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Review

Diatom Biorefinery: Comprehensive Resource Utilization and Economic Feasibility for Sustainable Development

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Abstract: Driven by global resource shortages and carbon neutrality strategies, diatom biorefinery technology has emerged as a key solution to reduce production costs and promote a green economy, thanks to its unique potential for comprehensive resource utilization. Diatoms are rich in high-value substances such as polyunsaturated fatty acids, fucoxanthin, polysaccharides, and phenolic compounds, and their siliceous cell walls hold significant application potential across various industries. However, their industrialization has long been hindered by high production costs, with single-component production models leading to low return on investment—a core bottleneck restricting their development. This review analyzes diatom biorefinery technologies and processes, including co-extraction, sequential extraction, and hierarchical utilization of whole biomass, which significantly enhance resource utilization efficiency and economic benefits. Economic feasibility analyses show that co-producing multiple bioactive substances effectively shares costs, increases profits, and reduces waste treatment expenses, demonstrating promising market prospects. Despite challenges such as upstream process regulation where environmental factors may exert multiple effects on metabolite production, and downstream green chemistry transformation, combining co-production of high-value products with technological innovation can effectively lower costs, achieve efficient resource utilization, and foster sustainable development. Diatom biorefinery processes are poised to achieve larger-scale commercialization, offering new approaches to address global challenges in energy, the environment, and human health.

Keywords: diatom; biorefinery; economic analysis; sustainable development

1. Introduction

Diatoms are single-celled algae with highly silicified cell walls, widely distributed in almost all water environments, including oceans, freshwater lakes, rivers, and even moist soil surfaces [1]. More than one million diatom species have been identified to date [2]. Thanks to their unique biological properties, diatoms exhibit enormous application potential in numerous fields and represent a microbial resource that cannot be ignored.

Diatoms contain various bioactive components with high added value. Their fatty acid composition includes myristic acid, palmitoleic acid, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) [3]. As representatives of Omega-3 polyunsaturated fatty acids, EPA and DHA have been confirmed to possess important physiological activities such as improving cardiovascular and cerebrovascular functions and promoting neural development [4], making them essential in the development of functional foods and pharmaceuticals. Additionally, diatoms typically contain high levels of fucoxanthin, a xanthophyll with multiple potential health-promoting properties, including antioxidant [5], anti-obesity [6,7], anti-tumor [8], and cancer-inhibiting effects [9–11]. Notably, compared with the main commercial source of fucoxanthin—large brown algae—the fucoxanthin content in diatoms is significantly higher [12], ranging from 0.2% to 2% of dry weight, which is more than 100 times that of large brown algae. Diatoms also contain chrysolaminarin, phenolic compounds, etc. Beyond intracellular active substances, diatom frustules (silicified cell walls) exhibit application potential in multiple fields due to their unique porous nanostructure. This natural biomaterial has a specific surface area of up to 200 m^2/g, and its micro-nano-scale pores can be functionalized through chemical modification. Combined with its high mechanical strength, unique optical properties, and excellent biocompatibility [13], diatom frustules have become a research hotspot, for example, in water purification [14], heavy metal adsorption devices [15], supercapacitors [16], solar cell components [17], and targeted drug delivery systems [18–20].

However, despite the numerous potential applications of diatoms, their high industrial application costs have become a key factor restricting large-scale industrialization, primarily due to high cultivation [21,22] and harvesting costs [23]. Studies show that harvesting costs account for approximately 30% of the total production cost of diatom biomass [24,25]. Traditional single-product production models often focus only on extracting one high-value component while neglecting the utilization of other components, leading to resource waste and increased costs. More importantly, this model generates substantial waste, further increasing treatment costs and environmental burdens. Therefore, reducing the cost of diatom industrial applications and achieving efficient resource utilization and sustainable development have become urgent issues to address.

Biorefinery aims to convert diatom biomass into multiple bioproducts, such as high-value chemicals and biomaterials, to improve return on investment (ROI) and the sustainability of process commercialization [26], holding profound potential value and significance. On one hand, biorefinery maximizes the utilization of diatom biomass to produce multiple valuable products, fully exploiting the rich biomass resources of diatoms. By optimizing biorefinery processes, various active components in diatoms can be converted into market-value products, improving comprehensive resource utilization. High-value bioactive substances in diatoms can be applied to produce high-value products in food, cosmetics, pharmaceuticals, and nutrition industries to meet people's demand for health products. On the other hand, diatom frustule residues after active ingredient extraction can further leverage their porous siliceous structure in applications such as heavy metal adsorbents, solar cell photosensitive materials, or targeted drug carriers. This review provides an in-depth review of the biorefinery potential of diatoms, comprehensively analyzes processes for co-producing multiple active substances from diatoms, and conducts a detailed economic feasibility analysis. It illustrates the process of converting biomass into multiple high-value products through biorefinery, emphasizing the critical role of product diversification in effectively allocating unit operation costs. Combined with energy efficiency improvements brought by technological innovations, this approach is expected to overcome the economic bottlenecks of traditional single-product models and significantly reduce costs. This not only provides innovative ideas and practical solutions for addressing global challenges such as energy, environment, and health, but also demonstrates the enormous potential and broad application prospects of diatom biorefinery processes in promoting sustainable development.

2. Biological Characteristics of Diatoms

2.1 Classification and Morphological Structure of Diatoms

Diatoms are highly diverse, primarily divided into two classes: Centricae (centric diatoms) and Pennatae (pennate diatoms) [27]. Centric diatoms typically have round or elliptical cells with radial symmetry, exemplified by genera such as *Coscinodiscus* and *Thalassiosira* (Figure 1a,b). Pennate diatoms are mostly elongated or lanceolate with bilateral symmetry, such as *Navicula* and *Pseudo-nitzschia* (Figure 1c,d). Diatoms exhibit unique morphological structures, with their most prominent biological feature being the siliceous cell wall, known as the frustule. Each frustule consists of three parts: the valve, girdle band, and connecting band. The upper valve (mother cell shell) and lower valve (daughter cell shell) are nested together via the girdle band, with the upper valve of the mother cell typically slightly larger than the lower valve of the daughter cell, forming a distinctive nested structure [28]. The frustule wall is composed of inner and outer layers, with various micro-nano structures (such as pores, spines, and raphes) distributed on the surface. The diversity in the morphology, size, and arrangement of these structures leads to highly variable macroscopic shapes [29]. Diatom frustules are intricately constructed from nanoscale silica through biomineralization, endowing diatoms with extremely high mechanical strength. This allows them to maintain morphological stability and resist external physical damage in complex and variable natural environments. Additionally, frustules have a rich porous structure with good toughness and elasticity (Figure 2), and their specific surface area exceeds 200 m^2/g [30,31]. This provides critical support for the diatoms' high-efficiency performance in processes such as substance adsorption and exchange, giving them unique advantages in the field of biomaterials. Meanwhile, the micron-scale size of the frustule and the nanoscale porosity matching the wavelength of visible light significantly enhance their optical scattering properties, making them suitable for use in optoelectronic devices [32].

