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REVIEW ARTICLE

Facets of diatom biology and their potential applications

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Abstract

Diatoms are the reservoir of bioactive compounds which have immense application in nutrition, industrial commodities and ecological studies. In the oceans, diatoms form a large bloom of silica under favourable conditions, whereas, in lentic and lotic systems, they colonize according to seasonal disturbances. Notably, the survival of diatoms in a stressed environment is because of their uniqueness; therefore, diatoms serve as an ideal candidate to understand the evolutionary paradigm and successional dynamics. This review outlines the biological uniqueness of diatoms, their role in biogeochemical cycles and the recolonization pattern of diatoms in anthropic disturbed habitats. Furthermore, a detailed discussion on different technologies for extracting valuable biomolecules with an emphasis on lipid extraction has been carried out. Moreover, the diatom-based photosynthetic biorefinery approach for a better understanding of the renewable usage of biomass is done.

Keywords Diatoms · High-value metabolites · Biological applications · Photosynthetic biorefinery

1 Introduction

Diatoms, the golden-brown algae, are ubiquitous in nature, that represent a significant part of the phytoplankton community, and responsible for 40% of entire primary production in oceans. They belong to the Heteronkontophyta clade, consisting of approximately 285 known genera and over 12,500 recognized species, but many of them still remain

Highlights

• Diatoms are unique photoautotrophs with promising biomolecules, useful in several biological applications
• Diatom biological and physiological mechanism to obtain high-value metabolites
• Silicious biomass harvesting processes and lipid purification techniques.
• Commercially relevant diatoms suitable for photosynthetic biorefinery approach

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to be described [1–3]. Being the primary producer, they capture solar energy to produce rapid biomass and initiate the grazing food chain [4]. The analysis of diatom studies has led to gain more insights into the lipid extraction process which ensure diatoms as a viable feedstock for sustainable biofuel production. The isolation of high-value metabolites (pigments, biogenic silica, oil, protein, etc.) from diatoms find a great market potential and future applications in the bioenergy, biomedical, bioremediation and as a biomarker tool to gain insights on a geological time scale [5]. The bioprospecting of diatoms was commenced in different aquatic reservoirs to spot strains with desired dispositions like faster reproduction, robust growth, metabolites of interest and easy to isolate and culture, which were subsequently required for the industrial applications [6, 7]. In this review, a brief account of diatom uniqueness regarding its magnificent role in ecological dynamics and succession, perturbing recolonization mechanism because of anthropic disturbances, reviewed to get more insights about diatom biology [8]. A general information about the high-value metabolites which can be commercially isolated, their chemical and molecular structure are enlisted, clearly describing the bioactivity of compounds, obtained from various diatom species. Now-a-days, there are several harvesting techniques employed to maximize the biomass yield, cell disruption methods to extract the lipids and their derivatives, followed by purification strategies. In a biorefinery system, the selection of strain is of prime importance as polycultures usually give rise to lower value products, whilst pure culture, with continuous monitoring over product quantity and quality control, will tend higher value products by biosynthesis pathways of diatom metabolism [9]. The extracted biomolecules find an immense potential in the medical sector, industrial biohydrocarbons, aquafeed, wastewater treatment facilities, nanodevices and other biotechnological applications. In a nutshell, to harness the potential silicious biomass, the engineering of photobioreactor design should meet the following criteria like high surface area-volume ratio, transparency of culture vessel, proper orientation, optimal gaseous exchange, the fixity of the construction elements, thermal regulations and LED illuminations [10, 11] (Tables 1, 2 and 3).

1.1 Distinctive traits of diatoms

Diatoms are surrounded by an intricately laced silica (hydrated silicon dioxide) cell wall termed as a frustule. They can alter the solar energy into biochemical energy via photosynthetic pathways, similar to plants, but this shared autotrophy evolved autonomously in both lineages [52, 53]. Diatom genome is chimeric in nature encompassing potential genes, derived from green algae [54], cyanobacterium and red algae [55] respectively. Consequently, a unique combination of genes exists that codes for non-canonical nutrient assimilation pathways and control of metabolites—for instance, metabolism of nitrogen in the urea cycle or coupling of photosynthesis and respiration [56]. Cyclins are largely encoded by the diatom genome, justifying their high efficiency for rapid multiplication and bloom formation [57].

1.1.1 Biological characteristics

- Diatoms are free living or colonized, range from being unicellular to multicellular, motile or non-motile, periphyton colonies which may be filamentous or mucilaginous [58].
- The frustules display an array of shapes and sizes like elliptical, triangular, circular or crescent shape. In symmetry, the frustules can be radial (centric) or bilateral (pennate), and the cell wall may possess secondary structures like spines and bristles [59].
- Diatoms exhibit a diplontic life cycle; mostly undergo vegetative (asexual) reproduction that results in size diminution, which is again restored by means of auxospore formation (sexual reproduction).

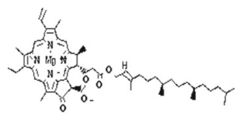
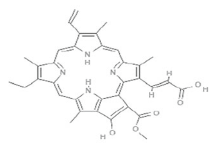
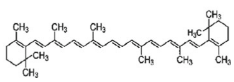
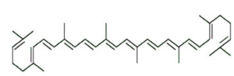
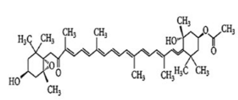
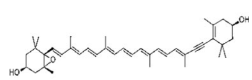
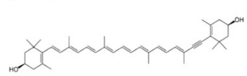
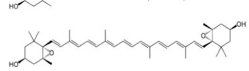
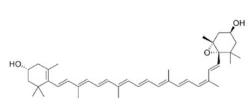
1.1.2 Biochemical characteristics

- The frustule is heavily impregnated with pectin composed of several polysaccharides.
- Plastids are double membrane bound and surrounded by four layers of chloroplast endoplasmic reticulum. The thylakoids are present in layers of three enclosed in a single girdle lamella.
- Main photosynthetic pigments are chlorophyll a, c_1 and c_2 and carotenoids include β-carotene and xanthophylls viz., fucoxanthin, diatoxanthin and diadinoxanthin. Fucoxanthin gives the plastid its characteristic brown colour.
- Food reserves include mainly chrysolaminarin—a carbohydrate dissolved in the vacuole of cell cytoplasm—oil and volutin [60].

