Chapter 11
Diatom Silica a Potential Tool as Biosensors and for Biomedical Field

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Abstract Brown algae, diatoms, have been the subject of extensive investigation in recent decades because they include active chemicals with a wide range of biological activities, including antibacterial, anticancer, antioxidant, anti-inflammatory, antidiabetic and antiparasitic capabilities. As of late, diatoms have many applications in biotechnology and are appropriate to deliver recombinant proteins/peptides, such as monoclonal antibodies, antibodies and presently for the generation of biosensors as well as sedate delivery specialist. Because of their biodegradability, ease of functionalisation, and moo-fetched and uncomplicated features compared to synthetics, diatom-based nanoparticles are used as drug delivery vehicles. Additionally, diatom-based nanoparticles are a viable option for delivering anticancer medications while also reducing cancer chemotherapy side effects. In this chapter, we attempted to compile the published data related to brown algae as a biosensor, medicate conveyance operator, focused on medicate conveyance utilising hereditarily built diatom biosilica.

Keywords Diatoms · Silicate cell wall · Biosensor · Drug delivery vehicle · Cancer therapy · Genetically engineered biosilica

11.1 Introduction

Diatoms are a big and diversified family of golden-brown algae that includes anything from minute filamentous forms to large, complex seaweeds (Phaeophyceae; Dhanker et al. 2022). Phaeophytes, like other Heterokontophyta members (Ochrophyta, Stramenopiles), have plastids with a girdle lamella, three-stacked thylakoids and chloroplast ER (endoplasmic reticulum). All have a heterokont motile stage (unequal flagella) and photosynthetic pigments such as chlorophylls a, c_1 and c_2, carotene, diatoxanthin and fucoxanthin (Andersen 2004).

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Fucoxanthin, a xanthophyll pigment, generally conceals the other pigments in phaeophytes, giving them their distinctive brown colour. Phaeophytes differ from most other heterokont groups in that they have (1) cellulose, alginic acid and various polysaccharides in their cell walls; (2) physodes, which are cellular inclusions of polyphenolic polymers; (3) chloroplasts with thylakoids in stacks of three, enclosed by a girdle lamella; and (4) laminarin, α-1,3-glucan as their main storage product (Pueschel and Stein 1983).

As storage reserves, several species create mannitol, sucrose, glycerol or oils. The nuclear envelope is separated by a peripheral endoplasmic reticulum. All Phaeophyceae members are multicellular in the vegetative phase, unlike other members of the phylum; none are unicellular in the vegetative phase, which is the prevalent morphology in other golden-brown groups. In most organisms, haploid and diploid generations alternate, which might be isomorphic or heteromorphic. Although there are many simpler filamentous forms, many are macroscopic seaweeds with sophisticated tissues and reproductive mechanisms (Guiry and Guiry 2014). Fewer than 1% of the class's estimated 1836 species in 285 genera have been identified in watery environments (Wilce 1966). Some freshwater organisms have adapted to life in brackish water. There are three to seven genera of freshwater brown algae and up to 13 species worldwide, according to various authors. In most organisms, haploid and diploid generations alternate, which might be isomorphic or heteromorphic. Although there are many simpler filamentous forms, many are macroscopic seaweeds with sophisticated tissues and reproductive mechanisms.

About two decades ago, the first characterisations of the biochemical processes and components involved in diatom silicification were made (Hildebrand et al. 2006; Kröger et al. 1999, 2000, 2002). More recent research has shed light on how higher-order silica structure construction might take place (Tesson and Hildebrand 2010, 2013; Scheffel et al. 2011). Recent publications have detailed the discovery of novel components engaged in higher-order processes, real-time imaging of dynamics and genetic modification of silica structure (Kotzsch et al. 2017; Tesson et al. 2017). These recent researches have offered strategies for not only identifying but also clarifying the connections and spatiotemporal dynamics of the components involved in silica cell wall formation. This type of holistic understanding will be required to have a better understanding of cell wall formation (Hildebrand et al. 2018).

The ability to selectively remove malignant cell populations while leaving healthy cells alone is a critical goal in anticancer therapy. Although the benefits of using nanoporous silica-based materials as drug delivery vehicles have recently been established, their production requires the employment of expensive and toxic chemicals. Nanoporous biosilica is generated from diatom microalgae to deliver chemotherapy medicines to cancer cells (Delalat et al. 2015). This chapter concentrates on the evolutionary history of brown algae, overview of brown algae's silicate cell, as well as the role of brown algae as a biosensor and its biomedical applications.