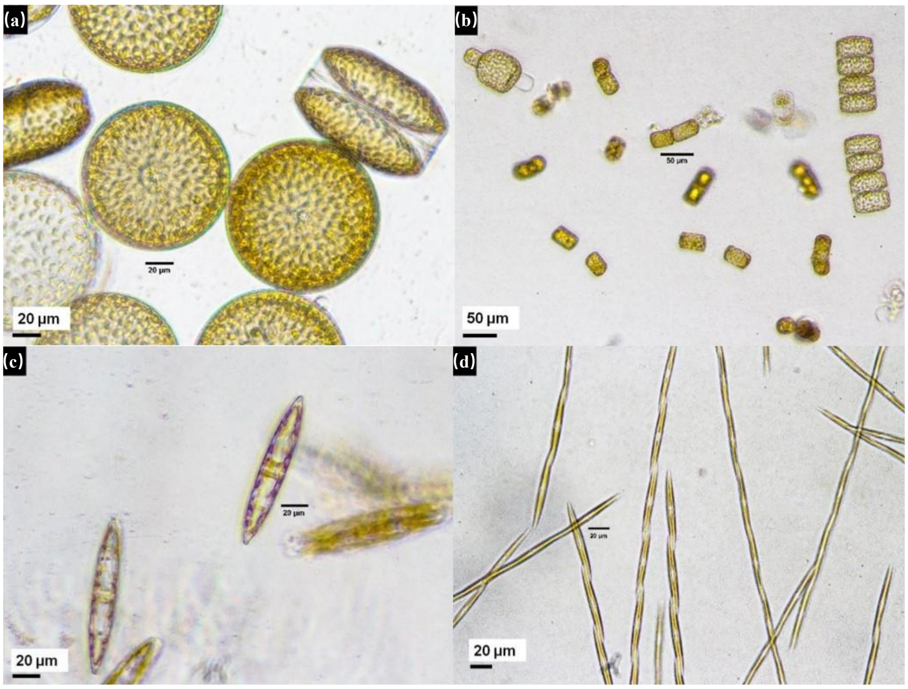

Figure 1. Microscopic images of some diatoms: (**a**) *Coscinodiscus* sp., (**b**) *Lauderia* sp., (**c**) *Navicula* sp. and (**d**) *Pseudo-nitzschia* sp. [26].

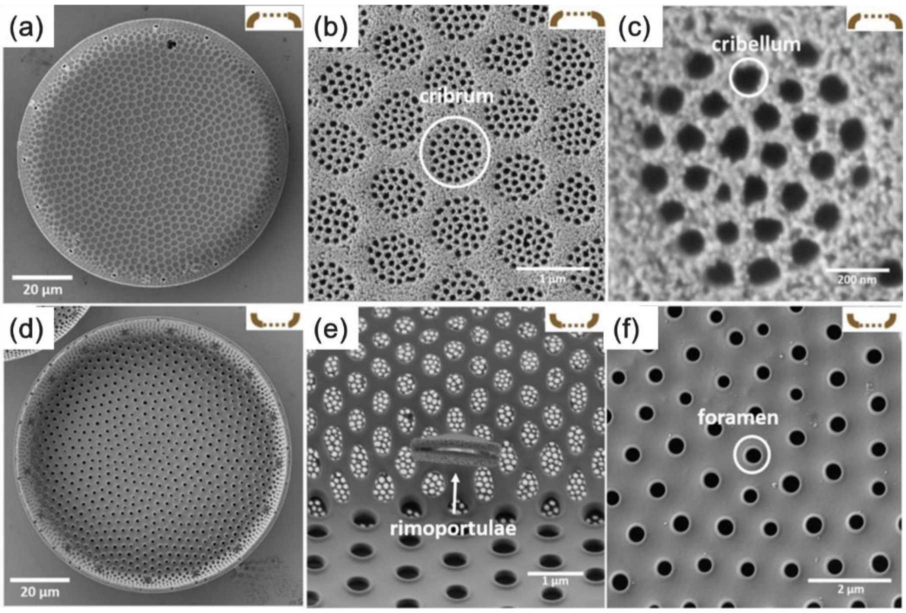

Figure 2. SEM images of diatom: (**a**) outer surface of the valve, (**b**) details of the external side of the valve: cribrum, (**c**) cribellum, (**d**) inner surface of the valve, (**e**) details of the internal side of the valve: rimoportulae, (**f**) foramen. [31].

2.2 Growth and Reproduction

Diatoms typically reproduce asexually via binary fission and sexually through gamete formation. During asexual reproduction, when a mother cell divides, each of the two daughter cells inherits one theca. One daughter cell remains the same size as the parent cell, while the other is slightly smaller. This division pattern leads to gradual cell size reduction. When cells reach a critical size (usually 50% of their initial size), they restore their original size through sexual reproduction, which involves gamete formation and fusion to produce a zygote, developing into a new initial cell (Auxospore). This process not only restores cell size but also introduces new genetic combinations. In sexual reproduction, the sex of Centricae diatoms is determined by cell size and environmental conditions, allowing homothallic reproduction (i.e., the same clone can produce both male and female gametes). In contrast, the sex of Pennatae diatoms is genetically determined, typically requiring heterothallic reproduction (i.e., mating between clones of different sexes following an MF/FF genetic model) [33]. Besides cell size reaching a critical threshold, environmental factors such as temperature, light, nutrients, and salinity also influence the triggering of sexual reproduction [34].

Light is a key factor in diatom growth. Guo et al. found that low light intensity promotes fucoxanthin accumulation in *Cyclotella cryptica*, but synthesis is inhibited when light intensity exceeds a certain threshold [35]. Iwasaki studied the effects of different colored lights on metabolic products (proteins, lipids, carbohydrates, etc.) in *Chaetoceros muelleri*. Results showed that diatoms cultured under blue light exhibited the best production efficiency for proteins, lipids, and carbohydrates with the highest cost-effectiveness, while microalgae cultured under red light had lower short-chain fatty acid content and lower photosynthetic efficiency [36]. In addition to light, nutrients are essential for diatom growth. For example, under nitrogen-limited conditions, diatom growth is significantly inhibited, with reduced growth rates and cell density. When external nitrogen sources are scarce, diatoms consume intracellular nitrogen reserves; once depleted, growth gradually stagnates. Meanwhile, nitrogen starvation induces significant changes in metabolic products—protein content decreases while lipid content increases significantly. Nitrogen limitation also significantly affects photosynthetic pigment synthesis, typically reducing pigment content and lowering photosynthetic efficiency [37].