1.1.3 Evolutionary characteristics

- Diatoms are secondary endosymbionts, having chloroplast derived from red alga but driven by green algal genes encoded in the nucleus [61].
- They survived Earth's most severe extinction—Permian Triassic mass extinction—where 96% of marine species were lost.

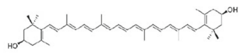
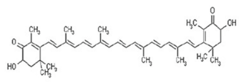
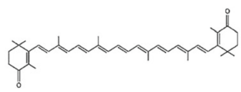
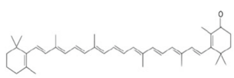
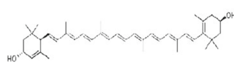
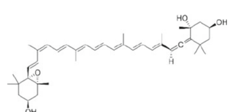
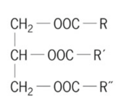
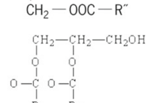
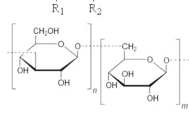
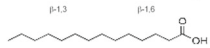
Table 1 High-value metabolites extracted from diatoms

Biochemicals	Chemical Formula	Molecular Structure	Biological Function	Bioactivity	References
Chlorophyll pigments	Chlorophyll-a Chlorophyll-b Chlorophyll-c1 Chlorophyll-c2 Chlorophyll-d Chlorophyll-f	—	Light energy absorption, form energy-rich compounds like carbohydrates or lipids	Control of geriatric patients, dietary supplement, anti-mutagenic, anticarcinogenic agent	[11]
Chlorophyll-a	$C_{55}H_{72}MgN_4O_5$		Conversion of photochemical energy	Appearance control agent for colours in food processing	[12]
Chlorophyll-c (most abundant - c1, c2)	$C_{35}H_{30}MgN_4O_5$		Effective participation in photosynthesis as an accessory pigment	-	[12]
β- carotene (lipophilic coloured compounds)	$C_{40}H_{56}$		Photoprotection, Photosynthetic component, Protect against lipid peroxidation, a stimulator of gap junctional communication	Nutritional supplement, A precursor of Vit. A (Retinol), prevents night blindness, liver fibrosis, cardioprotective, anti-oxidant, anti-cancer, protects skin against UV and sunlight	[12,13]
Lycopene	$C_{40}H_{56}$		Intermediate in the biosynthesis of carotenoids	Anti-cancer, prevent cardiovascular diseases, radiation protection, anti-oxidant	[12]
Fucoxanthin (main carotenoid)	$C_{42}H_{58}O_6$		Forms FCP (fucoxanthin-chlorophyll protein) that performs a light-harvesting function	Anti-oxidant, anti-obesity, functional food, anti-cancer, anti-inflammatory, anti-diabetic, anti-angiogenic, anti-metastatic	[11,12]
Diadinoxanthin (Ddx)	$C_{40}H_{54}O_3$		Photoprotection	-	[12]
Diatoxanthin (Dtx)	$C_{40}H_{54}O_2$		Photoprotection	-	[12]
Violaxanthin (Vx)	$C_{40}H_{56}O_4$		May be involved in Photoprotection Photosynthetic component	Anti-inflammatory Anti-cancer	[11,12]
Antheraxanthin (Ax)	$C_{40}H_{56}O_3$		May be involved in Photoprotection	-	[12,14]

1.2 Role of diatoms in biogeochemical cycles

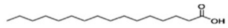
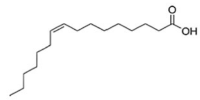
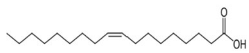
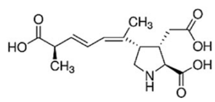
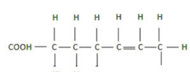
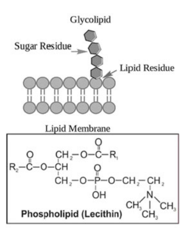
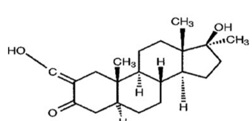
Diatoms are the principal contributors to global primary productivity, accounting for 40% of total primary production in oceans; these microscopic algae are responsible for carbon export in the marine systems [62]. They are the key components of the biogeochemical cycling of silica owing to their characteristic property of biogenic silica synthesis. The leading role of diatoms in net primary production and carbon transport, particularly in coastal areas having low temperature,

Table 1 (continued)

Zeaxanthin (Zx)	$C_{40}H_{56}O_2$		May be involved in Photoprotection Photosynthetic component	The colouration of the macula lutea, protect against age-related muscular degeneration, anti-oxidant, food colourant, fish feed, and nutraceutical	[11,12]
Astaxanthin	$C_{40}H_{52}O_4$		Protect photosynthetic components in the cell from photooxidation, stabilise the integrity of lipid membrane from peroxidation, provide superior antioxidant defence	Strong anti-oxidant, anti-inflammatory, anti-cancer, cardioprotective, neuroprotective, anti-diabetic	[11]
Canthaxanthin	$C_{40}H_{52}O_2$		Protect photosynthetic components in the cell from photooxidation, stabilise the integrity of lipid membrane from peroxidation	Anti-oxidant produces a tan colour	[11]
Eichinenone	$C_{40}H_{54}O$		Protect photosynthetic components in the cell from photooxidation, stabilise the integrity of lipid membrane from peroxidation	-	[11]
Lutein	$C_{40}H_{56}O_2$		Photosynthetic component	Prevents cataract and age-related muscular degeneration, cardiovascular diseases, have antioxidant, anti-cancer, anti-inflammatory properties, protects skin against UV and sunlight	[11]
Neoxanthin	$C_{40}H_{56}O_4$		Photosynthetic component	-	[11]
Marennine (an unusual water-soluble blue-green pigment) and Linoleic acid	NA*	NA*	Greening of oyster gills	Allelopathic, antioxidant, antibacterial, antiviral, anti-proliferative effect on lung cancer model, growth-inhibiting properties, anti-coagulant	[12,15]
Lipids and their derivatives (TAGs - Triacylglycerides)	—		Carbon storage	Production of plant oils, FAAEs (fatty acid alkyl esters), green diesel, commercial glycerol	[16,17]
Diacylglycerols	$C_{37}H_{70}O_5$		Energy storage	Anti-oxidant Anti-cancer	[11]
Chrysolaminarin (carbohydrate)	$C_{18}H_{32}O_{16}$ (β Glucan)		Carbohydrate food reserve	Anti-oxidant, food supplement	[4,18]
Myristic acid (C14:0)	$C_{14}H_{28}O_2$		Main FA	Cosmetics, personal care products, biomarker	[17]

high oxygen and nutrient concentration, have been revealed by regression-based analysis on the entire metabarcoding data set currently available from the *Tara* oceans project [63]. Besides, the presence of abundant carbon-rich deposits of diatoms from ancient sediments led to the formation of petroleum rocks as well [64].

