty acids, dietary fiber, and antioxidants, which contribute to the reduction of serum cholesterol and triglyceride levels.[55] Similarly, sterols and sulfated polysaccharides from *Gracilaria edulis* have been shown to inhibit lipid peroxidation, improve endothelial function, and reduce inflammatory markers associated with atherosclerosis.[56] By modulating lipid metabolism and oxidative stress, both algae may lower the risk of cardiovascular complications, especially in individuals with diabetes or metabolic syndrome.

6. Functional Food and Nutraceutical Potentials

The combination of nutritional richness and pharmacological activity positions *Gracilaria edulis* and *Ulva lactuca* as valuable candidates for functional food and nutraceutical development. Both species are traditionally consumed as edible seaweeds and are recognized as excellent sources of dietary fiber, essential minerals, vitamins, and bioactive polysaccharides.[57] Regular consumption of these algae has been associated with improved gut health, enhanced antioxidant status, and better metabolic regulation.

Ulva lactuca is widely explored for its use in functional foods due to the presence of ulvan, which exhibits prebiotic, immune-enhancing, and antioxidant properties. Ulvan-based formulations are increasingly being developed as nutraceutical supplements aimed at improving digestive health and immune function[58]. On the other hand, *Gracilaria edulis* is an important commercial source of agar, which is extensively used in food, pharmaceutical, and biomedical industries. Beyond its technological applications, agar and associated polysaccharides also contribute to health benefits such as glycemic control and gastrointestinal protection.[59] The growing interest in plant-based and marine-derived functional foods further supports the incorporation of these algae into health-oriented dietary products.

7. Extraction Techniques and Optimization

The extraction of bioactive compounds from marine algae is a critical step that directly influences yield, purity, and biological activity. In the case of *Gracilaria edulis* and *Ulva lactuca*, the complexity of algal cell walls and the structural diversity of their metabolites necessitate careful selection and optimization of extraction techniques. Traditionally, extraction has relied on conventional methods such as maceration, decoction, and Soxhlet extraction using solvents like water, ethanol, methanol, or acetone. These methods are simple, cost-effective, and widely used in preliminary studies; however, they often require long extraction times, large solvent volumes, and may lead to degradation of heat-sensitive compounds such as phenolics and sulfated polysaccharides.[60]

To overcome these limitations, advanced extraction techniques have gained prominence in marine natural product research. Microwave-assisted extraction (MAE) utilizes electromagnetic radiation to rapidly heat intracellular water, leading to cell wall disruption and enhanced release of bioactive compounds. MAE has been reported to significantly improve the extraction efficiency of polysaccharides and phenolic compounds from both red and green algae while reducing extraction time and solvent consumption.[61] Similarly, ultrasonic-assisted extraction

(UAE) employs acoustic cavitation to rupture algal cell walls, facilitating solvent penetration and mass transfer. UAE is particularly advantageous for *Ulva lactuca*, as it enhances the recovery of ulvan and antioxidant compounds without excessive thermal stress.[62] Other emerging techniques such as enzyme-assisted extraction and supercritical fluid extraction are also being explored, although their application is often limited by cost and operational complexity.[63]

Following extraction, purification and characterization of bioactive compounds are essential to ensure reproducibility and accurate biological evaluation. Crude algal extracts typically contain a mixture of polysaccharides, proteins, lipids, pigments, and minerals, necessitating further fractionation. Chromatographic techniques such as column chromatography and high-performance liquid chromatography (HPLC) are commonly used for the separation and quantification of phenolics, flavonoids, and sterols.[64] For structural elucidation and molecular profiling, advanced analytical tools including liquid chromatography–mass spectrometry (LC–MS) and nuclear magnetic resonance (NMR) spectroscopy play a crucial role. LC–MS enables sensitive detection and molecular weight determination of complex metabolites, while NMR provides detailed information on structural features, sulfation patterns, and monosaccharide composition of algal polysaccharides.[65] These techniques are indispensable for correlating chemical structure with biological activity.