11.2 Evolutionary History of Brown Algae

Brown algae (Phaeophyceae) are complex photosynthetic entities with an evolutionary history that is substantially distinct from that of green plants, to which they are only distantly related. These seaweeds are the most common species in rocky coastal ecosystems, and they have a variety of remarkable adaptations to their typically harsh surroundings. Brown algae are also one of the few eukaryotic lineages with sophisticated multicellularity (Cock et al. 2010; Dhanker and Tiwari 2021).

The old, twentieth-century understanding of brown algal categorisation, which was based on a combination of life cycle organisation, thallus architecture and gametic features, was invalidated by molecular phylogenies. For example, phylogenetic evidence clearly refuted the long-held theory that the physically more complex orders were diverged from filamentous Ectocarpales early in the brown algae's development. The Ectocarpales, on the other hand, were near cousins of the Laminariales, one of the most morphologically complex groups of brown algae. Based on molecular phylogenies, ancestral state reconstructions show that parenchymatous growth has returned to filamentous growth several times (Trevor et al. 2020). Similarly, life history features and gametic differentiation show complex evolutionary patterns, with transitions from isogamy to anisogamy to oogamy occurring multiple times independently, with the genetic basis just recently identified. Because of this versatility, molecular data has been crucial in accurately characterising brown algal relationships.

The genome of Ectocarpus has revealed indications of its ancient evolutionary background as well as more recent events related to the origin of the brown algal lineage. The former includes the various origins of the genes that make up the genome, many of which were acquired through endosymbiotic events, whereas the latter includes the recent emergence of new gene families and the evolution of an unusual genome architecture, both in terms of gene structure and organisation (Cock et al. 2010). It's likely that events on both periods influenced the genesis of sophisticated multicellularity in brown algae. The long-term preservation of completeness and diversity within essential gene families, such as the brown algal receptor kinase family, appears to have been just as significant as the more recent development of novel proteins (Cock et al. 2010).

Early in the evolutionary history of brown algae, the orders Discosporangiales and Ishigeales diverged from the other brown algal lineages at the beginning of the Mesozoic Era (~250 Ma). These two orders have only 11 species, yet they are very different from other brown algae.

The SSDO clade diverged from the lineage that gave origin to the remaining existing brown algae orders during the Mid-Mesozoic (approximate timeframe for the Jurassic period, 200–145 Ma) and diversified into what are now four orders: Sphacelariales, Syringodermatales, Dictyotales and Onslowiales. The most prominent of these lineages is Dictyotales, which today comprises a large number of brown algal species (Trevor et al. 2020).

The life cycle is a fundamental biological element that drives the evolution of many properties such as reproductive systems and dispersal modes, and it must be considered in order to properly comprehend a species' biology. Brown macroalgae have a diverse range of life cycles, sexual systems and reproduction strategies (Trevor et al. 2020). Their life cycles range from isomorphic haplodiplontic life cycles (e.g. *Dictyota dichotoma*), in which both the gametophyte and sporophyte display identical levels of multicellular development, to diplontic life cycles, in which only the diploid generation is multicellular (e.g. *Fucus* spp.) The cycle is called heteromorphic when the gametophytes and sporophytes have distinct morphologies. Except in a few taxa, such as *Scytosiphon*, where the haploid phase is a big, upright thallus and the diploid phase is a prostrate crust, the diploid sporophyte is generally dominant (i.e. larger) than the haploid gametophyte (Heesch et al. 2021; Trevor et al. 2020).

The primordial form of brown algal sexual reproduction was haplodiplontic, with identical haploid and diploid phases, according to phylogenies based on morphological and molecular features (i.e. isomorphic; Heesch et al. 2021; Trevor et al. 2020). Several lineages have experienced changes to this isomorphic life cycle, including a reduction in the size of the gametophyte generation (transition to a heteromorphic cycle, e.g. Syringodermatales, prior to the ancestor of the BACR) or the loss of this haploid generation (transition to a diplontic life cycle, e.g. Ascoseirales, Fucales, genus *Tilopteris* in Tilopteridales). There have been no transitions back to a haplodiplontic life cycle, implying that conversions to diplontic cycles were irreversible. Multiple transitions from heteromorphic to isomorphic life cycles, on the other hand, have happened (Trevor et al. 2020). The study of the evolutionary processes that drive these transformations is still a fruitful field of study for brown algae.

11.3 Emerging Application of Microalgae

11.3.1 Brown Algae as Biosensor

11.3.1.1 Biosensors

Biosensors or organic sensors are tools made from a transducer and bioreceptor that can pick out analytes and flip that data right into a measurable sign.

There are elements of biosensors such as bioreceptor and transducer (Brayner et al. 2011):

1. Bioreceptor: Bioreceptor can be created from any enzyme, antibody, nucleic acid, complete cell, tissue and microorganism.
2. Transducer: Transducer is the opposite of a biosensor and having optical, electrochemical, thermal, mass-based, ion—susceptible and resistant (Mona et al.