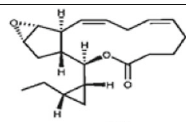
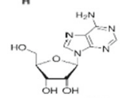
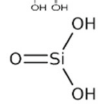
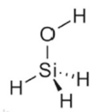
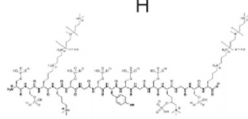
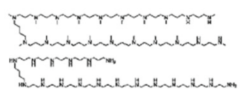
Table 1 (continued)

Palmitic acid (C16:0)	$C_{16}H_{32}O_2$		Energy storage	Production of soaps, cosmetics, industrial mould release agents, Antimicrobial	[11,19]
Palmitoleic acid (C16:1n-7)	$C_{16}H_{30}O_2$		Main FA	Anti-bacterial	[17]
Stearic acid (18:0)	$C_{18}H_{36}O_2$		Energy storage	Antimicrobial	[17]
Oleic acid	$C_{18}H_{34}O_2$		Energy storage	Excipient in pharmaceuticals, emulsifying agent in aerosol products	[20]
Eicospentaenoic acid (EPA) (PUFA)	$C_{20}H_{30}O_2$		Omega-3 FA	Anti-inflammatory, better neural function, alleviate conditions like arteriosclerosis, hypertension, inflammation, psychiatric disorders, microbial, viral, tumour activity, protect the vision, cardiovascular system	[12,21]
Domoic acid (Amino acid derivative)	$C_{15}H_{21}NO_6$		Toxin	Neuroexitary, the antagonist of the neuroexcitatory glutamate receptors that are fatal upon accumulation in shellfish, Efficiently reduce Ascaris, pinworms infection	[12,22]
Unsaturated FAs 16:3n-4, 16:1n-7	—	 Unsaturated Fats	Minor components of FA fractions	Highly active against Gram +ve bacteria	[17]
Polar lipids (Glycolipids + Phospholipids)	—		**Glycolipids**: present in chloroplasts **Phospholipids**: component of the cell membrane	**Glycolipids**: anti-inflammatory, antitumor, antibacterial, antiviral **Phospholipids**: functional foods, cosmetics, pharmaceuticals	[16,17]
Steroids	$C_{19}H_{28}O_2$		-	Anti-inflammatory, anti-trypanosomal, anti-mycobacterial, cytoxic	[17]

1.2.1 Carbon export

The biological export of atmospheric CO_2 due to the activity of photosynthetic organisms from the surface to ocean floors as either organic matter, by being consumed by oceanic grazers as planktonic biomass, or, as inorganic calcium carbonate, is known as biological pump. According to Fu et al. [65], diatoms were initially thought to be abundant only in regions with high nutrient concentration and high turbulence (Margalef's mandal) and modern remote-sensing technologies, and other tools reveal the presence of diatoms in mesoscale processes and sub-mesoscale fronts. They also

Table 1 (continued)

Oxylipins	$C_{20}H_{32}O_3$		Chemical mediators in ecological and physiological processes	Anti-mitotic, anti-inflammatory, antimicrobial, anti-cancer, pro-apoptotic	[17]
Adenosine	$C_{10}H_{13}N_5O_4$		Helps in physiological adaptation	Cytotoxic, blood platelet inhibitory	[12]
Silica (Hydrated Silicon Dioxide) and Proteins	H_2O_3Si		Mechanical protection, defence against pathogens, easy movement, molecular sieving for nutrient uptake, enhancing optical scattering	Detects N2 pollution, nanomaterial composites for energy storage, catalysts, adsorbents, nanobiotechnological products, Bioactive glasses, ceramics, microdevices for drug delivery systems	[11,23,24]
Silanol	SiH_4O		Surface reactivity, cellular toxicity, ROS production	Drug delivery, biosensor	[11]
Silaffins	-NH-(CH_2) n-CO-		Silica biogenesis	Produce silica nanospheres, encapsulate enzymes	[25]
LCPAs (Long Chain Polyamines)	$C_4H_{11}N$		Silica biogenesis	Potential anti-cancer, useful in microalgae research	[26]

**NA*, not available

significantly contribute to the dense vegetation found at the deep chlorophyll maximum (DCM). Their potential to replicate at a rapid rate, their low nutrient affinity, escape from grazers due to their silicified walls and their ability to outcompete other phytoplanktons makes diatoms thrive and, consequently, contribute significantly to biomass production and carbon export [66]. The euphotic zone of oceans witnesses the fixation of inorganic carbon dioxide to organic biomass by microplanktons, especially diatoms. This biomass is taken up by planktonic grazers and is similarly passed on to higher trophic levels. The sinking particles when settles with seafloor sediments to form a carbon sequestration layer depend on multi-stress factors for the community structure, ocean productivity and nutrients export [67].