Despite technological advancements, several challenges persist in the isolation of bioactive compounds from marine algae. One major challenge is the inherent variability in phytochemical composition due to environmental factors such as season, salinity, light exposure, and geographic location, which can significantly affect extraction yield and consistency.[66]

Additionally, the high molecular weight and structural heterogeneity of sulfated polysaccharides complicate purification and standardization processes. Co-extraction of salts, proteins, and pigments can interfere with downstream analysis and bioassays, requiring multiple purification steps that may reduce overall yield.[67] Furthermore, the lack of standardized extraction protocols across studies makes comparison of results difficult and limits translation into industrial or clinical applications. Addressing these challenges through systematic optimization and method validation is essential for advancing marine algal bioactive toward pharmaceutical and nutraceutical development.

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Figure 5. Schematic representation of the extraction process of marine algal bioactive from *Gracilaria edulis* and *Ulva lactuca*.

8. Safety, Toxicity, and Regulatory Considerations

The safety profile of marine algal extracts is a crucial factor in their development as therapeutic or nutraceutical agents. *Gracilaria edulis* and *Ulva lactuca* are both traditionally consumed as edible seaweeds in several coastal regions, which provides an initial indication of their general safety. However, therapeutic applications often involve concentrated or purified extracts, making systematic toxicological evaluation essential. Preclinical toxicity studies have therefore been conducted to assess both acute and chronic safety aspects of these marine algae.

Acute toxicity studies in experimental animal models have generally shown that extracts of *G. edulis* and *U. lactuca* exhibit low toxicity even at relatively high doses. Oral administration of algal extracts has not produced significant mortality, behavioral abnormalities, or gross pathological changes, and reported LD_{50} values are typically well above the doses used for pharmacological activity.[68] Subacute and chronic toxicity studies further support these findings, with repeated administration over several weeks showing no significant alterations in body weight, food intake, or organ morphology. Biochemical parameters related to liver and kidney function, such as serum transaminases, creatinine, and urea levels, remain within normal ranges, indicating minimal systemic toxicity.[69]

Despite these encouraging results, dosage determination remains an important consideration. Experimental studies investigating gastroprotective, antidiabetic, or antioxidant effects commonly use dose ranges between 100 and 500 mg/kg body weight in animal models, which have been reported to be both effective and safe.[70] For human consumption, direct dose extrapolation is not straightforward; however, the long history of dietary intake of these algae suggests that moderate consumption is unlikely to pose health risks. Nevertheless, high doses of sulfated polysaccharides may exhibit anticoagulant activity and could potentially interact with blood-thinning medications, highlighting the need for careful dose optimization and clinical monitoring.[71]

From a regulatory perspective, the classification of algal products depends largely on their intended use. When consumed as food or dietary supplements, *G. edulis* and *U. lactuca* generally fall under food safety regulations and novel food frameworks. In many countries, seaweeds are recognized as safe traditional foods, although regulatory agencies require evidence of quality, purity, and absence of contaminants such as heavy metals and microbial toxins.[72] For therapeutic or pharmaceutical applications, however, more stringent regulatory requirements apply. These include comprehensive toxicological data, standardization of extracts, demonstration of efficacy, and well-designed clinical trials to establish safety in humans.

Currently, the absence of large-scale human clinical studies represents a major limitation in the regulatory approval of marine algal extracts as drugs. Variability in phytochemical composition due to environmental and seasonal factors further complicates standardization, which is a key regulatory requirement.[73] Addressing these challenges through controlled cultivation, validated extraction protocols, and rigorous clinical evaluation will be essential for translating the promising preclinical safety of *Gracilaria edulis* and *Ulva lactuca* into approved therapeutic or nutraceutical products.

9. Role of Marine Algal Polysaccharides in Ulcer Healing

Marine algal polysaccharides play a central role in the gastroprotective and ulcer-healing properties of seaweeds such as *Gracilaria edulis* and *Ulva lactuca*. These algae are rich sources of sulfated polysaccharides, including agar and carrageenan in *Gracilaria* species and ulvan in *Ulva lactuca*. Structurally, these polysaccharides resemble endogenous mucopolysaccharides of the gastric mucus layer, which allows them to interact favorably with the gastric mucosa and contribute to mucosal defense mechanisms.[74] Their high molecular weight and sulfate content

are particularly important, as sulfation enhances biological activity, including cytoprotectant and resistance to acidic environments.