3. Application Potential of Diatoms in Biorefinery

As a microalga with enormous application potential, diatoms exhibit unique advantages in the field of biorefinery. Diatoms are rich in various high-value active substances, including polyunsaturated fatty acids (PUFA), fucoxanthin, polysaccharides, and phenolic compounds (Table 1). Among them, polyunsaturated fatty acids, fucoxanthin, and polysaccharides are the most common high-value products in diatoms, possessing unique biological activities. Additionally, the natural siliceous cell walls of diatoms provide them with unique structural and functional properties, further enhancing their application potential in biorefinery.

Table 1. Bioactive compound of diatoms.

Strain	Bioactive compound	Contents	References
Phaeodactylum tricornutum	Fucoxanthin	1.22%	[38]
Phaeodactylum tricornutum	Fucoxanthin	NA	[39]
Chaetoceros calcitrans	Fucoxanthin	0.53%	[40]
Hyalosynedra toxoneides	Fucoxanthin	0.33%	[41]
Nitzschia laevis	Fucoxanthinol	NA	[42]
Cyclotella meneghiniana	Lipid	30.1%	[43]
Nitzschia palea	Lipid	NA	[44]
Tabularia affinis	PUFAs	NA	[45]
Anomoeoneis sp.	PUFAs	15.54% TFA	[46]
Phaeodactylum tricornutum	PUFAs	61.92% TFA	[47]
Phaeodactylum tricornutum	EPA	NA	[48]
Pinnularia borealis	EPA	32% TFA	[49]
Gyrosigma sp.	Palmitic acid	48.6% TFA	[50]
Synedra acus	Chrysolaminaran	0.35%	[51]
Phaeodactylum tricornutum	Chrysolaminarin	21.2%	[52]
Phaeodactylum tricornutum	Chrysolaminarin	5.46%	[53]
Didymosphenia geminata	Crude polysaccharides	NA	[54]
Phaeodactylum tricornutum	Crude polysaccharides	6.85%	[55]
Navicula directa	Sulfated polysaccharide	NA	[56]
Hyalosynedra toxoneides	Sulfated polysaccharides	NA	[41]
Nitzschia palea	Phenolic compounds	34.6%	[57]

NA = Not available (Data not available in the cited reference).

3.1. Fatty Acids

Diatoms contain a diverse array of fatty acids (Figure 3) [58–82], with common examples including myristic acid (C14:0), palmitic acid (C16:0), palmitoleic acid (C16:1 n-7), DHA, and EPA [83]. Under normal growth conditions, fatty acids typically account for 15–25% of diatom dry weight [84]. Among these, Omega-3 polyunsaturated fatty acids (PUFAs) such as EPA and DHA are particularly notable for their high value.

Humans have a limited potential to synthesize these PUFAs efficiently and primarily rely on dietary intake. For years, fish oil has been the main commercial source of Omega-3 PUFAs like DHA and EPA [85,86], but its application faces multiple limitations. First, global fishery resources struggle to meet growing market demands—the pollution of marine environments where fish live has caused fish oil production to decline, and current global fish oil output cannot satisfy consumer needs [87]. Second, fish oil has applicability constraints: its characteristic fishy odor deters some consumers, and it cannot meet the special needs of vegetarians or individuals with fish allergies [88]. Therefore, there is an urgent need for new, sustainable alternative sources of Omega-3 PUFAs. Notably, fish, as secondary accumulators of EPA and DHA, obtain all their Omega-3 PUFAs from microalgae, such as diatoms and dinoflagellates, at the base of the food chain [89] (Table 2).

Table 2. EPA and DHA content of diatoms.

Strain	EPA (% Total Fatty Acid)	DHA (% Total Fatty Acid)	References
Haslea ostrearia	18.28	3.4	[90]
Nitzschia lecointei	20.3	NA	[91]
Nitzschia sp.	1.92	0.26	[92]
Nitzschia sp.	14.11	1.9	[93]
Odontella aurita	26.1	3.8	[94]
Odontella aurita	38.91	4.95	[95]
Phaeodactylum tricornutum	24.8	10.3	[96]
Phaeodactylum tricornutum	30.26	0.98	[97]
Phaeodactylum tricornutum	15.99	8.83	[98]
Phaeodactylum tricornutum	30.8	NA	[99]
Phaeodactylum tricornutum	4.72	0.52	[100]
Porosira glacialis	33.8	6	[101]
Porosira glacialis	23.66	5.75	[102]
Skeletonema costatum	22.2	5.2	[103]
Skeletonema costatum	9.35	1.97	[104]
Thalassiosira binata	22.04	3.45	[105]
Thalassiosira pseudonana	19.3	2.2	[106]
Thalassiosira weissflogii	3.23	12.63	[107]
Thalassiosira weissflogii	22.5	1.9	[108]

NA = Not available (Data not available in the cited reference).

This ecological transfer mechanism indicates that bypassing the fish intermediate and directly developing Omega-3 PUFA-producing microalgae could significantly shorten the production chain and reduce resource loss. Thus, diatoms (e.g., *Phaeodactylum tricornutum*), as primary producers of fatty acids like EPA and DHA [109], offer a promising alternative for commercial PUFA production by directly accumulating Omega-3 PUFAs [110,111], avoiding the food chain dependency and ecological risks of fish oil production [111–115].

Omega-3 fatty acids play a vital role in human health [116], particularly in the prevention and treatment of cardiovascular health, inflammatory responses, and neurodegenerative diseases. Omega-3 PUFAs can effectively reduce blood triglyceride and cholesterol levels, decrease low-density lipoprotein (LDL), and increase high-density lipoprotein (HDL), thereby lowering blood lipid levels and reducing the risk of cardiovascular diseases. Omega-3 PUFAs such as EPA, DHA, and docosapentaenoic acid (DPA) can inhibit platelets from producing thromboxane-A (TXA2), thereby reducing thrombus formation and preventing cardiovascular diseases such as atherosclerosis and coronary heart disease [117]. Regarding anti-inflammatory responses and immune regulation, Omega-3 PUFAs exhibit remarkable efficacy—they exert anti-inflammatory effects by reducing the production of pro-inflammatory leukotrienes. As substrates for cyclooxygenase (COX), EPA and DHA can mitigate inflammatory reactions [118].

In the prevention and treatment of neurodegenerative diseases, DHA generates signaling molecules such as neuroprotectin D1 (NPD1) under conditions of cell damage or disease. These molecules protect neurons by regulating gene expression, reducing neuroinflammation and dendritic spine damage, and have preventive and therapeutic effects on Alzheimer's disease and Parkinson's disease [119–123]. In addition, Omega-3 PUFAs are crucial for the brain and visual development of fetuses and infants. Intake of DHA by pregnant women during pregnancy and lactation can reduce the risk of poor visual and neural development in infants [124]. Omega-3 PUFAs also have the effects of lowering blood glucose and increasing the body's sensitivity to insulin [125,126].