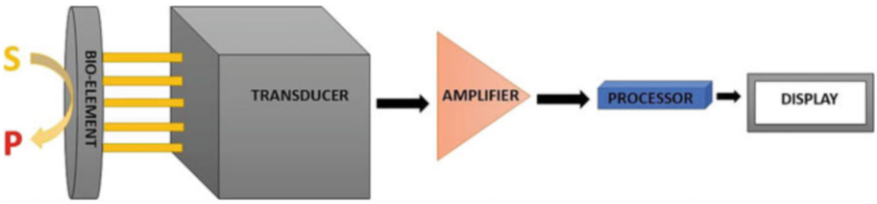

Fig. 11.1 Schematic diagram of biosensor

2020). Selectivity and specificity rely upon an organic popularity gadget related to appropriate transducers (Fig. 11.1).

Basic precept of biosensor is especially concerned with three elements:

- Biological popularity detail
- Transducers discover and transduce signs from organic goal
- Then transduction of indicators from organic to electric powered indicators (Mona et al. 2020)

11.3.1.2 Need of Algal Biosensor

This technique quickly and accurately detects low concentrations of pollutants in fluids, water and air. Environmental safety issues require fast, accurate and efficient technology. Bio-algae biosensors are based on microalgae and cyanobacteria (turquoise algae). Algae biosensors detect herbicides, volatile organic compounds (VOCs), heavy metals and more. Algae biosensors measure various metabolic activities of an organism. Toxic and dangerous substances have a great influence on the metabolic activity of cells, and this effect is transmitted in the form of signals. The main purpose of these sensors is to detect pesticides, herbicides and fungicides. Algae are used in bioassays for aquatic risk management and environmental monitoring (Kashem et al. 2019; Dhanker et al. 2021, 2022; Mathew et al. 2021). Algae are so sensitive and reproducible that they are used to eliminate toxicity (Durrieu et al. 2004; Dhanker et al. 2022; Mathew et al. 2021). However, biosensors have been developed to assess aquatic toxicity. Photosynthetic activity is inhibited by electrochemical oxygen reduction and chlorophyll fluorescence. The alternative activity of algae protoplasts and the gravity or phototaxis of algae are electrochemically monitored (Tatsuma et al. 2009). The main advantage of biosensors is that they are highly selective for each type of contaminant. Heavy metals inhibit enzyme synthesis as an inhibitor of alkaline phosphatases and esterases and inhibit pesticide attack on PSII as chlorophyll fluorescence released from photosynthetic activity (Durrieu et al. 2004).

11.3.1.3 Types of Biosensors

Primarily there are two sorts of biosensor:

1. **Natural:** These algal strains happen in common conditions. These organisms generally work in living beings (*Chlorella vulgaris*). Characteristic algal biosensors are for the most part working on the photosynthetic action of green growth. In these sorts of biosensors, the movement of photosynthesis in living cells is affected due to the nearness of different poisons. A few biosensors are based on the fluorescence of chlorophyll put away in chloroplasts. Algal biosensors right now utilise the chlorophyll fluorescence as the quantifiable flag. Chlorophyll fluorescence is utilised to measure the herbicides that influence the photosynthesis at PSII for illustrating triazines and atrazine (Durrieu et al. 2004).
2. **Hereditarily altered:** They are hereditarily altered quality of any microorganism. Manufactured biosensors have so numerous focal points. Natural biosensors have certain limitations, but to overcome these problems, biotechnological modified strains of biosensors are used, work with high efficiency and are easily detectable. According to Shao et al. (2022) a freshwater Cyanobacteria, *Synechocystis* sp. strain PCC6803, was genetically modified with the gene *Lucia luciferase* of firefly (a novel bioluminescent alga) which is sensitive to a wide range of compounds like herbicides and other pollutants. Important application of these biosensors is important for quick screening of water samples or determining toxicity of pollutants to harm the environment (Guleri et al. 2020; Shao et al. 2022). The biosensors could also help to indicate the type of pollutant and potential of pollutant to harm.

11.3.1.4 Working of Algal Biosensors

Biosensor consists of a bioreceptor that senses a biological element and transducer which determines the signals (biochemical) and converts it into an optical or electrical signal. Biosensors facilitate fast, accurate, rapid and low concentration screening of a number of compounds. Depending on the type of biological element used, the response/signal varies. The signal is then amplified and filtered using a signal processing unit (SPU), and the outcome of the SPU is an analog signal which is equal to the biological quantity measured. However, specifically in algal biosensors, the fluorescence emitted by the photosynthetic activities of algae is used to facilitate the detection of toxic substances. The identical signals are obtained with optical and conducto-metric transducers. This device is planned to watch different synchronous metabolic exercises of immobilised green growth (Durrieu et al. 2006).