1.2.2 Silica cycle

Diatoms account for major biogenic silica production [68], although it is affected by several physiochemical factors such as temperature and incorporation of trace elements like

Table 2 Potential applications of diatoms

Application	Diatoms	Bioactive compounds	References
Wastewater treatment	*Gyrosigma* sp., diatoms consortium	Lipids, nano-silica	[27–29]
Health and cosmetics	*Nitzschia thermalis*, *Phaeodactylum tricornutum*	Fucoxanthin, gallic acid (phenolic acid), rutin (flavonoid), EPA (eicosapentaenoic acid), arachidonic acid, DHA (docosahexaenoic acid)	[30–32]
Biohydrocarbons	*Navicula crytocephala*, *Phaeodactylum tricornutum*	FA (fatty acids) and TAGs (triglycerides)	[20, 33, 34]
Antiviral potency	*Navicula directa*, *Haslea ostrearia*	Naviculan, marennine	[35, 36]
Aquafeed	*Chaetoceros sp.*, *Skeletonema costatum*	PUFAs, EPA, diatom-derived EPA	[38, 39]
Nanobiotechnology and biomedical	*Coscinodiscus wailesii*, *Thalassiosira weissflogii* and *Cyclotella cryptica*	Silicon oxide nanoparticles	[40–42]

Table 3 Diatoms as a rich source of fatty acids (lipids) suitable for biofuel production

S. no.	Diatoms	References
1	*Amphora exigua*	[43]
2	*Biddulphia* sp.	[43]
3	*Chaetoceros gracilis*	[43]
4	*Cyclotella cryptica*	[39, 44]
5	*Cylindrotheca fusiformis*	[12, 45]
6	*Fragilaria* sp.	[43]
7	*Fistulifera solaris*	[46]
8	*Navicula cincta*	[47, 48]
9	*Navicula cryptocephala*	[49]
10	*Navicula inserta*	[43]
11	*Navicula muralis*	[43]
12	*Navicula pelliculosa*	[43]
13	*Nitzschia closterium*	[43]
14	*Nitzschia palea*	[45]
15	*Nitzschia longissima*	[43]
16	*Nitzschia closterium*	[50]
17	*Nitzschia frustulum*	[43]
18	*Phaeodactylum tricornutum*	[6, 46]
19	*Thallasiosira weissfloggi*	[51]
20	*Skeletonema costatum*	[48]

aluminium and specific surface area, and biogenic silica dissolves at rates fivefolds (5×) faster than those silicate minerals brought by rivers and streams by weathering of mineral rocks. Thus, most of such silica produced gets refluxed in the upper layers as silicic acid and is reutilized in-wall genesis, with only some of it reaching to the sub-photic layers [69], that the dissolution of silica in the upper layers was less than two-thirds (2/3) of the total production, indicating a considerable amount of silica sinking. It has been observed that diatom silicification is higher when the cell size is larger and colonial in nature [70, 71].

Based on their growth rate and degree of silicification, diatoms have been classified as [72]:

1. C-sinkers/group I species—lightly silicified, small, fast-growing, chain-forming diatom growing is growing in an iron-rich environment.
2. Si sinkers/group II species—heavily silicified, large, colony-forming diatoms are growing in an iron-deficit environment. Their growth rate is slow. Due to heavy silicification in their wall, they are resistant to zooplankton grazing.

Reproductive cycles also impact the Si:C ratio for export. Auxospore formation favours settling of diatoms onto the ocean floors; thus, carbon export in many coastal, upsurge and exposed ocean regions takes place significantly [73].

1.3 Eco-physiological dynamics of diatoms

According to the *Tara* oceans project, amongst the diatoms, *Chaetoceros* is the most abundant and diverse genus, followed by *Fragilariopsis*, *Thalassiosira* and *Corethron* [60]. A large amount of data collected from ocean colour remote sensing reveals the abundance of diatoms in coastal areas because of a continuous silica supply in the form of silicic acid from the rivers [63]. Diatoms help to understand the energy flux, mineral cycling, sedimentation patterns, etc. in the lotic and lentic water systems; additive factors like immigration and cell reproduction positively affect colonization, whereas negative factors, including abiotic stress, leading to a reduction in density and cell-count due to death or sloughing or being grazed by consumers [74–76].

1.4 Anthropogenic stress on diatom community

Anthropogenic stresses have been detrimental to all kinds of biological systems. They cause the vulnerability of species to a variety of changes including the extinction of some species [77, 78].

1.4.1 Ocean acidification

With the advent of the industrial revolution, global CO_2 concentrations have continued to increase and have spiked up in the recent past. Oceans serve as huge reservoirs to absorb CO_2 in the environment and reduce its accumulation in the atmosphere. But with the increase in CO_2 concentration, oceans are constantly being more and more acidified due to the dissolution of more CO_2 and the formation of more bicarbonate [57]. Thus, increased ocean acidification might eventually lead to a change in diatom community structure, ocean productivity and biogeochemical cycling and export of carbon and silicon.

1.4.2 Oil spills and their effects

The accidental leakage of a large amount of crude and other types of oils in water bodies is called an oil spill. This oil spill may remain on the surface of oceans for a long time if it remains unchecked and untreated. The oil can settle down at the base of the ocean by some of the mechanisms like direct mixing of oil in sediments by wave action and then sinking to the bottom due to increased density, mixed with faecal pellets after being ingested by zooplankton, and by adsorption of oil particles on particles suspended in water columns, culminating in sinking to the bottom. Phytoplanktons take up non-volatile aromatic hydrocarbons whilst heavyweight aromatic hydrocarbons do not undergo degradation and accumulate along with the sediments. The benthic organisms take up these hydrocarbons, preferentially heavy over light weighted as the larvae feed. These accidental leakages interfere with vital metabolic processes of both flora and fauna of aquatic systems and cause chemical intoxication [79].

Oil spills when occurring near coasts also affects the diatom communities as they are richly present in the coastal and upwelling regions. The studies have also shown that oil spills have brought about not only an increase in the number of diatom species but also an increase in the taxa number. The motile guild diatoms—comprising of fast-moving, competitively stronger species—have been found to dominate the oil-enriched zones [80]. Many times, changes in temporal gradients along with oil spills also have an impact on diatom communities. The rainfall causes disturbance in the inorganic layer and moves sediments, thereby causing shading and limiting light and nutrient availability to the periphytic communities. This favours the formation of long, tube and chain-forming, filamentous, stalked periphyton attached to a solid substratum, most sensitive to light and nutrient availability. Thus, it can be inferred those biological traits of dominating diatom species densities are detrimental to bioturbation activity and may prevent natural propagule resuspension and recolonization which is driven by currents [81].