Figure 3. Fatty acid composition of diatoms [58–82].

3.2 Fucoxanthin

Pigments in diatom cells typically consist of two categories—chlorophylls and carotenoids. Among them, fucoxanthin is the most attractive carotenoid. Due to the presence of active groups such as allene structures, epoxide groups, and conjugated carbonyl groups [127] (Figure 4), these structures endow fucoxanthin with a high degree of unsaturation. Benefiting from this, fucoxanthin exhibits extremely strong antioxidant capacity, making it a research hotspot in the fields of pharmacology and food health.

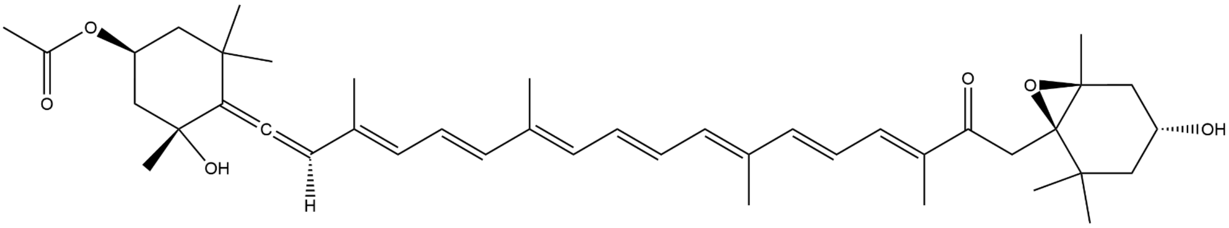

Figure 4. Structure of fucoxanthin.

Fucoxanthin is primarily found in brown algae and diatoms. Currently, commercial fucoxanthin is mainly derived from brown algae such as *Laminaria*, *Cladosiphon*, *Sargassum*, and *Undaria* [128,129]. However, brown algae suffer from long production cycles, low fucoxanthin content, and inefficient extraction due to thick cell walls and high algal gum content, making it difficult to meet market demand [130]. By contrast, diatoms can contain 100 times more fucoxanthin than brown algae (Figure 5) [131–159]. They also exhibit fast growth rates, short culture cycles, strong adaptability, and can be cultivated on a large scale in photobioreactors. Additionally, diatom production can co-produce high-value byproducts such as Omega-3 fatty acids, which are widely used in pharmaceutical and health fields [160]. Combining economic viability and sustainability, diatoms have become a preferred alternative to traditional brown algae.

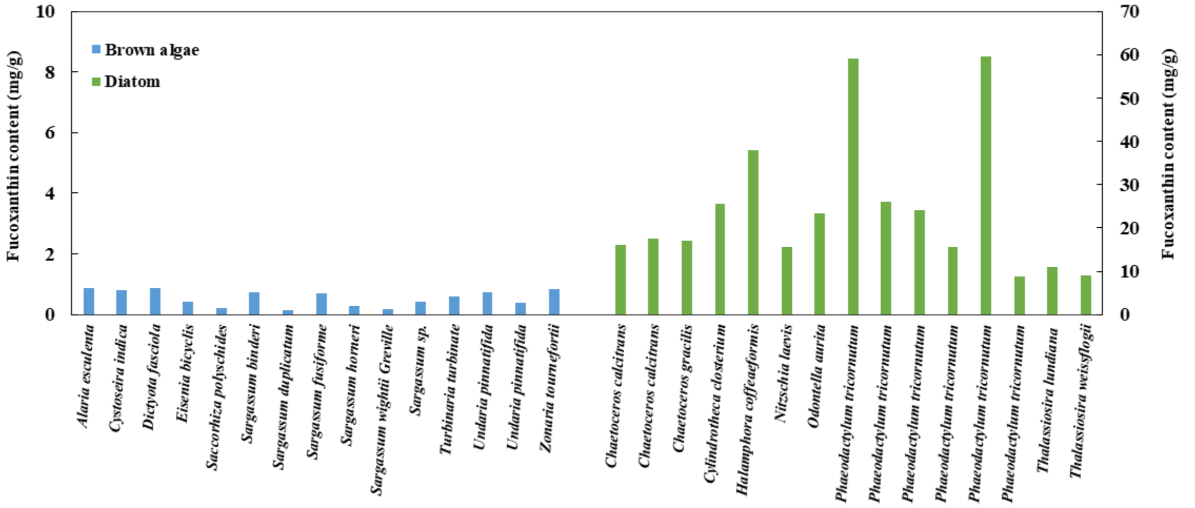

Figure 5. The fucoxanthin content of different algae [131–159].

Numerous studies have shown that fucoxanthin exhibits unique biological activities in anti-obesity, anti-cancer, anti-tumor, and antioxidant aspects. Fucoxanthin combats obesity by influencing lipid metabolism. Studies have found that fucoxanthin can inhibit adipogenic factors such as PPARγ, FABP-4, and C/EBPα, thereby significantly suppressing fat accumulation [161]. In addition to inhibiting fat synthesis, fucoxanthin also promotes fat breakdown. It enhances the expression of β3-adrenergic receptors and uncoupling protein-1 (UCP1), promotes fatty acid oxidation and energy expenditure, and accelerates fat decomposition [162,163]. Fucoxanthin has demonstrated significant potential in anti-tumor applications. Mei et al. studied the anti-lung cancer mechanism and effects of fucoxanthin and confirmed that it inhibits cancer cell proliferation by regulating the expression of apoptosis-related genes and proteins (p53, p21, Fas, PUMA, Bcl-2, and caspase-3/8) [164]. Ye et al. confirmed through in vitro cell experiments that fucoxanthin can significantly inhibit the expression of HIST1H3D, thereby suppressing cervical cancer cell proliferation and colony formation, promoting cancer cell apoptosis, and causing cell cycle arrest [165]. Additionally, fucoxanthin has potential preventive and therapeutic effects on gastric cancer [166], breast cancer [167], and other malignancies. Due to its unique chemical structure, fucoxanthin possesses extremely strong antioxidant activity and free radical scavenging capacity [168]. Studies have shown that fucoxanthin significantly enhances intracellular catalase activity, promotes the elimination of intracellular reactive oxygen species (ROS), prevents DNA damage and cell apoptosis caused by H_2O_2 accumulation, and protects cultured cells from iron-induced oxidative stress.

Furthermore, fucoxanthin also holds promising development value in anti-diabetes [169], anti-inflammation [170,171], and improving gut microbiota [172].