11.3.2 Diatoms-Based Sensors

11.3.2.1 Hierarchical Porous Structure

Diatom frustules feature a remarkable permeability structure, with pores dispersed at different scales from nano to micro. They can be thought of as prefabricated 3D nanodevices. More than 10^5 unique diatom species have been depicted. They are easily processed, yielding large quantities of hereditarily regulated silica frustules. These three-dimensional silica shells could thus serve as the foundation for novel electronic devices, such as gas sensors that can detect contamination faster and more effectively than conventional devices (Livage and Sicard 2011). The subject of optical microsensors for unstable compounds will be a fascinating application of diatom frustules. An expansive surface range is a critical feature for an optical transducer that must be sensitive to vapors and glasses in order to provide a genuinely successful interaction with a few adsorbates. Because the diatom pores' measurements are accurate within a nanometer range, a wide range of unstable chemicals (solvents, hydrocarbons, etc.) and even pure gases can penetrate and condense within them. Diatoms' varied levels of porosity enable hint mixing between the explanatory gas test and the locator, allowing for appealing biomolecular intuitive observation. Silica is known to have photoluminescent capabilities within the visible range, around 2.2 eV, due to Si–O organisation abandons (Livage and Sicard 2011).

For silica diatom frustules, similar photoluminescence (PL) emanation within the yellow region is also monitored. Surface-oxygen stoichiometric surrenders are linked to this glow activity. It can thus be impacted by even minor changes in the surrounding gas environment. Within the thickness of luminous states, gas particles are adsorbed on these surrenders, leading them to an altar. As a result, the presence of gases can either quench or boost photoluminescence (PL) emission. Gas detection at low concentrations is very sensitive, and for diatom frustules with the highest specific surface area, a detection limit of 50 ppb was achieved. Recent research using the silica skeleton of the marine diatom *Thalassiosira rotula* has revealed that photoluminescence (PL) is greatly influenced by the environment. In the visible area, silica frustules have a broad emission band centred at roughly 2.26 eV, with a full width at half maximum of 600 meV. The strength of the PL signal decreases when exposed to NO_2. The PL flag has been deactivated because NO_2's electrophilic capabilities can attract electrons from the silica substrate. *Thalassiosira rotula* frustules have been observed with a notable variation of PL concentrated at low (sub-ppm) NO_2 concentrations (shown as $[NO_2]$), and immersion of the extinguishing impact occurs at NO_2 concentrations of the order of 10 ppm (Lettieri et al. 2008; De Stefano et al. 2005). Gases and natural vapors affect both the optical escalated and crest placements. A few compounds, such as acetone or ethanol, extinguish the glow, while others, such as pyridine, successfully improve it, depending on their electronegativity and polarising capability. These miracles allow for the separation of various chemicals and were utilised to create the first

diatom-based photoluminescence gas-sensing devices (Steraro 2007). As a result, these genuine living beings are excellent candidates for optical detecting materials for dangerous gas detection or contamination testing. By providing distant components inside the culture media, the photoluminescent characteristics of silica frustules can be changed.

For example, germanium can be metabolically implanted in *Pinnularia* sp. frustule biosilica. Within the blue range, between 450 and 480 nm, a few Si atoms are replaced by tetravalent Ge, and germanium-doped frustules display both photoluminescent and electroluminescent features (Jeffryes et al. 2008; Qin et al. 2008). Titanium has also been metabolically implanted into silica frustules using a two-stage cell-cultivation process (Jeffryes et al. 2008), resulting in the formation of a semiconducting TiO_2 coating.

In this situation, conductivity estimates can be used to limit the total amount of distant gases like NO_2. The modified frustule functions as a microelectrode. The hydrated silica $SiO_2 \cdot nH_2O$ in diatom frustules is unknown. Si–OH receptive hydroxyl bunches enable chemical surface modification and subsequent silica shell functionalisation. Later research has shown that the frustule surface of *Coscinodiscus wailesii*, a diatom with spiral symmetric valves, may be chemically changed and covalently attached to several types of bioprobes, acting as a helpful support in the development of fluorescence biosensors. Antibodies have been linked to the frustules of *Coscinodiscus concinnus*, a marine diatom. According to fluorescence estimates, these antibodies can still recognise their antigens when attached to the hazy silica surface of diatom microshells. Changes in the photoluminescence emission of diatom frustules reflect the specific antibody–antigen recognition (De Stefano et al. 2008; Gale et al. 2009). Diatom frustules appear to be used as layouts for the production of nanostructured materials as well.

Silica shells can be chemically transformed into different oxide materials while retaining their three-dimensional nanostructure. Through a shape-preserving gas–silica uprooting response, silica has been transformed into a contemporary composition in this preparation, currently known as fundamental 'bioclastic and shape-preserving inorganic transformation'.