2 High-value metabolites from diatoms

2.1 Pigments

Majorly, the kinds of pigments present in diatoms are chlorophyll and carotenoids. Amongst the chlorophyll pigments, chlorophyll a and chlorophyll c are the main pigments that take part in the photosynthesis process. Chlorophyll c is present in two forms—chlorophyll c1 and chlorophyll c2 [13]. Namely, carotenes and xanthophylls are the prominent classes of carotenoids found in diatoms. According to Maeda et al. [5]; Leyland et al. [17] and Bayu et al. [12], fucoxanthin, β-carotene, astaxanthin, lipid droplets, lycopene and proteins are commercially important compounds with bioactivities beneficial to human nutrition.

2.2 Lipids and its derivatives

Lipids serve the purpose of energy storage and are available as TriAcylGlyceride (TAGs), fatty acids, chrysolaminarin and other forms. These various chemical compounds are industrially viable as they are into the production of green diesel, fatty acids, glycerol and many other valued chemicals. Major fatty acids found are myristic acid, eicosapentaenoic acid, palmitoleic acid and docosahexaenoic acid (DHA), which are used prominently in the health and biofuel industry. Lipids also encompass compounds like polar lipids, steroids, oxylipins and isoprenoids, all with significant biological functions and bioactivities aiding in human health [18, 118].

2.3 Silica

Silica cell wall confers mechanical protection as well as biological shield against microbes like viruses and bacteria. It predominantly contains silaffins, silacidins, pleuralins, long-chain polyamines and other proteins. Biosilica has extensive potential as a biotechnological material as it forms highly pure porous nanospheres of different architectural designs. Diatom biosilica is employed to manufacture bioactive glasses, ceramics, drug delivery systems and many other microdevices [23, 41, 82].

3 Biomass harvesting techniques

The biomass harvesting involves the removal of culture medium and water to concentrate the grown biomass. Some important techniques of biomass harvesting involve filtration, centrifugation, flotation and flocculation.

3.1 Flocculation

In this method, the algal cells are aggregated in lumps through circumventing their net negative surface charges using flocculants, which are cationic exopolymeric macromolecules that reduce the intermolecular force and aggregate the microalgal cells in suspension [83]. This method works well for freshwater environments but not so effective for saline culture conditions where the high metallic charged ions cover up the cell surface charge [84]. Polyelectrolyte salts such as aluminium or iron salts are the most commonly used flocculants but their addition is not so desirable, as they may affect further downstream processes [85]. The easiest way of flocculation is induced through the diversion of pH. At the increasing pH (more alkaline levels), the net negative charge of the cell surface gets reduced and may turn into positive resulting in auto-flocculation. Another technology described by Poelman et al. [86] is electro-flocculation, where electrode surface is charged by electric current but it is of limited use because of several technical demerits like huge energy cost, the toxicity of flocculants, lumps formation, etc.

3.2 Centrifugation

Within centrifuge, sedimentation frequency is accomplished with the enhanced gravitational force to raise the sedimentation amount to get concentrated cell pellets. The biomass recovery through centrifugation relies on the magnitude of centrifugal force biomass sedimentation rate and temperature. However, for harvesting large-scale cellular suspension, the centrifugation system is not considered because of high maintenance cost of centrifuges and high installation cost using the specialized materials of construction which is durable and anti-corrosive alloys [83].

3.3 Floatation

Floatation is one of the premium approaches to take the algal biomass aside from pond water before its use for drinking purposes. In this procedure, the algal biomass floats on the top surface of the culture medium and is later harvested as a froth. Mainly, the floatation technique can be done in two ways: froth floatation and dissolved air floatation (DAF) respectively. "Froth floatation is a method of separating algal cells from the medium by adjusting pH and bubbling air through the column to create algal froth on the surface of the medium" ([87]), whereas, in the DAF method, mainly the water is ozonized, and then, the sensitized cells are treated with small amounts of polyelectrolyte salts. This results in the production of fine bubbles through the relaxation of pressurized fluid. These fine bubbles provide the floccules ultimate buoyancy through their adherence to it and causing their floatation over the surface of a separating vessel. The consequent high-density cell froth (7–10% dry weight) is then obtained as a semi-liquid mixture [88].

3.4 Filtration

Several modes are there to aggregate the extremely fragile frustules through filtration, of which the simplest one is dead-end filtration, where the dilute cell suspension is passed through a membrane packed with filters (different media combinations or sand particles). This type of filtration is restricted by the rheological characteristics of the cultured strain as they can easily obscure the filtration pathway through the formation of a compressible algal mat over it. Ultrafiltration is an advanced way of membrane filtration and is typically used for both biomass harvesting and separation of metabolites [89].

4 Cell disruption methods

To efficiently recover intracellular materials such as lipids from the cell interior, the disruption of the cell is commonly required. There are different approaches to extract intracellular components from the dried harvested algal biomass (Fig. 1).

4.1 Mechanical approach

There are two major processes to disrupt the dried algal biomass mechanically; they are as follows:

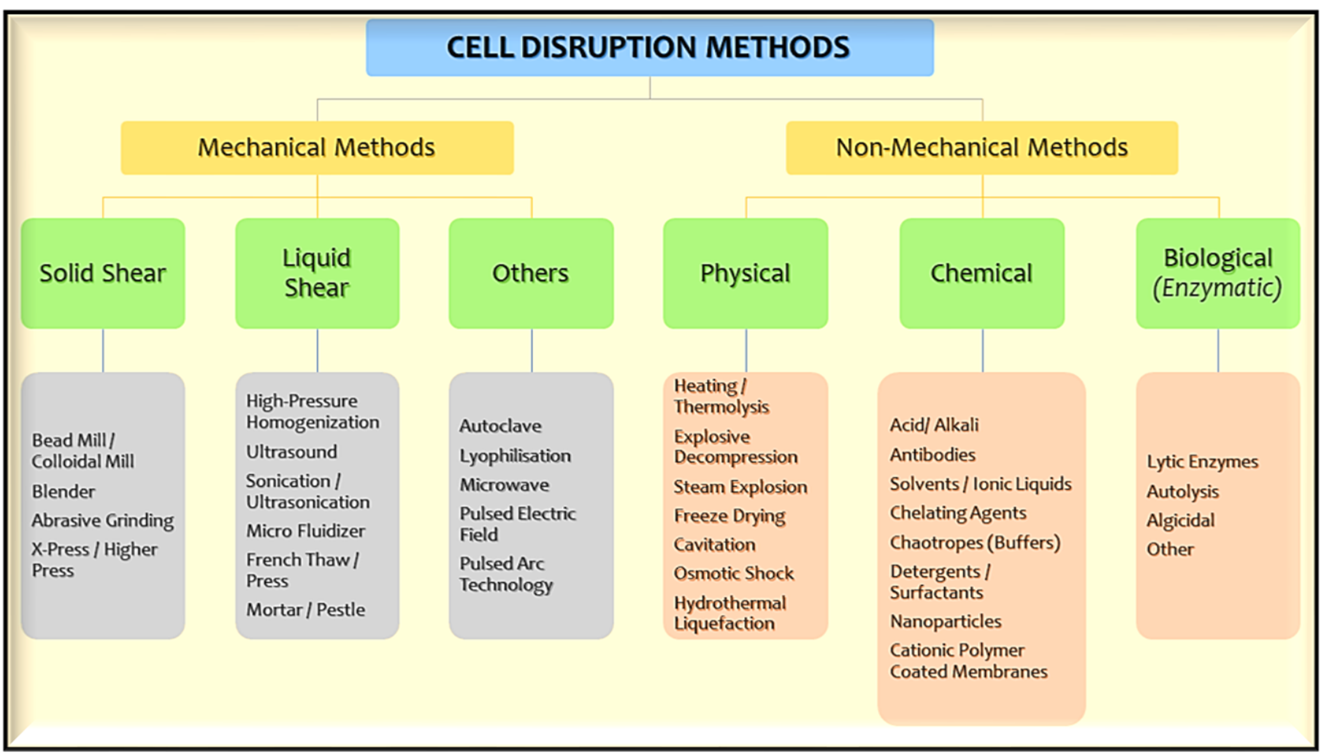


Fig. 1 Cell disruption methods

4.1.1 Bead milling

In this approach, a large vessel is filled with tiny glass beads and then agitated at high speed, which causes mechanical damage to the cells and leads to their disruption. The bead beating technique depends upon the residence time in the system, shape and size of cells and the strength of their cell wall [90]. This process is greatly used both in the laboratory as well as for industrial purposes.

4.1.2 High pressurized homogenisation

The high pressurized cell homogenisation involves the entry of fluid being strongly processed through a small perforation, thereby generating a rapid pressure, which impinges on the microalgal cell resulting in cellular disruptions. The rate of disruption caused is directly reliant on the pressure applied and the strength of the algal cell walls. The application of high osmotic pressure using a 10% NaCl solution as a breakage buffer decreases apparent cell strength and is also very effective to crack cell walls [91].

4.2 Physical approach

Physically, cell disruption can be accomplished through various treatments such as the pulsed-electric-field (PEF), ultrasound (UT) and microwave-assisted technique (MAT). The pressure and temperature are very minimal in the PEF method, providing very shear stress on microalgae as they have a rigid or elastic cell wall and protecting them from mechanical damage [92]. The UT method confers high shear pressure and can be performed at low operating temperatures, but the high-cost factor makes it not a viable option for large-scale biomass production. In MAT procedure, a high-frequency wave is applied to disrupt the algal cells whose cavitation effect generates the cracking of cells in sonication-based for lipid extraction.

4.3 Biochemical approach

Biochemical routes comprise of enzymatic digestion and alkali/acid treatments, which are cell-disruptive methods commonly employed to break microalgal cells. But this approach proves to be costly and inefficient, as it can even degrade some of the components of interest, so not used at the industrial level. Also, the enzymatic action of proteases often causes loss of protein molecules [92]. A mixture of several degrading enzymes (sulfatase, chitinase and lysozyme), coupled with PEF, may improve the permeability of some microalgal cells facilitating the cellular disruption.

4.4 Thermochemical approach

The process of hydrothermal liquefaction (HTL) or pyrolysis is the advanced method of extraction of value-added bio-products. In this approach, several sequential reactions, dealing with the decarboxylation of carbohydrates to sugars and fragmentation to aldehydes, lipid hydrolysis to fatty acids and deamination and depolymerization of proteins, take place to fragment bigger hydrocarbons, and other biomolecules, into smaller and more desirable hydrocarbons in the presence of a size-selective catalyst. HTL processing of algal biomass has been proved to be less energy-expensive and potentially measurable [93]. Also, here repolymerization of the resultant fragments into larger oil components is favourable. The major steps of HTL involve batch liquefaction, gas analysis, aqueous phase analysis and crude bio-oil analysis. The leftover crude bio-oil can be separated and filtered out from the solid phase, using chloroform solvent. Later on, the solvent was evaporated with a rotary evaporator at high temperature [94]. It is beneficial over the conventional methods as it does not require any complex separation step of the biomass fractions.

5 Lipid extraction

There are three major lipid extraction techniques like organic solvent extraction, supercritical fluid extraction and switchable solvent polarity system-based extraction.

5.1 Organic solvent-based extraction

The organic solvent-based extraction method is primarily performed using chloroform/methanol (1/2 *v*/v) solvent, but due to the cytotoxic effects of chloroform, it has restricted usage. The mechanism works on the principle of intermolecular forces, where a non-polar solvent infiltrates via the intracellular membrane into the cytoplasm and interacts with the neutral lipids to form an organic solvent lipid complex as per their concentration gradient. An alternate to chloroform which is the hexane/isopropanol (3/2 v/v) solvent is preferred because of its low cytotoxicity in the laboratories. This extraction procedure has several disadvantages, such as high energy requirement for solvent dissolution and the toxicity of organic solvents, so difficult to handle and possess health risks on exposure. Therefore, the modified organic solvent extraction method is compulsory to improve the yield in time and convenience [95].

5.2 Supercritical fluid extraction

The supercritical fluid extraction (SFE) method relies on the separation technique of one component to the other, using supercritical fluid as the solvent. The extraction procedure requires no energy for solvent removal at the highest temperature, pressure and supercritical CO_2 ($SCCO_2$) for the lipid extraction. $SCCO_2$-based lipid extraction is considered safe due to its low flammability, lack of reactivity and low toxicity at the cellular level [95].