3.3 Chrysolaminarin

Chrysolaminarin is a class of water-soluble β-1,3-glucans primarily derived from marine microalgae such as diatoms. As a product of microalgal photosynthesis, it is typically stored in the vacuoles of algal cells and serves as the main carbon storage material in diatoms. Studies show that chrysolaminarin generally accounts for 10% to 20% of the total cellular carbon in diatoms, but its content increases significantly under nitrogen-limited growth conditions, even reaching up to 80% of total cellular carbon [173]. Chrysolaminarin exhibits biological activities unique to β-glucans, such as antioxidant, antitumor, hypoglycemic, hypolipidemic, and immune-enhancing effects [174]. Additionally, it has high immunological activity and can be used as an immunostimulant and prebiotic, holding broad application potential in functional foods and animal feed [175].

3.4 Phenolic Compounds

Phenolic compounds are a class of important compounds produced by diatoms during secondary metabolism. Studies have shown that phenolic compounds in diatoms exhibit antioxidant and anti-inflammatory effects, effectively scavenging free radicals and reducing cellular damage caused by oxidative stress. Additionally, phenolic compounds can act as photoprotectants, protecting cells from light stress [176]. These properties enable phenolic compounds to play a critical role in the survival and environmental adaptation of diatoms, while also offering potential value for their applications in functional foods, cosmetics, and pharmaceutical development.

3.5 Frustules

Diatom frustules possess unique properties such as high strength, porosity, good biocompatibility, and special spectral absorption. These characteristics endow them with enormous application potential in adsorbents, drug carriers, and photovoltaic materials (Figure 6).

As a promising new type of adsorbent material, diatom frustules exhibit excellent adsorption performance for cationic dyes like methyl violet and rhodamine B, with removal rates exceeding 90%. Additionally, Qin et al. found that diatom frustules have significant adsorption capacity for heavy metal Cu^{2+}—under optimal conditions, the adsorption rate for Cu^{2+} can reach as high as 99% [177].

In the field of drug sustained-release carriers, the porous structure of diatom frustules enables efficient loading of drug molecules [178]. Aw et al. investigated the application potential of diatom frustules in drug delivery by combining porous frustules with the water-insoluble drug indomethacin. The study showed that diatom frustules exhibit remarkable performance in drug delivery, with a drug loading efficiency of approximately 22% and the ability to sustain drug release for more than two weeks [179]. This demonstrates that diatom frustules excel as drug-sustained-release carriers, providing a feasible alternative to traditional synthetic nanocarriers.

In the photovoltaic field, traditional dye-sensitized solar cells (DSSCs) primarily rely on TiO_2 nanoparticles as photoanodes, with performance optimization focusing on improving the structure of TiO_2 in photoanodes, photosensitive dyes, and electrolytes. Studies have found that applying diatom frustules or diatom frustule-metal oxide composites to photoanodes can enhance DSSC efficiency [180–182]. The addition of diatom frustules imparts the porous TiO_2 layer with high dielectric contrast and light scattering within pore arrays. The photonic crystal and light-scattering properties of diatom frustules help enhance light trapping, thereby improving photoelectric conversion efficiency [183,184].

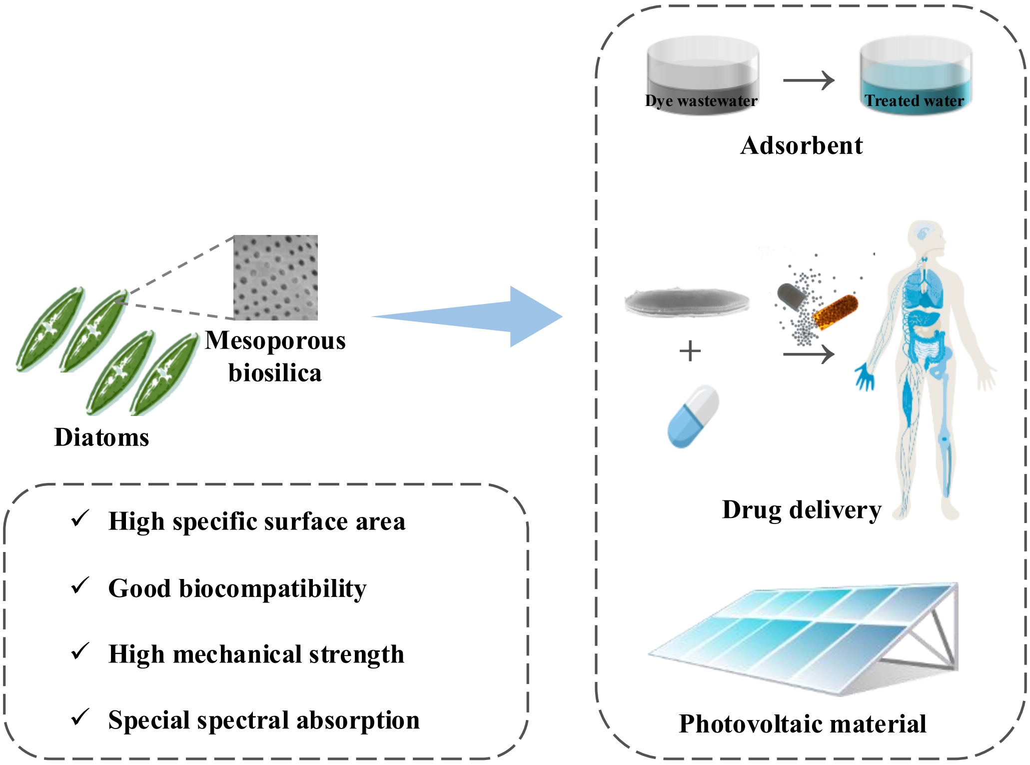

Figure 6. The application of frustule.

4. Technologies and Processes of Diatom Biorefinery

Biorefinery is a process of obtaining biofuels, energy, and high-value-added products through biomass conversion technologies. It uses renewable biomass as raw material, processes it through a series of chemical, biological, and physical methods to convert it into intermediate compounds, and then produces a range of chemicals, energy, pharmaceuticals, etc., through microbial fermentation or biocatalysis [185]. This new industrial production model enables full and efficient utilization of biomass and maximizes output value [186].

One of the most well-known examples of biorefinery is the comprehensive utilization of crop straw. For instance, sorghum straw has enormous development potential, and its stepwise refining process is based on sequential treatment of component characteristics. Fresh straw is first pressed to directly ferment its soluble sugars into ethanol. The cellulose/hemicellulose in the pressed residue is then converted into biogas through anaerobic digestion. Finally, the residual lignin is transformed into biobased materials [187]. The full-component biorefinery of straw achieves its high-value utilization, converting agricultural waste into multiple high-value products, realizing efficient resource utilization of agricultural waste, and reducing secondary environmental hazards caused by incomplete utilization of single components.

The core of biorefinery lies in fully tapping the utilization potential of specific biomass while minimizing waste generation. Microalgae stand out due to their unique advantages. Microalgae growth does not rely on precious arable land and does not compete with food crop cultivation. Compared with terrestrial plants, microalgae lack highly tough cell wall components and do not have structures such as stems or roots. This structural simplicity makes it easier to extract and utilize various valuable biological compounds from microalgae [188].