The silica shell can be converted to MgO by heating it in magnesium vapour at 900 °C for 4 h (Sandhage et al. 2002). As a result, a variety of additional nanostructured oxide materials (TiO_2, ZrO_2, $BaTiO_3$) have been created (Bao et al. 2007). Silica can be reduced to permeable silicon, resulting in previously unimagined microelectronic consequences. A synergistic combination of natural nanostructures and synthetic chemical functionalisation could result in a large variety of 3D micro/nanostructures with chemistry and characteristics that can be designed for detection applications (Guleri et al. 2020; Livage and Sicard 2011).

11.3.2.2 Photonic Crystals Made of Diatom Frustules

A few diatoms continue to function as 'living opals', with glowing qualities arising from their unusual porous structure. They then occasionally transport moo (gaps)

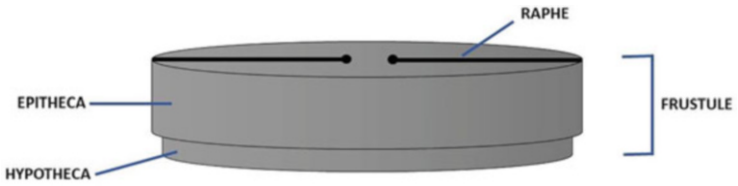

Fig. 11.2 Schematic diagram of diatom

and tall (silica) dielectric stable materials with grid measurements close to the wavelength of visible light. In *Coscinodiscus granii*, a hexagonal cluster of pores with a large grid within the valve and a square cluster with a small cross section within the support (Fuhrmann et al. 2004) have been discovered. As a result, diatom frustules might be depicted as 'living photonic crystals'. Between light and matter, something solid may happen intuitively. In 'photonic crystals', light behaves similarly to electrons in semiconducting materials. As a result, diatom frustules take on the appearance of opals (Fig. 11.2).

Silica frustules typically hold light in the blue region, a feature that protects diatoms from excessive illumination and improves their photosynthetic behaviour (Yamanaka et al. 2008). This is due to a specific assimilation resulting from the occasional conveyance of pores inside the silica frustule, which continues to function as a photonic precious stone piece waveguide. These diatomic nanostructures can be used to locate unstable chemicals in photonic microsensors. The capillary condensation of natural vapors inside the pores causes a change in the normal refractive file, which can be detected using a few optical techniques (De Stefano et al. 2009). Lin et al. (2010) have described diatom-based sensors for fast label-free electrochemical localisation of cardiovascular biomarkers. A cluster of gold nanoelectrodes on a silicon chip make up the biosensor. Each sensor is covered with a diatom frustule, resulting in a thick layer of nanowells. Their permeable structure facilitates the spread of biospecies and allows for true management of 'molecular flow'. At low pg/mL levels, fiery indicators in the human blood have been found, with affectability sufficient to identify patients at risk of cardiovascular infection (Livage and Sicard 2011).

11.4 Brown Algae as Drug Delivery Agent

Lipids, carbohydrates, peptides and carotenoids, which are derived from brown algae and have anticancer and antibacterial properties, are used in biomedicine and pharmaceutical biotechnology. Photosynthetic marine microorganisms have biotech uses and are also suitable hosts for the production of recombinant peptides such as monoclonal antibodies and vaccines. Diatom is a brown algae that is eukaryotic and has a distinctive cell wall called frustule. The silica frustule structure possesses unique advantages for drug administration, including well-organised

three-dimensional pores, microchannels, chemical inertness and a homogeneous nanopore structure. Frustules could be easily designed, shielded and functionalised for medication delivery and loading in the future (Khavari et al. 2021). Because of their easy functionalisation, biodegradability, low cost and simple features compared to manufactured silica nanoparticles, diatom-based nanoparticles are exploited as drug delivery vehicles (Vona et al. 2015). As a result, diatom-based nanoparticles can be used to deliver anticancer medications while also reducing the negative effects of cancer chemotherapy. Diatom-based nanoparticles have been employed in drug delivery systems in recent years. Biodegradability, wide surface area and low toxicity are the key advantages of these nanoparticles over other carriers. Diatoms are utilised in the production of growth factors, antibodies, vaccines, hormones and immunological regulators in medical and pharmaceutical biotechnology (Yan et al. 2016; Aw et al. 2012).

11.4.1 Diatom-Based Nanocarriers in Drug Delivery

Drug delivery systems are created to deliver medications or genes to specific cells, such as cancer cells. Patients with genetic diseases frequently have a missing or damaged genome. In this context, silicon nanoparticles (NPs) have been found to be a successful technique (Dolatabadi and de la Guardia 2011). As they transport medications to specific tissues in the body, sophisticated drug delivery systems can now overcome the constraints of conventional pharmaceuticals (e.g. poor solubility/stability and high toxicity). Micelles, liposomes and silicon oxide NPs are some of the most utilised drug carriers, each with its own set of advantages and disadvantages (Dhanker et al. 2021).