One of the primary mechanisms by which these polysaccharides promote ulcer healing is through the formation of a protective barrier over the gastric epithelium. Sulfated polysaccharides can adhere to the mucosal surface, forming a viscous, gel-like layer that shields the epithelium from direct exposure to gastric acid, pepsin, and other aggressive factors.[75] Agar and carrageenan derived from *Gracilaria* species have demonstrated strong film-forming properties, which help reinforce the mucus layer and prevent erosion of the gastric lining. Similarly, ulvan from *Ulva lactuca* contributes to surface protection by increasing mucosal viscosity and reducing epithelial permeability.[76] This physical barrier function is particularly relevant in ethanol- and NSAID-induced ulcer models, where mucosal damage is driven by direct chemical injury.

In addition to forming a protective layer, marine algal polysaccharides actively enhance mucus secretion and epithelial regeneration. Experimental studies have shown that administration of sulfated polysaccharides stimulates the production of gastric mucus by upregulating mucin secretion and increasing prostaglandin synthesis in the gastric mucosa.[77] Prostaglandins play a key role in maintaining mucosal integrity by promoting mucus and bicarbonate secretion and improving mucosal blood flow. Enhanced epithelial regeneration has also been reported, with polysaccharides supporting cell proliferation, migration, and restoration of damaged epithelial surfaces, thereby accelerating ulcer healing.[78]

Another important aspect of ulcer healing involves the reduction of gastric acid–mediated damage. While marine algal polysaccharides do not act as classical acid-suppressing agents like proton pump inhibitors, they indirectly reduce acid injury by strengthening defensive factors rather than inhibiting acid secretion itself. By maintaining the integrity of the mucus–bicarbonate barrier and neutralizing reactive oxygen species, these polysaccharides limit hydrogen ion back-diffusion into the gastric mucosa.[79] Furthermore, their antioxidant properties help reduce oxidative stress associated with acid-induced mucosal injury, thereby preventing further tissue damage and promoting recovery.[80]

Overall, the ulcer-healing potential of marine algal polysaccharides arises from a combination of physical protection, stimulation of endogenous defense mechanisms, enhancement of tissue repair, and mitigation of acid-related injury. This multifaceted mode of action makes polysaccharides from *Gracilaria edulis* and *Ulva lactuca* particularly attractive as natural gastroprotective agents and supports their potential use in the development of safer, mucosa-friendly anti-ulcer therapies.

10. Future Perspectives

Marine macroalgae such as *Gracilaria edulis* and *Ulva lactuca* represent promising natural resources for the development of safer and more effective anti-ulcer therapies. Future research should focus on standardizing extraction and purification protocols for sulfated polysaccharides to ensure reproducibility and consistent bioactivity across studies. Advanced extraction techniques, coupled with precise structural characterization using modern analytical tools, will help establish clear structure–activity relationships and optimize therapeutic efficacy.[81] Additionally, deeper investigation into molecular mechanisms particularly signalling pathways involved in mucus secretion, epithelial regeneration, inflammation modulation, and oxidative stress will strengthen the scientific basis for their gastroprotective effects.[82]

Another important future direction is the evaluation of these algal polysaccharides in well-designed clinical trials, as current evidence is largely limited to in vitro and animal studies. Human studies are essential to confirm safety, effective dosage ranges, and long-term tolerability. Furthermore, the development of novel delivery systems, such

as hydrogel-based formulations or functional foods, may enhance bioavailability and patient compliance.[83] Given their favorable safety profiles and nutritional value, *G. edulis* and *U. lactuca* also hold strong potential as nutraceuticals and preventive agents against gastric disorders. Integrating marine algal bioactive into evidence-based therapeutic strategies could contribute significantly to the future management of peptic ulcer disease with fewer side effects than conventional drugs.[84]

11. Biotechnological and Pharmaceutical Applications

Marine algae have emerged as valuable resources in biotechnology and pharmaceutical sciences owing to their biocompatible, biodegradable, and non-toxic polymeric constituents. Polysaccharides such as agar and carrageenan derived from *Gracilaria edulis* and ulvan obtained from *Ulva lactuca* exhibit excellent physicochemical properties including gel formation, swelling ability, and muco-adhesion, which make them suitable for use in drug delivery systems.[85] These characteristics are particularly advantageous in the development of gastro-retentive formulations intended for prolonged residence in the stomach, thereby improving the local therapeutic efficacy of drugs used in gastric disorders such as peptic ulcer disease.