Common microalgal biorefinery processes are mainly applied to *Spirulina* and *Haematococcus pluvialis*. The biorefinery based on *Spirulina* aims to offset the high costs of separation and purification in traditional processing through the collaborative development of high-value product phycocyanin (C-PC) and multiple byproducts. In recent years, introducing industrial wastewater and high-concentration CO_2 flue gas into the *Spirulina* cultivation system has proven to be a new scheme combining economic and environmental benefits—industrial waste can replace traditional culture media to reduce raw material costs and provide a cheap carbon source for *Spirulina* photosynthetic carbon fixation. Additionally, the remaining *Spirulina* biomass after protein extraction is still rich in various metabolites, which can be further extracted for full-component utilization. For example, studies have shown that after protein extraction, value-added utilization can be achieved by recovering other valuable metabolites (including lipids, polysaccharides, and pigments) from the remaining *Spirulina* biomass to produce biofuels, biomaterials (such as bioplastics), and animal feed [189].

Furthermore, *Haematococcus pluvialis* is one of the richest natural sources of astaxanthin (AXT), while also containing high-value components such as proteins, lipids, and carbohydrates. Research shows that AXT extracted from *Haematococcus pluvialis* exhibits good antioxidant activity and has great potential in cosmetic applications. The remaining biomass after AXT extraction is rich in proteins, carbohydrates, and nutrients, making it a natural biofertilizer that can significantly improve plant nutrient absorption efficiency and promote plant growth and development [190].

This biorefinery model of full-component utilization and zero-waste discharge, built around microalgae, not only provides a paradigm for microalgal resource development but also opens up ideas for the comprehensive utilization of other algae.

Biorefinery processes are also applicable to the development of diatoms rich in bioactive substances. Diatoms contain high-value resources such as fatty acids, fucoxanthin, and polysaccharides, and possess a natural porous silica structure, holding enormous potential in the field of biorefinery. Currently, most industrial production of diatoms focuses on single compounds, while other potentially high-value components are often discarded. To improve the economic viability of diatom bioactive substance production, it is necessary to maximize the utilization of their valuable components and establish and optimize diatom-based biorefinery processes. Specifically, co-producing active substances such as fucoxanthin, PUFAs, and polysaccharides while recycling diatom frustules can achieve hierarchical utilization of resources and significantly enhance comprehensive benefits.

In recent years, domestic and international studies have carried out extensive explorations around this goal. From green improvements in co-extraction processes to integrated upgrades of multi-product sequential extraction, and then to hierarchical utilization of whole biomass, these studies provide important references for breaking through the limitations of single-component production.

First, regarding the green improvement of co-extraction processes, a study by Delbrut et al. provides a synergistic extraction approach for diatom biorefinery [191]. Initially, methanol was used to extract active substances from *Phaeodactylum tricornutum*, with yields of FX, EPA, and DHA being 13.3 $mg \cdot g^{-1}$ DW, 29.1 $mg \cdot g^{-1}$ DW, and 1.2 $mg \cdot g^{-1}$ DW, respectively. Subsequently, the extraction process was optimized using the green solvent ethanol, ultimately achieving a 95% FX extraction rate and an 89% EPA extraction rate compared to the original method. Ethanol is significantly safer than methanol, establishing a green process. Based on co-extraction technology, Zhang et al. further developed a sequential extraction process to gradually extract and purify FX, EPA, and chrysolaminarin from *Phaeodactylum tricornutum* [192]. The yields of these three components (weight of purified compound/absolute weight of algal biomass, %) reached 34.03%, 23.00%, and 43.54%, respectively. Additionally, the purity of FX was $\geq$98%, and the purity of EPA was increased from 19.30% to 80.70%. The sequential extraction technology maximizes the utilization of *Phaeodactylum tricornutum* biomass, combining environmental and economic values.

Another study expanded its scope to whole biomass development. Paidi et al. simultaneously extracted high-value bioactive compounds such as FX, chlorophyll, DHA, and EPA from *Thalassiosira lundiana*, and processed the remaining biomass after extraction to recover porous biosilica [149]. The yields and purities were as follows: DHA yield was 6.41 $mg \cdot g^{-1}$ DW with 78% purity; EPA yield was 15.56 $mg \cdot g^{-1}$ DW with 79.69% purity; chlorophyll a yield was 7.22 $mg \cdot g^{-1}$ DW with >95% purity; FX yield was 11.1 $mg \cdot g^{-1}$ DW with >92% purity. Meanwhile, the residual biomass after active substance extraction is acid-washed to recover porous biosilica. The biomass waste is converted into biosilica materials, which can be used as natural adsorbents, achieving full utilization of biomass.

However, although both co-extraction and sequential extraction technologies significantly improve diatom resource utilization, their inherent limitations deserve attention. Specifically, while simultaneous extraction of multiple components in co-extraction improves initial efficiency, it inevitably increases subsequent separation and purification time and costs. Sequential extraction can achieve directional enrichment of components (e.g., extracting lipid-soluble FX/PUFAs first, then water-soluble polysaccharides), but pre-extraction solvents may deplete subsequent target products.

Based on an in-depth analysis of the limitations of existing technologies, constructing a more economically viable and resource-efficient diatom biorefinery process has become a priority. The core strategy is to reasonably plan the extraction order according to the market value, stability, and separation difficulty of target products—prioritizing the extraction of high-value components, followed by relatively low-value or easily separable components. For example, in sequential extraction, FX extraction and purification are placed at the beginning of the process to avoid significant FX loss caused by prioritizing EPA extraction. In whole-component utilization, high-value bioactive substances are separated first, and finally, siliceous cell walls are recovered from residues and converted into high-value biosilica materials (Figure 7). This strategy not only reduces co-extraction separation costs and minimizes cross-loss in sequential extraction but also achieves the biorefinery goals of high recovery rates for high-value components and full utilization of low-value components, laying a solid foundation for the large-scale and efficient development of the diatom industry.