Silica-based NPs like SBA-15 and MCM-41 offer chemical and physical qualities include tailorable pore size, thermal ability, a large surface area and high loading capacity. The limitations of NPs have been noted as being time-consuming and costly, as well as requiring toxic ingredients and a lot of energy (Aw et al. 2012; Maher et al. 2018). The use of marine resources in biomedicine is becoming increasingly popular (Chao et al. 2014). Diatom biotechnology has received a lot of interest in recent years as a major field for research and manufacturing of high-value molecules with therapeutic uses (Gordon et al. 2009). As previously stated, microalgae are a major source of different polysaccharides such as carrageenan, laminarin, fucoidan and alginate, which can be transformed into NPs and interact with biomolecules via hydrophilic groups on the surface (Shankar et al. 2016).

The production of diatoms (brown algae) with an amorphous silica shell is both expensive and simple. Porous silica (SiO_2) NPs can be found in their fossils [frustules/diatomaceous earth (DE)]. DE and living diatoms have also been found to be sources of silica NPs, with DE having more frustules (Maher et al. 2018; Sasirekha et al. 2019). Amino group functionalisation preserves plasmid DNA while also delivering it to the nucleus. Park et al. (2008) found that receptor-mediated endocytosis reduced cytotoxicity and improved transfection effectiveness.

Furthermore, Aw et al. (2011) examined the oral delivery of a hydrophilic drug (gentamicin) and a hydrophobic drug (indomethacin) through porous silica diatoms and found that indomethacin loading (smaller than gentamicin) was higher and had a stronger interaction with DE, while both drugs' drug release behaviour was similar (Aw et al. 2011). Bariana et al. (2013) modified diatoms with phosphonic acid and organosilanes for co-delivery of hydrophilic (gentamicin) and hydrophobic medicines (indomethacin). They discovered that hydrophilic modifications like 16-PHA (16-phosphono-hexadecanoic acid) and OTS (7-octadecyltrichlorosilane) improved drug loading and controlled release of gentamicin, whereas hydrophilic modifications like APTES (3-aminopropyltriethoxysilane) and 2-CEPA (2-carboxyethyl–phosphonic acid) increased drug loading and controlled release of indomethacin. Modifications to diatomaceous earth (diatomite, DE) could change and improve its properties; for example, oligo(ethylene glycol) methacrylate copolymers on diatom microcapsules make these agents stimulus-responsive carriers for the delivery of levofloxacin, an antibiotic used against *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Vasani et al. 2015).

Furthermore, diatom frustules treated with DOPA/Fe_3O_4 (dopamine-terminated Fe_3O_4 NPs) used their magnetic characteristics to control an external magnetic field (Losic et al. 2010). Sasirekha et al. (2019) used chitosan to functionalise *Amphora subtropica* for doxorubicin (DOX) release and loading in their study. Furthermore, Janićijević et al. (2015) reported that diatomite treated with aluminium sulphate is an efficient carrier for diclofenac sodium, resulting in higher adsorbent loading and longer release than the control.

A disulfide bond was used to attach cargo molecules in biomimetic silica carriers (e.g. bioactive peptides/proteins, medicines) with R5 silaffin peptide in another work. After that, R5-cargo conjugates were entrapped in silica particles, and it was discovered that reductive and acidic conditions were beneficial for cargo release from this complex (Lechner and Becker 2013). Natural silica NPs produced from *Coscinodiscus concinnus* (diatom) for the administration of streptomycin (hydrophilic drug), comparing the drug release efficiency time of the treated diatoms to the untreated diatoms. Due to surface adsorption, streptomycin was also absorbed inside the pores and into the hallow diatom structure (Gnanamoorthy et al. 2014). According to Vona et al. (2015), increasing silanol on diatom surfaces improved drug encapsulation of ophiobolin A, a fungi-derived anticancer chemical. Surface functionalisation was found to be an effective technique for drug loading on diatoms in a previous study, and ophiobolin A release was reported to be prolonged (Vona et al. 2015; Delasoie and Zobi 2019), as shown in Table 11.1. In a work by Cicco et al. nanoporous silica-based particles were functionalised with cyclic nitric oxide 2,6,6-tetramethylpiperidine-*N*-oxyl and loaded with antioxidant, antibiotic (ciprofloxacin) and antibacterial effects on fibroblast and osteoblast-like cell development (Cicco et al. 2015). The combined effects of diatom surface functionalisation and shape on drug loading and release qualities were studied by Bariana et al. (2013). Diclofenac sodium (DS) is a nonsteroidal anti-inflammatory medication (NSAID) used to treat inflammation and pain (Table 11.1).