5.3 Switchable solvent polarity system-based extraction

In this system, the reversible action of the liquid solvent is possible, from non-ionic (alcohol and an amine base) to ionic form (salts), under a suitable environment exposed to carbon dioxide, nitrogen or argon gas. This process includes multiple steps of separation, for the optimum production of valuable products. Also, the solvent's properties can be adjusted in the reaction vessel to utilize the same solvent in consecutive steps and make it an economically viable process [96]. The switchable solvents are applied in the "green" synthesis of various high-value products such as pharmaceuticals and nutraceuticals.

6 Biological applications of high-valued metabolites of diatoms

The advancement in molecular technologies has revealed the genomes of diatoms, which helped humans to study them as model organisms, using different culturing conditions and modified photobioreactors and helped in understanding the practical applications of diatoms and their valued products. This has ultimately created a niche for diatoms for their multiscale biorefinery approaches. A step closer to this, many companies have already started working on novel substances/biomolecules isolated from diatoms, which can be used as a carbon-neutral green fuel, nanotechnological products, wastewater treatments, health and cosmetic products and many more on a wider scale (Fig. 2).

6.1 Wastewater treatment

Diatom consortium is used in waste material degradation as they possess unique physiology of being sensitive to environmental change. An investigation was conducted by Wan Maznah and Mansor [97] where different diatom species were stationed at selected sampling points to monitor specific community structure and sensitivity to pollutants. The findings depicted the abundance of biological indicator species of diatoms concerning the water quality of the Penang River. As per Govindan et al. [27], palm oil mill effluent (POME) can be used in medium to culture Diatom *Gyrosigma* sp., which under optimized conditions produced lipid content of 70.71 ± 6.0% by dry weight. In this manner, POME wastewater, a highly polluting industrial effluent, could be treated by generating essential compounds for biodiesel, rather than

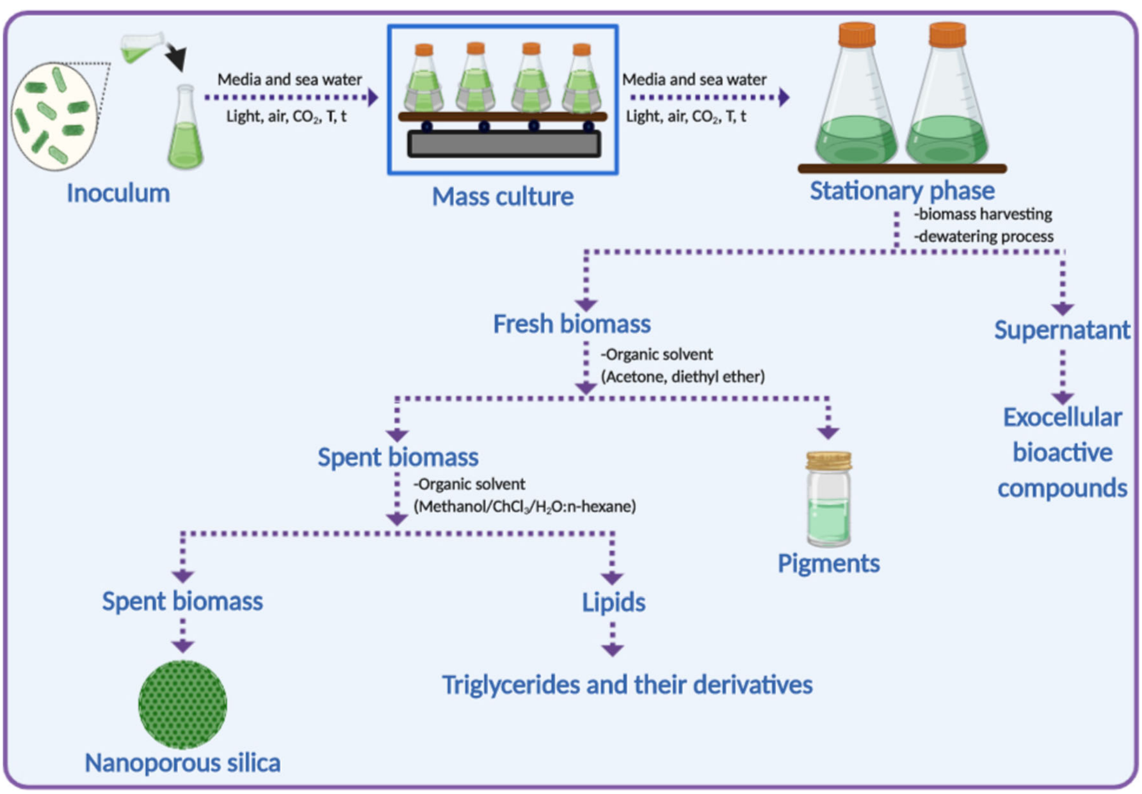


Fig. 2 A multiscale biorefinery approach of diatoms

discharging into the environment. The urban wastewater treatment, using Algal Floway (AFW) technology based on dominating pennate diatom community, works on silica enrichment of untreated water bodies and removes nutrient load cost-effectively and sustainably. The periphyton community forms dense biofilms which support mechanical stability in a high current of sewage waters [28, 29].

6.2 Health and cosmetics

Lately, microalgae are being valued for their applications in the health and cosmetic industry and the nutritional value is almost equivalent to the vegetable sources [98]. Most of the chemicals extracted from diatoms exhibit potential benefits to human health [99]. It contains nutritionally relevant biomolecules, fucoxanthin, β-carotene, astaxanthin, marennine, domoic acid, EPA, DHA omega-3 fatty acids and many more, which are commercially used to treat diseases and are taken as supplements to promote a healthy lifestyle. Studies conducted by Urikura et al. [32] revealed that the most abundant carotenoid, fucoxanthin, protects the skin from harmful UV radiation and reduces wrinkle formation, hence used in moisturizer or oral medication as an anti-photoaging agent.

6.3 Antiviral potency

Several of the diatom chemical compounds possess potential antiviral activity and are being researched extensively for pharmaceutical applications [100]. For instance, *Haslea ostrearia*, a marine diatom, is rich in blue pigment, marennine, which showed antiviral activity at the laboratory scale [36, 37]. Also, naviculan, a sulfated polysaccharide found in *Navicula directa*, is regarded as an antiviral agent against herpesviruses (HSV-1, HSV-2) and influenza virus [35].