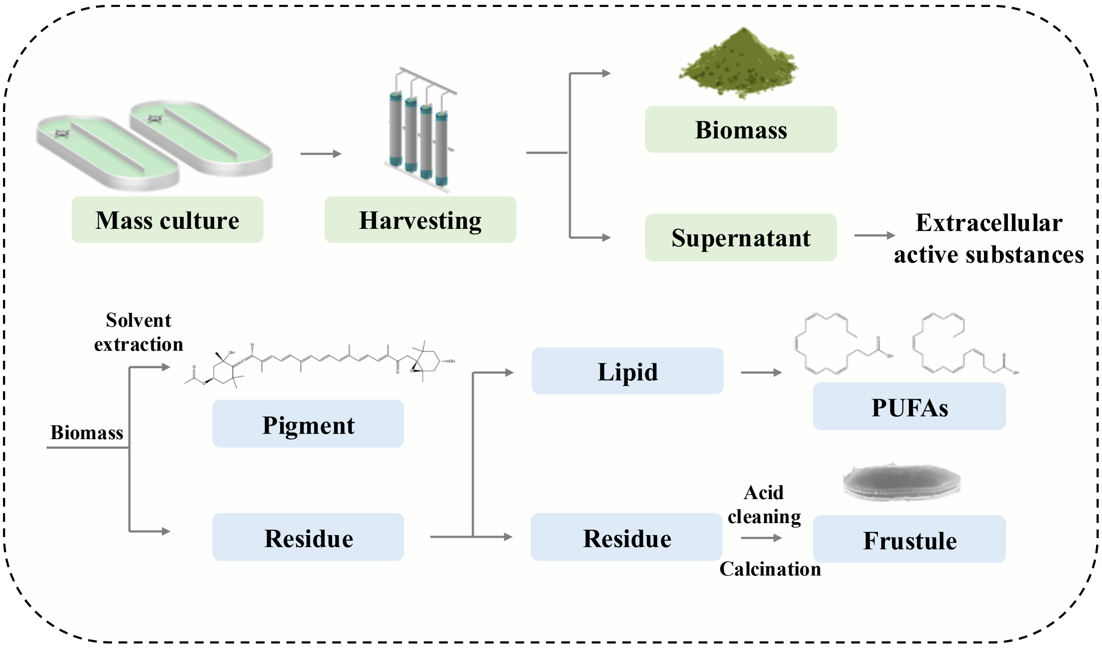

Figure 7. A biorefinery approach of diatoms.

5. Economic Feasibility Analysis

5.1 Market Demand Analysis

Fucoxanthin has extensive applications in food, health products, cosmetics, and other fields. The food industry represents its largest downstream market, where fucoxanthin is used as a natural pigment and functional additive to enhance food nutrition and health benefits, accounting for approximately 80% of the market share. The Asia-Pacific region is the world's primary producer of food-grade fucoxanthin. According to YH Research, the global food-grade fucoxanthin market was valued at approximately CNY 210 million in 2024 and is expected to grow steadily, reaching nearly CNY 290 million by 2031, with a compound annual growth rate (CAGR) of 4.4% over the next six years [193].

The market application of Omega-3 PUFAs has expanded from traditional health products to food, pharmaceuticals, cosmetics, and animal nutrition. The global Omega-3 PUFA market was valued at approximately CNY 109.1 billion in 2023 and is projected to grow steadily, approaching CNY 140.8 billion by 2031, with a CAGR of 3.6% over the next six years [194]. Meanwhile, diatom frustule materials, due to their unique physicochemical properties, hold significant application potential in environmental, medical, and materials science fields. The global diatomite market was valued at approximately CNY 8.83 billion in 2024 and is expected to grow steadily, reaching nearly CNY 12.55 billion by 2031, with a CAGR of 5.2% over the next six years [195]. According to Expert Market Research, 50% of diatomite produced in 2023 was used for filtration products, approximately 50% for applications such as adsorbents and fillers, and less than 1% for biomedical and pharmaceutical purposes [196].

In summary, the sustained growth in market demand for fucoxanthin, Omega-3 PUFAs, and diatom frustules provides broad development space for diatom biorefinery processes. Biorefinery not only meets the growing market demand for these products but also enhances market competitiveness through efficient diatom resource utilization and cost optimization, with promising application prospects in food, healthcare, cosmetics, materials, and other industries, providing strong support for related industrial development.

5.2 Cost Composition and Profit Analysis

Based on the analysis of diatoms' biorefinery application potential, it is evident that the rich bioactive substances and porous siliceous frustules in diatoms are highly profitable. Single-extraction models incur high costs, requiring additional expenses for waste treatment while causing useful substances to be wasted, which not only increases processing costs but also hinders green and sustainable development. In contrast, the co-production model significantly enhances the output value of unit biomass by simultaneously extracting multiple bioactive substances. Additionally, reusing diatom frustules from residual biomass after extracting high-value substances not only achieves efficient resource utilization but also aligns perfectly with the concept of green sustainability.

Taking the extraction of high-value products FX and EPA, from *Phaeodactylum tricornutum* as a classic example, this section compares the cost-effectiveness of single-product extraction and multi-product co-production to reveal the economic advantages of the collaborative production model.

Gilcher et al. used supercritical carbon dioxide (ScCO$_2$) to extract high-value compounds from *Phaeodactylum tricornutum* and optimized extraction efficiency and purity through different extraction sequences [197]. According to the study's data, when extracting FX alone, the unit output value was $332.80-$665.60/kg dry weight (DW), with a maximum profit of $649.27/kg DW under optimal cost control. In contrast, co-producing FX and EPA increased profits to $788.47-$938.87 /kg DW, a profit increase of approximately 21.44%-44.60% per unit biomass. Furthermore, Weickert et al. verified the economic feasibility of the co-production process through an FPA-PBR cultivation system [198]. Based on their analysis, under baseline conditions of an annual biomass output of 497.53–613.62 t and fixed production costs of 101–124.56 M€, the extraction cost for FX was €16,111.02 /kg (annual output: 10 t), and the extraction cost for EPA was approximately €80.56 /kg (annual output: 24.12 t). Economic analysis based on these parameters showed that the co-production model increased annual profits from 114.33–137.9 M€ in the single-FX production model to 117.21–140.78 M€, with a total cost increase of only 0.68%-0.74%. From a cost-effectiveness perspective, the unit product cost in the co-production model dropped significantly by approximately 70.34% compared to the single-product model due to cost sharing.

Combining data from both studies, the co-production model of FX and EPA demonstrates significant cost-effectiveness advantages: on one hand, the profit per unit biomass in the co-production model increases by 21.44%-44.60% compared to the single-product model; on the other hand, through cost sharing, the unit product cost decreases by 70.34% with a total cost increase of less than 1%, fully reflecting the critical value of co-production processes in enhancing economic efficiency during diatom biorefinery. Although specific cost structures such as equipment depreciation and labor costs were not included in the calculation discussion, the co-production model still holds significant importance.

Co-production processes typically focus on developing high-value products in diatoms but often overlook the potential value of siliceous frustules in diatom residues. Current methods for synthesizing industrial silica materials are often time-consuming, energy-intensive, and involve toxic precursors and harmful byproducts. In contrast, using diatom frustules as a natural silica source is not only safe and non-toxic but also generates minimal waste. Recycling diatom frustules from residual biomass after extracting bioactive substances and converting them into high-value materials (e.g., adsorbents, drug carriers) can significantly reduce waste treatment costs while creating additional economic benefits. Specifically, due to their unique porous structure, diatom frustules exhibit excellent filtration capabilities, leading the filtration industry with a 66.8% market share in 2023 [196]. Siliceous frustules can effectively remove pollutants from media and improve cost-effectiveness, achieving efficient conversion of waste in diatom co-production processes and balancing economic and environmental benefits.