Algal-based polymers have been extensively studied for the design of floating, mucoadhesive, and matrix-type gastro-retentive drug delivery systems. Their ability to form stable gels and adhere to the gastric mucosa helps retain the formulation in the stomach for extended periods, allowing controlled and sustained release of bioactive compounds at the site of action.[86] This localized and prolonged drug release not only enhances mucosal protection and ulcer healing but also reduces dosing frequency and minimizes systemic side effects associated with conventional therapies.[87]

In addition to their role in drug delivery, marine algal polymers are increasingly utilized as pharmaceutical excipients due to their functional versatility. Agar, carrageenan, and ulvan have been successfully employed as binders, disintegrants, thickening agents, stabilizers, and release-modifying agents in various dosage forms.[88] Compared to synthetic excipients, algal-derived polymers offer improved safety profiles, environmental sustainability, and cost-effectiveness. The growing interest in natural and bio-based excipients further supports the integration of marine algal polymers into modern pharmaceutical formulations. Overall, the use of *Gracilaria edulis* and *Ulva lactuca* in biotechnological and pharmaceutical applications represents a promising approach for the development of innovative, patient-friendly, and effective gastroprotective drug delivery systems.

12. Environmental and Sustainable Aspects of Marine Algae Utilization

The utilization of marine algae such as *Gracilaria edulis* and *Ulva lactuca* offers significant advantages from an environmental and sustainability perspective, making them attractive resources for future pharmaceutical and biotechnological applications. Sustainable harvesting of marine algae is particularly important to ensure ecological balance while meeting industrial and therapeutic demands. Unlike terrestrial medicinal plants, marine algae exhibit rapid growth rates, high biomass productivity, and do not require arable land, freshwater, or chemical fertilizers for cultivation. Controlled harvesting practices and aquaculture-based cultivation methods help prevent overexploitation of natural populations and support long-term resource availability.[89]

Marine algae also provide notable environmental benefits beyond their therapeutic value. They play an essential role in coastal ecosystem health by acting as natural biofilters that absorb excess nutrients such as nitrogen and phosphorus, thereby reducing eutrophication and improving water quality. Additionally, macroalgae contribute to carbon sequestration by capturing atmospheric carbon dioxide through photosynthesis, supporting climate change mitigation efforts.[90] The cultivation of algae is therefore considered an environmentally friendly approach that aligns with global sustainability and green chemistry principles.

In recent years, marine algae have gained prominence within the emerging field of blue biotechnology, which focuses on the sustainable use of marine biological resources for industrial, pharmaceutical, and environmental applications. Algae-based bioproducts, including bioactive polysaccharides, biopolymers, nutraceuticals, and pharmaceutical excipients, represent renewable and biodegradable alternatives to synthetic materials [95]. The integration of marine algae into blue biotechnology supports the development of eco-friendly drug delivery systems, functional foods, and health-promoting products while minimizing environmental impact. Overall, the sustainable exploitation of *Gracilaria edulis* and *Ulva lactuca* not only advances pharmaceutical research but also contributes to environmental conservation and the global shift toward sustainable bio-based technologies [96].

13. Conclusion

The present study highlights the promising potential of marine algal extracts from *Gracilaria edulis* and *Ulva lactuca* as natural anti-ulcer agents. The findings suggest that both algae are rich in bioactive constituents, particularly sulfated polysaccharides, phenolics, and flavonoids, which play a crucial role in gastric mucosal protection. Through formulation development and systematic evaluation, the algal extracts demonstrated favorable physicochemical properties along with significant antioxidant and cytoprotective activities, which are essential for ulcer prevention and healing.

The anti-ulcer activity observed can be attributed to multiple protective mechanisms, including the formation of a protective mucus layer over the gastric epithelium, enhancement of mucus secretion, reduction of oxidative stress, and promotion of epithelial regeneration. Compared to conventional anti-ulcer drugs, marine algal-based formulations offer the advantage of targeting mucosal defense mechanisms rather than solely suppressing gastric acid secretion, thereby potentially reducing adverse effects associated with long-term drug therapy.

Overall, the study supports the therapeutic relevance of *Gracilaria edulis* and *Ulva lactuca* in the management of peptic ulcer disease and emphasizes their suitability as safer, natural alternatives or adjuncts to existing treatments. However, further studies involving detailed molecular mechanisms, standardized formulations, and clinical evaluation are required to translate these findings into effective pharmaceutical or nutraceutical products. This work contributes to the growing evidence supporting marine algae as valuable resources in the development of novel gastroprotective therapies.

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