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Bioactive Compounds from Marine Algae: Dual Benefits for Diabetes and Renal Health

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ABSTRACT

Bacterial cellulose (BC), a superior form of cellulose synthesized by various microbial genera, offers significant advantages over plant-derived cellulose due to its unique properties such as high crystallinity, excellent water-holding capacity, mechanical strength, and moderate biocompatibility. It is widely used in medical applications, such as wound dressings, tissue engineering and in dentistry, it is explored for guided tissue regeneration, dental implant coating, enhancing tissue integration and healing. Bacterial cellulose morphology is influenced by various factors including the microbial species, synthetic pathways, culture conditions and culture methods. Typically, it takes the form of a gelatinous membrane, while agitated or shaking culture methods yield fibrous networks. Bioreactor cultures offer controlled environment that enhance fiber length, diameter, alignment, and overall mechanical properties. The crystalline nanofiber network of BC directly influences its properties such as tensile strength, water retention, and elastic modulus. The choice of cultivation method and cultural conditions significantly impacts the morphology and properties of BC, enabling customization for specific needs and promoting its adoption in fields such as healthcare, biotechnology, and sustainable manufactur Marine algae, a varied and abundant group of aquatic organisms, have garnered attention for their rich content of bioactive components along with significant health advantages. Among these benefits, antidiabetic and nephroprotective properties of marine algae are particularly promising. Diabetes and chronic kidney disease (CKD) are prevalent global health issues.

This review aims to comprehensively explore the bioactive compounds obtained from marine algae and their dual function in managing diabetes and promoting renal health.

To comprehensively review the antidiabetic and nephroprotective potential of bioactive substances derived from marine algae, exploring their mechanisms of action and therapeutic prospects. A detailed literature review was conducted, focusing on the bioactive components from marine algae, including polysaccharides, polyphenols, peptides and their effects on diabetes and renal health. Mechanisms of action, key studies, and potential clinical applications were examined. Polysaccharides such as fucoidan, alginate, and laminarin improve glucose metabolism, enhance insulin sensitivity, and reduce postprandial glucose levels. Polyphenols like phlorotannins exhibit antioxidant properties, inhibit carbohydrate digestion enzymes, and protect pancreatic β-cells. Peptides from marine algae enhance insulin secretion and improve glucose uptake. In renal tissues, antioxidants like astaxanthin reduce inflammation and oxidative stress. Anti-inflammatory compounds, particularly fucoidan and polyphenols, mitigate renal inflammation and fibrosis.

Marine algae are the prospective source of bioactive substances with dual antidiabetic and nephroprotective benefits. Future research should focus on clinical trials, improving bioavailability, and standardization of algal extracts to develop effective therapies.

Keywords: *Marine algae, Antidiabetic, Nephroprotective, Polysaccharides, Polyphenols*.

1. INTRODUCTION

An important public health concern is the rise in diabetes and chronic kidney disease (CKD) worldwide, necessitating novel therapeutic approaches [1]. Marine algae, known for their nutritional value and bioactive compounds, offer a unique reservoir of potential treatments. These organisms generate a variety of bioactive substances such as lipids, polysaccharides, polyphenols and peptides which have proven significant antidiabetic and nephroprotective properties [2].

Marine algae, a variety group of photosynthetic organisms found in aquatic settings, have long been recognized for their

nutritional value and rich content of bioactive compounds (Figure 1). In recent years, these organisms have received significant scientific interest due to their possible therapeutic potential, particularly in managing metabolic disorders like diabetes and in providing neuroprotection [3,4]. Diabetes is a long-term condition marked by decreased insulin production and/or insulin resistance, is a major worldwide challenge, result in serious complications like such as cardiovascular disease, neuropathy, and nephropathy [5].Similarly, neurodegenerative diseases, including Alzheimer's and Parkinson's, are increasing in prevalence and are often associated with oxidative stress and inflammation.