By integrating the production of high-value bioactive substances with the recycling of diatom frustules from residual biomass, diatom biorefinery processes enhance unit product profitability. This biorefinery model fully utilizes the rich components of diatoms and their unique siliceous cell wall properties to achieve full-component utilization of biomass. Through cost sharing, the cost per unit biomass is significantly reduced, greatly enhancing the economic feasibility of biomass refining. Both experimental data and economic models indicate that diatom biorefinery processes are a key strategy for commercial production, not only improving resource utilization efficiency but also providing strong support for sustainable development.

6. Challenges and Future Prospects

6.1 Upstream Processes

Although diatom-based biorefinery processes can simultaneously or sequentially produce high-value-added products, scaling up from laboratory to industrial scale still faces several bottlenecks [199].

For example, in photobioreactors, microbial contamination and light attenuation pose significant challenges, limiting diatom photosynthesis and growth efficiency. To address this issue, optimizing reactor design is essential to enhance the feasibility and economic viability of large-scale cultivation.

Moreover, environmental conditions are known to significantly influence diatom growth rates, biomass accumulation, and the accumulation of bioactive metabolites [200]. Therefore, regulating growth conditions is crucial for diatom cultivation, but environmental factors often exhibit multiple regulatory effects on the metabolism of bioactive substances in diatoms. For example, Mus et al. found that under nitrogen-limited conditions, *Phaeodactylum tricornutum* significantly increased lipid content while decreasing photosynthetic pigments [35]. Zhao et al. demonstrated that different salinities had little effect on the biomass, fucoxanthin, and EPA of *Cyclotella cryptica*, but DHA content decreased with increasing salinity, while salinity changes also caused significant variations in the morphological characteristics and silicification degree of frustules [201].

In addition to regulating growth conditions, mutation breeding strategies such as genetic modification and adaptive laboratory evolution (ALE) [202–204] are effective means to obtain high-yielding algal strains for bioactive substances [205]. For instance, overexpression of lipid synthesis-related genes (e.g., *LPAAT1*, *DGAT2*) in *Phaeodactylum tricornutum* increased EPA content by 4-fold and 1.8-fold compared to wild-type strains, respectively. Similarly, overexpression of *DXS* and *PSY* genes enhanced fucoxanthin content in *Phaeodactylum tricornutum* by 2.4-fold and 1.8-fold compared to wild-type strains [160].

In large-scale industrial production, the synergistic application of environmental factor regulation and genetic modification strategies is key to improving target product synthesis efficiency. However, it is important to note that the limited metabolic resources within cells are competitively allocated among different synthetic pathways, potentially leading to two typical issues. On one hand, synthetic pathways for different bioactive substances may compete for shared precursors, resulting in trade-offs. On the other hand, high accumulation of products may be accompanied by significant decreases in biomass, failing to substantially increase overall target product yields. Therefore, to achieve large-scale industrial application of diatom biorefinery processes, it is necessary to balance the yields of different products and select appropriate cultivation methods based on specific needs and cost-benefit analyses to maximize benefits.

6.2 Downstream Processes

Due to the increasingly strict environmental regulations at present and in the future, traditional organic solvents face application restrictions due to their potential toxicity and environmental risks. Against this backdrop, developing safe and sustainable extraction processes has become a key challenge in the downstream processes of the biorefinery field. Although traditional solvent extraction methods have certain advantages in efficiency, issues such as flammability and residual toxicity not only threaten the health of operators but also run counter to global carbon neutrality goals. Therefore, constructing efficient extraction systems that comply with green chemistry principles has become an urgent industry need.

In recent years, new green technologies such as supercritical carbon dioxide (Sc-CO_2), ultrasonic-assisted extraction (UAE), and microwave-assisted extraction (MAE) [206] have been widely used for the separation of bioactive components. Specifically, UAE technology is renowned for its ability to shorten extraction time and reduce solvent usage, making it a more economical and energy-efficient alternative to traditional techniques. However, the UAE relies on ultrasonic vibrations to disrupt cell walls and promote the release of intracellular bioactive chemicals. While this can obtain target products more rapidly and safely, the siliceous cell walls of diatoms are damaged in the process. Similarly, studies have shown that MAE technology can rapidly extract FX from *Phaeodactylum tricornutum*, even completing the process in just 1–2 min [207]. However, Akyıldız et al. found that the high temperatures in MAE easily cause FX degradation, resulting in low extraction efficiency [208]. On the other hand, these technologies generally suffer from high equipment investment costs and significant energy consumption. The purchase, installation, and maintenance of advanced equipment require a significant amount of upfront capital. Meanwhile, the notable energy consumption not only escalates operational costs but also raises concerns about the sustainability of the processes, conflicting with the goals of energy conservation and emission reduction. Consequently, these factors collectively pose challenges and, to some extent, limit the large-scale application and industrialization of diatom biorefinery processes.

Furthermore, given that high-value products from diatoms are mostly used as food additives in the market, food safety is a critical threshold that downstream processes must overcome. This imposes strict requirements on extraction and purification processes, which are not only related to product quality but also a key factor determining market competitiveness.

Therefore, the green transformation of downstream processes has become an irreversible trend in diatom biorefinery. There is an urgent need to explore technological processes that balance multiple needs—reducing the implementation cost of green processes and enhancing their economic feasibility while ensuring the yield and quality of target products. Additionally, strengthening the construction of food safety evaluation systems is crucial for the sustainable development of diatom biorefinery processes. The expansion from laboratory to industrial scale faces many technical and economic challenges, and the path of diatom biorefinery from laboratory to industrialization still needs to overcome many obstacles.

7. Conclusions

As a single-celled alga with abundant resources, diatoms possess enormous application potential in food, pharmaceuticals, and other fields due to their rich content of high-value bioactive substances. However, the high cost of industrial diatom applications primarily stems from the failure of single-production models to achieve diversified development of diatom resources, resulting in low return on investment and resource waste. Biorefinery-based co-production of multiple high-value products not only shares production costs, significantly improves the resource utilization efficiency and economic value of diatom biomass, but also reduces waste treatment costs, providing new ideas for achieving green and sustainable development. Although diatom biorefinery processes still face technical and economic challenges in industrial applications, their potential in developing high-value products and efficiently utilizing resources cannot be ignored. They are expected to drive large-scale commercialization through technological innovation in the future.

Author Contributions

Q.X: visualization, methodology, writing—original draft preparation; K.Y.: supervision, writing—reviewing and editing, funding acquisition. L.G.: writing—reviewing and editing; S.W.: conceptualization, supervision, validation, writing—reviewing and editing, funding acquisition. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement

Data will be made available on request.

Conflicts of Interest

The authors declare no conflict of interest.

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