Table 11.1 Some pharmaceutical products and drug candidates from brown algae

Compound (product)	Preparation technology	Biological activity and pharmaceutical application
Magnesium alginate/$NaHCO_3$ (Gastrotuss® baby syrup)	Pharmaceutical excipient	Children and infants from the first days of life reflux treatment
Sodium alginate/$KHCO_3$ (Algicid® suspension/tablets)	Pharmaceutical excipient	Adult reflux treatment
Sodium alginate/$NaHCO_3$/$CaCO_3$ (Gaviscon Double Action Liquid®)	Pharmaceutical excipient	
Sodium alginate oral suspension sachet	Pharmaceutical excipient	
Alginate-based reflux suppressant	Pharmaceutical excipient	Heartburn in pregnancy
Polyethylene glycol matrix/hydrated alginate (Flaminal Forte® gel)	Functional modification: hydrogel	Leg and diabetic ulcers, pressure sores, complex grazes, burns, oncology and wound dermatosurgery
Propylene glycol sodium/calcium alginate (Saf-Gel® gel)	Functional modification: hydrogel	Dry and sloughy necrotic wounds, pressure and venous ulcers, second-degree burns, cuts, abrasions and skin tear, noninfected diabetic foot ulcers
Ester of hyaluronic acid/sodium alginate (Hyalogran® dressing)	Pharmaceutical excipient	Variety of exuding wounds including leg ulcers, pressure sores, ischaemic and diabetic wounds, particularly those which are covered with slough and necrotic tissue or areas that are difficult to dress
Calcium alginate (SeaSorb® dressing)	Functional modification: hydrogel	Heavily exuding wounds including leg and pressure ulcers, diabetic ulcers and second-degree burns, cavity wounds
Calcium/sodium alginate (Kaltostat® dressing)	Functional modification: hydrogel	Moderately to highly exuding chronic and acute wounds and for wounds with minor bleeding
Sodium alginate/poloxamer (Guardix-SG® adhesion barrier)	Pharmaceutical excipient	In spine and thyroid surgeries to reduction of the incidence postoperative adhesions
Sodium alginate (Natalsid® suppositories)	Pharmaceutical excipient	Chronic haemorrhoids, proctosigmoiditis and chronic anal fissures after surgical interventions in the rectum
Propylene glycol alginate/enamel matrix derivative (Emdogain® gel)	Esterification: gel	1-, 2- and 3-wall intrabony defects, class II mandibular furcation defects with minimal interproximal bone loss, recession defects
Alginate oligosaccharide (OligoG®)	Chemical depolymerisation	Cystic fibrosis, treatment of chronic obstructive pulmonary disease (COPD), improvement of antibacterial and antifungal therapy, antifungal activity
Propylene glycol alginate sodium sulfate oligosaccharides (PSS)	Chemical depolymerisation and sulfation	Anticoagulant and antithrombotic activity, blood viscosity reduction

(continued)

Table 11.1 (continued)

Compound (product)	Preparation technology	Biological activity and pharmaceutical application
Propylene glycol mannuronate sulfate (PGMS)	Chemical depolymerisation and sulfation	Hyperlipidemia and ischaemic cardiovascular and cerebrovascular diseases
Oligomannuronates (GV-971)	Chemical depolymerisation	Alzheimer's disease and neurodegenerative diseases
Polymannuroguluronate sulfate (HS911)	Chemical depolymerisation and sulfation	HIV/AIDS, hepatitis B virus
Oligomannurarate sulfate (JG3)	Chemical depolymerisation and sulfation	Inhibition of tumour angiogenesis, metastasis and tumour growth
Polyguluronate sulfate sodium (PGS)	Chemical depolymerisation and sulfation	Kidney stones and bladder stones; anti-inflammatory

11.4.1.1 Cancer Therapy with Diatom-Based Nanocarriers

DSNs (diatomite silica nanoparticles) are suitable for cancer therapy. Anticancer chemicals are efficiently transported into the cytoplasm of human epidermoid carcinoma cells by DSNs (Ruggiero et al. 2014). Liposomes and polymeric nanoparticles have recently been employed in chemotherapy, and dual-drug delivery may be used with two or more medicines (Nouri et al. 2017). When the concentration of DOX is higher than PTX, for example, paclitaxel (PTX) and DOX have shown synergistic interactions in the treatment of solid tumours. Because of their self-assembly and ease of production, DE particles are ideal for the regulated release of these medicines (Kabir et al. 2020).