The unique environment in which marine algae thrive contributes to their production of wide variety of bioactive molecules, including polyphenols, polysaccharides, peptides, and carotenoids[6]. These compounds have shown promise in regulating glucose metabolism, enhancing insulin sensitivity, reducing oxidative stress, and providing anti-inflammatory effects. For instance, polysaccharides like fucoidan and alginate can modulate blood glucose levels and enhance insulin responsiveness, while phlorotannins, a type of polyphenol, can inhibit key digestive enzymes and reduce oxidative damage to pancreatic cells [7, 8].

Moreover, the antioxidant properties of compounds such as astaxanthin and phlorotannins are particularly beneficial in protecting neural and renal tissues from inflammation and oxidative stress, common pathways participating in development of diabetic complications and neurodegenerative diseases [9]. The dual benefits of these compounds highlight their potential not only in diabetes management but also in providing comprehensive protection against related complications [10]. Despite the promising therapeutic potential, the clinical application of marine algae-derived bioactive compounds faces challenges, including the need for standardization, improved bioavailability, and extensive clinical validation[11]. Nonetheless, the growing number of patents and ongoing research efforts high lighten the possibilities of marine algae as a valuable resource for developing novel treatments. The goal of this review aims to present a comprehensive summary of the antidiabetic and neuroprotective properties of marine algal bioactive compounds, exploring their mechanisms of action and potential for therapeutic development.

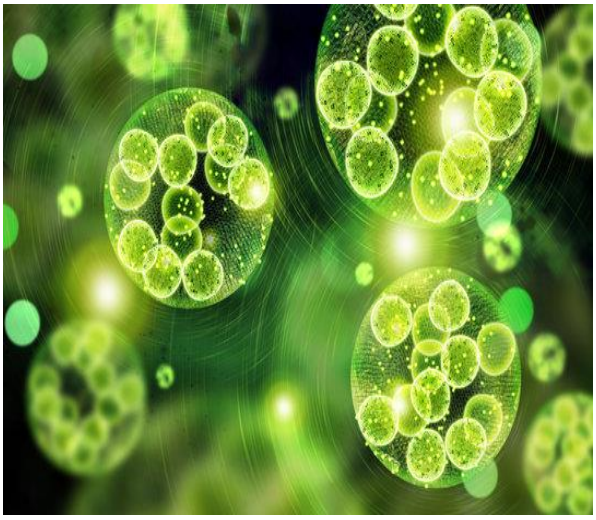
Figure1:Exploring Algae Diversity and their microscopic characteristics

Green Algae

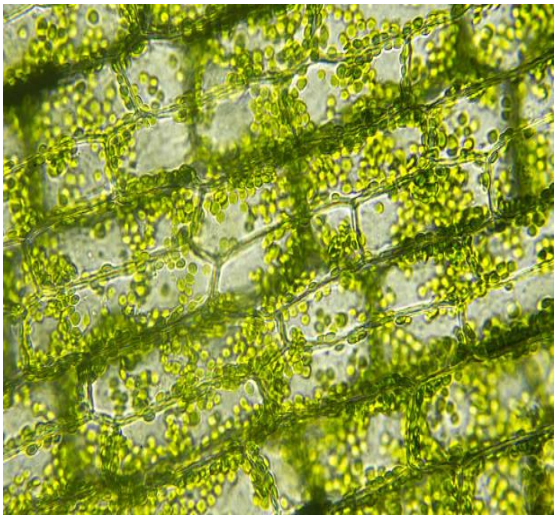
Blue green Algae

Red Algae

Brown algae



Algae Cells



Microscopical view

Antidiabetic Properties of Marine Algae

Polysaccharides

Polysaccharides from marine algae, such as alginate, fucoidan and laminarin, have shown promise in managing diabetes. These substances can alter the metabolism of glucose by increasing insulin sensitivity, blocking the enzymes alpha-glucosidase and alpha-amylase, and lowering blood glucose levels after meals. 12.