6.4 Biohydrocarbons

Diatoms could be an efficient source of oil for biodiesel production. According to Schenk et al. [33], the sonication method showed a yield of 0.364 g/g of dry mass, higher than the soxhlet method of extraction. In the diatom *Navicula cryptocephala* occurrence of fatty acids such as palmitic acid, oleic acid, triacylglycerides (TAGs) like OLL (dilinoleoyloleoylgylcerol), are the major components for biofuels. However, in the nitrogen- and phosphorus-deprived conditions, *Phaeodactylum tricornutum* showed higher TAG contents in the cells. This can be due to the protective mechanism where cell divisions slow down and fatty acids are deposited as TAGs [20].

6.5 Aquafeed

Diatoms are considered as the ideal meal in the fishery and hatchery cultivation. They have a short life cycle with good nutritional property, leaving a good amount of residual biomass after harvesting, rich in lipid, protein and polysaccharides contents [101]. In the aquaculture production units, with the use of emerging algal cultivation techniques, the biomass is a good source of polyunsaturated fatty acids (PUFAs) and omega-3 fatty acids, like linoleic acid and α-linoleic acid which are key nutrients for aquaculture. These algal pellets make the fish healthy and more significant in size, hence turning fish farming into a profitable business in a short period. According to Debelius et al. [102], "*Nannochloropsis gaditana* has great potential as aquafeed, as they are easy to culture for Atlantic salmon, common carp and white leg shrimp". Another study by Catarina and Xavier [103], diatom *Chaetoceros sp.* is considered most suitable for the rearing of bivalves, under standard laboratory conditions. These raw materials are rich in secondary metabolites such as PUFAs and EPA (eicosapentaenoic acid and DHA (docosahexaenoic acid) which gives a good yield and market value.

6.6 Nanobiotechnology

The complex structure and interesting patterns of diatoms are prominently used in nanotechnology to produce nanomaterials. These biosilica nanoparticles, nanofibers and nanopolymers are used extensively due to their unique optical, mechanical, chemical and thermostable characteristics. Also, the biosilica synthesized by species of *Coscinodiscus*, *Thalassiosira* and *Cyclotella* microcapsule structures which are modified at the nanoscale to create natural living nanodevice [10, 41]. They have medical applications as contrast agents for magnetic resonance and ultrasound medical imaging and as a therapeutic platform for targeting the release of drugs, enzymes, antibodies and nucleic acids [104, 105].

Diatom silica deposition may also prove to be of great value to nano(bio)technology. An artificial selection procedure (micro-electrochemical system) based on phototropism guides diatoms to slide towards chemostat template. This approach can be commercialized at the nanoscale to mass produce a 3D fabric with matching patterns [22, 106]. Also, diatoms can be used as an important component of solar cells by replacing photosensitive TiO_2 for the SiO_2, naturally used by diatoms to build their cell walls. Diatoms could even increase solar efficiency by many folds when thin-film solar cells are coated with diatoms which trap the light inside the nanoscale pores [107]. The recent advancement in silica nanotechnology can be utilized in biosensing, biomimetics, drug and gene delivery, and formation of complex metal nanostructures biofuel producing solar panels [40, 108, 109].

7 Diatoms as a photosynthetic biorefinery

The living diatoms possess natural biosynthetic machinery, to create novel value-added products, which are used in a variety of applications. They are considered as a photosynthetic biorefinery because the energy is harnessed from the solar radiation whilst assimilating the carbon dioxide using earth-abundant minerals (N, P, Si, etc.), all within the same organism to produce valuable fuel and other bio-products [110]. The production of these bio-products (proteins, pigments, nanoporous silica, secondary metabolites and many more) can improve the economic viability and adds service value to the biorefinery concept [51]. Diatoms need biogenic silica to survive and grow; without a source of silicon, the frustules are not able to perform protein synthesis, no cell division and therefore die. But, once the cell has sufficient silicon to make a new cell wall and divide, its photosynthetic machinery takes over to make energy-dense lipids which can be converted into biodiesel or liquid hydrocarbon transportation fuels [111]. A typical diatom contains 10% silica, 50% lipids and 40% other biochemicals under normal environmental conditions; but under the controlled environmental conditions, the lipid content may reach up to 90% of the total dry weight of the biomass [112, 113]. According to Dunstan et al. [114], the presence of high lipid content in the cells, along with membrane-bound polar lipids, triglycerides and free fatty acids, makes them ideal for biofuel generation.

In the biorefinery approach, multiple steps are followed like cultivation, harvesting, cell disruption, extraction and purification process which are tailored in such a way that can further improve, optimize and recover the bio-oil and bio-char (residue). Some of the companies like Algatech (Czech Republic), Phytobloom, Necton (Portugal), Solix biofuels (USA), PetroSun Biofuels (Texas, USA) and even government funding started to invest in diatom research and diatom-based techno-economic valuable products. The fatty acid (FA) profile of diatoms shows that they are rich in monosaturated FA such as palmitoleate (16:1) or oleate (18:1) that release more energy on oxidation and stable as biofuels due to their combustion, lubricity and viscosity [62, 115]. The screening of the diatoms as a good source of lipids is suitable for bioenergy applications and can replace fossil fuels, as they have lower greenhouse gas emission, non-toxic, biodegradable and grown with ease in non-arable areas [116]. To ensure the commercial availability and reduction in the production cost of green biofuels, several industries and governments are providing funds to the diatom research.

8 Conclusion

Diatoms have played a decisive role in the ecosystem for millions of years as one of the foremost sets of oxygen synthesizers on earth and as a primary source of biomass in oceans. The recent biotechnological breakthrough has revealed the potential pathways of diatom cell factories to isolate the bioactive compounds of greater significance. The engineered diatom strains with optimized fatty acid chain for biodiesel production are considered an economically viable substitute for fossil fuels and conventional oilseed crops [45]. The understanding of diatom biology and their life cycle analysis plays an important role in screening the ideal diatom strain for commercial biomass production. The homogeneous culture enhances the photosynthetic productivity in photobioreactors, under high light radiation and nutrient limitations, and also decreases the susceptibility towards photodamage [117]. In the biorefinery approach, the isolation of high-value compounds (pigments, biogenic silica, bio-oil, protein, etc.) from diatoms finds great market potential and future applications in the bioenergy sector.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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