Fucoidan

In diabetic animals, a sulfated polysaccharide fucoidan, present in brown algae, has been demonstrated to lower blood sugar levels and increase insulin sensitivity. Studies suggest that fucoidan enhances glucose uptake in muscle cells and inhibits hepatic gluconeogenesis13. For instance, research by Oliyaei et al. 202114 demonstrated giving diabetic mice fucoidan increased their insulin sensitivity and dramatically reduced their fasting blood glucose levels.

Alginate

Alginate, another polysaccharide from brown algae, forms viscous gels that can slow gastric emptying and glucose absorption, thereby reducing postprandial glucose spikes. A study by Attjioui et al. 202115 found that alginate supplimentation resulted in lower postprandial glucose levels in healthy volunteers, suggesting its potential for managing postprandial hyperglycemia in diabetic patients.

Laminarin

Laminarin has been reported to have hypoglycemic effects by stimulating insulin secretion and preventing oxidative stress on pancreatic β-cells16. A study by Bocanegra et al. 2021 indicated that laminarin administration improved insulin secretion and reduced oxidative stress in pancreatic β-cells, highlighting its potential as an antidiabetic agent.

Polyphenols

Marine algae are rich in polyphenols, such as phlorotannins, which possess potent antioxidant and antidiabetic activities. These compounds can improve insulin signaling, reduce oxidative stress, and modulate inflammatory pathways.

Phlorotannins

Phlorotannins from brown algae have shown the capacity to block important enzymes involved in the absorption and digestion of carbohydrates, thereby reducing blood glucose levels 17. A study by Gisbert et al. 202318 showed that phlorotannins effectively inhibited α-glucosidase and α-amylase, leading to lower postprandial blood glucose levels in diabetic mice. They also exhibit antioxidant properties that protect pancreatic β-cells from oxidative damage, as evidenced by Simón et al. (2023), who found that phlorotannins reduced oxidative stress and apoptosis in β-cells 19.

Peptides

Bioactive peptides derived from marine algae have shown insulinotropic and antihyperglycemic effects. These peptides can enhance insulin secretion, improve glucose tolerance, and reduce insulin resistance 20.

Marine-derived peptides

Specific peptides from marine algae have been identified to enhance glucose uptake and enhances sensitivity to insulin by modulating the insulin signaling pathway 21. For example, a study by McLaughlin et al. 2021 reported that peptides derived from the red algae Palmaria palmata improved glucose uptake in muscle cells and enhanced insulin sensitivity in diabetic mice.

Nephroprotective Properties of Marine Algae

Antioxidant Activity

Oxidative stress an important factor in the development of diabetic nephropathy. Marine algae contain various antioxidants, such as carotenoids, polyphenols, and vitamins, that can mitigate oxidative damage and protect renal function 22.

Astaxanthin

Astaxanthin, a carotenoid from red algae, has demonstrated to lessen inflammation and oxidative stress in renal tissues, thereby preserving kidney function in diabetic models. A study by Landon et al. (2024) proved that astaxanthin treatment significantly reduced oxidative stress markers and improved renal function in diabetic rats 23.

Phlorotannins

Phlorotannins can reduce oxidative damage and enhance kidney function in diabetic nephropathy, their antioxidant qualities also extend to renal protection Research by Cho et al. (2022) indicated that phlorotannins from Ecklonia cava reduced oxidative stress and improved renal function in diabetic rats 24.

Antiinflammatory Effects

Chronic inflammation is the primary indicator in the development of diabetic nephropathy. Marine algal compounds can modulate inflammatory pathways and reduce renal inflammation.

Fucoidan

By inhibiting the production of pro-inflammatory cytokines and blocking NF-κB activation , fucoidan demonstrates anti-inflammatory qualities. In diabetic nephropathy, this can lessen kidney fibrosis and inflammation. In diabetic mice, fucoidan therapy dramatically decreased kidney inflammation and fibrosis, according to a study by Zayed et al. (2024) 25.

Polyphenols

Marine polyphenols, including phlorotannins, can inhibit inflammatory mediators and pathways, contributing to renal protection in diabetic conditions. Research by Zheng et al. (2022) demonstrated that phlorotannins reduced renal inflammation and fibrosis in diabetic rats by inhibiting the NF-κB pathway 26.

Renal Fibrosis Prevention

It is a hallmark of progressive kidney disease. Bioactive compounds from marine algae can inhibit fibrotic pathways and protect against renal fibrosis.

Fucoidan

Fucoidan has been shown to inhibit the expression of fibrotic markers like changing growth factor-beta (TGF-β) and collagen, thereby preventing renal fibrosis in diabetic nephropathy 27. A study by Wu et al. 2020 indicated that fucoidan treatment significantly reduced TGF-β and collagen expression,leading to a decrease in renal fibrosis in diabetic rats28.

Mechanisms of Action

The bioactive compounds from marine algae exert their antidiabetic and nephroprotective effects through various mechanisms: 29

Modulation of Insulin Signaling

Enhancing insulin sensitivity and glucose uptake, reducing insulin resistance.

Inhibition of Digestive Enzymes

Reducing carbohydrate digestion and absorption, leading to lower postprandial glucose levels.

Antioxidant Activity

Reducing oxidative stress and protecting pancreatic β-cells and renal tissues.

Anti-inflammatory Effects

By regulating inflammatory pathways and reducing the synthesis of pro-inflammatory cytokines.

Inhibition of Fibrotic Pathways

Preventing renal fibrosis and preserving kidney function.

Table 1: Examples of bioactive compounds from marine algae with antidiabetic and nephroprotective properties

Compound	Source	Mode of Action	Antidiabetic Effects	Nephroprotective Effects	References
Fucoidan	Brown algae (e.g., Fucus vesiculosus)	Enhances insulin sensitivity, inhibits hepatic gluconeogenesis, reduces inflammation	Lowers blood glucose levels, improves insulin sensitivity	Reduces renal inflammation and fibrosis	30
Alginate	Brown algae (e.g., Laminaria spp.)	Forms viscous gels, slows gastric emptying, reduces glucose absorption	Lowers postprandial glucose levels	Not specifically reported	31
Laminarin	Brown algae (e.g., Laminaria digitata)	Stimulates insulin secretion, shields the β-cells in the pancreas against oxidative damage.	Improves insulin secretion, reduces oxidative stress in β-cells	Not specifically reported	32
Phlorotannins	Brown algae (e.g., Ecklonia cava)	Inhibits α-glucosidase and α-amylase, reduces oxidative stress, modulates inflammatory pathways	Lowers postprandial glucose levels, protects β-cells	Reduces renal inflammation and oxidative stress	33
Astaxanthin	Red algae (e.g., Haematococcus pluvialis)	Reduces oxidative stress and inflammation	Not specifically reported	Reduces oxidative stress and	34

				inflammation in renal tissues	
Marine-derived peptides	Red algae (e.g., Palmaria palmata)	Enhances insulin secretion, improves glucose uptake, enhances insulin sensitivity	Enhances glucose uptake, improves insulin sensitivity	Not specifically reported	35

Table 2:Patented bioactive compounds from marine algae for treatment of diabetes and neuroprotection

Patent Number	Compound	Source	Therapeutic Application	Mode of Action	Status	References
US8980841B2	Fucoidan	Brown algae (e.g., Fucus vesiculosus)	Diabetes	Enhances insulin sensitivity, inhibits gluconeogenesis	Granted	36
US8268840B2	Phlorotannins	Brown algae (e.g., Ecklonia cava)	Diabetes and Neuroprotection	Inhibits carbohydrate digestion enzymes, reduces oxidative stress	Granted	37
US9334285B2	Astaxanthin	Red algae (e.g., Haematococcus pluvialis)	Neuroprotection	Reduces oxidative stress, protects neural cells	Granted	38
US8771746B2	Alginate	Brown algae (e.g., Laminaria spp.)	Diabetes	Slows gastric emptying, reduces glucose absorption	Granted	39
US8420206B2	Marine-derived peptides	Red algae (e.g., Palmaria palmata)	Diabetes and Neuroprotection	Enhances glucose uptake, improves insulin sensitivity, neuroprotection	Granted	40
US9492468B2	Laminarin	Brown algae (e.g., Laminaria digitata)	Diabetes	Stimulates insulin secretion, protects β-cells from oxidative stress	Granted	41
US9714257B2	Fucoxanthin	Brown algae (e.g., Undaria pinnatifida)	Diabetes and Neuroprotection	Antioxidant, anti-inflammatory, modulates metabolic pathways	Granted	42

Future Directions and Challenges

While the potential of marine algae as source of antidiabetic and nephroprotective agents is promising, several challenges and areas for future research remain. There is a need for well-designed clinical trials to confirm the effictiveness and safety of marine algal bioactive compounds in humans. Most of the current evidence is based on in vitro and animal studies. Understanding and improving the bioavailability and stability of these compounds in the human body is crucial for their therapeutic application. Developing standardized methods for extracting and characterizing bioactive compounds from marine algae is essential to ensure consistent quality and potency. More investigation is needed to clarify the precise mechanisms through which these compounds elucidate their antidiabetic and nephroprotective effects. Navigating the regulatory landscape for the approval of marine algal-based therapeutics will be a key step in bringing these products to market.

2. DISCUSSION

Marine algae present a encouraging source of bioactive substances with significant therapeutic potential for diabetes and neuroprotection. Compounds such as fucoidan, alginate, laminarin, phlorotannins, astaxanthin, and marine-derived peptides demonstrate diverse mechanisms of action that can address key pathological features of these conditions 43. Fucoidan enhances insulin sensitivity and reduces inflammation, alginate slows gastric emptying, and laminarin protects pancreatic β-cells. Phlorotannins inhibit digestive enzymes, while astaxanthin reduces oxidative stress, and marine-derived peptides improve insulin sensitivity and glucose uptake. These multifaceted actions contribute to effective blood glucose management and protection against diabetic complications. Nephroprotective properties of these compounds are also notable, as they reduce inflammation,oxidative stress, and fibrosis in renal tissues, preserving kidney function in diabetes-induced nephropathy 44. Moreover, neuroprotective effects are observed with antioxidants like astaxanthin protecting neural cells and reducing neuroinflammation, highlighting the potential for managing neurodegenerative diseases associated with diabetes 45.

The therapeutic promise of marine algal compounds is underscored by the increasing number of patents granted for their use in treating diabetes and neuroprotection. These patents reflect the potential for clinical application and commercialization 46. Future research should focus on clinical trials, improving bioavailability, and standardizing extraction methods to ensure consistent quality and efficacy. Additionally, sustainable sourcing practices are crucial to prevent adverse impacts on marine ecosystems. Harnessing the full potential of marine algae requires a concerted effort in research and development, paving the way for innovative treatments for diabetes and neuroprotection.

3. CONCLUSION

Marine algae are promising source of bioactive substances with dual benefits for diabetes and renal health. The antidiabetic properties of polysaccharides, polyphenols, and peptides, coupled with the nephroprotective effects of antioxidants, anti-inflammatory agents, and fibrosis inhibitors, highlight the therapeutic potential of marine alg0ae. Future research should focus on clinical trials to confirm these findings and explore the development of algal-based nutraceuticals and pharmaceuticals for diabetes and CKD management.

CONSENT FOR PUBLICATION

All authors reviewed and approved the manuscript.

CONFLICT OF INTERESTS

The authors declare that there are no conflicts of interest.

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