DNPs functionalised with ATPES (3-Aminopropyl) triethoxysilane and polyethylene glycol (PEG) had greater cellular absorption and a longer drug release profile (Terracciano et al. 2015). Curcumin is an anti-inflammatory, antioxidant and cancer-fighting compound. Curcumin's medicinal use is currently limited by issues such as low bioavailability, fast dimerisation and poor absorption. In cancer therapy, natural diatoms treated with polydopamine are effective carriers for curcumin administration (Uthappa et al. 2019). Furthermore, diatomites activated by oxidising acids have been used as an ophiobolin A carrier (a fungal anticancer molecule) to extend the release of this agent (Vona et al. 2015).

Todd et al. (2014) found that diatoms loaded with iron oxide NPs might be employed as smart carriers for the delivery of small molecules and pharmaceuticals by manipulating an external magnetic field using their magnetic characteristics (Todd et al. 2014). This compound binds to HCT-116 colorectal cancer cells at the pH of the GI (Gastro Intestinal) tract, and the anticancer drug is slowly released under light irradiation, resulting in a twofold increase in cytotoxicity against HCT-116 (Delasoie et al. 2020). Free diatoms, on the other hand, have exhibited extremely low cytotoxicity against Caco-2, HT-29 and HT-116 (colon cancer cells),

resulting in increased prednisone and mesalamine release and penetration in the GI tract (Zhang et al. 2013). Two medications have been delivered using diatom silica microparticles in the treatment of GI disorders. In GI diseases, prednisone and mesalamine have a longer half-life. Furthermore, drug permeability across Caco-2/HI-29 cells has been reported to improve, indicating that these particles are viable options for colon cancer treatment (Zhang et al. 2013). Diatomite NPs are similarly effective at transporting siRNA to suppress gene expression inside human epidermoid cancer cells (H1355).

11.5 Targeted Medication Delivery Using Genetically Modified Diatom Biosilica

The capacity to selectively target malignant cell populations while leaving healthy cells untouched is a key goal in anticancer therapy. Although the use of nanoporous silica-based materials as drug delivery vehicles has proven to be beneficial, their manufacture needs harmful and expensive chemicals. Chemotherapeutic medicines are delivered to cancer cells using nanoporous biosilica produced from diatom microalgae. *Thalassiosira pseudonana* has been genetically modified to display an IgG-binding domain of protein G on the surface of biosilica, allowing cell-targeting antibodies to be attached. Biosilica showing specific antibodies sorbed with drug-loaded nanoparticles specifically targets and kills B-lymphoma and neuroblastoma cells. In a subcutaneous mouse xenograft model of neuroblastoma, treatment with the same biosilica causes tumour growth regression. These findings suggested that genetically modified biosilica frustules could be employed as adaptable 'backpacks' for delivering poorly water-soluble anticancer medicines to tumour locations (Delalat et al. 2015).

Because of their longer drug release profiles and great efficacy in delivering hydrophobic medicines, research on porous silica-based particles has verified their applicability for drug-delivery applications.

1. The utilisation of nanoporous silica materials for drug delivery is a cornerstone of the rapidly growing field of nanomedicine.
2. Oxidised porous silicon and mesoporous silica have been the most extensively studied silica materials for drug delivery.
3. Both have thermal stability, a large surface area, configurable pore size, great biocompatibility, chemical inertness and biodegradability (at least in the case of porous silicon).
4. One significant disadvantage of using these materials is that their synthesis requires toxic chemicals (namely, silanes and hydrofluoric acid) and is both expensive and time-consuming.

The goal of this research was to provide a general approach for attaching antibodies and hydrophobic medicinal molecules to diatom biosilica without using

covalent cross-linking or chemical solvents. This method's strategy entails (a) genetic engineering of antibody-binding protein domains into diatom biosilica and (b) the insertion of medicinal molecules into silica-binding carriers (Delalat et al. 2015).

To achieve (a), the currently developed method known as live diatom silica immobilisation (LiDSI) (Poulsen et al. 2007; Sheppard et al. 2012) is used to incorporate GB1, an immunoglobulin G (IgG)-binding domain of protein G19, into the biosilica of the diatom *T. pseudonana* in vivo and investigate IgG antibody attachment to the genetically engineered biosilica.

To achieve (b), hydrophobic drug molecules are encapsulated in cationic micelles and liposomes (Tanaka et al. 2010; Blanco et al. 2013) then their biosilica-binding characteristics are investigated, and the drug molecules are released. Because loading the diatom frustules with a hydrophobic chemical from an organic solvent would denature the antibody, this two-step technique is critical. Once the biosilica has adhered to tumour cells, drug-loaded nanoscale vehicles can be deployed (Delalat et al. 2015).

11.6 Conclusion and Future Perspectives

Brown algae have been broadly investigated for giving inexhaustible and profoundly esteemed items for more than a century, and the brown algal polysaccharides have an extraordinary potential for pharmaceutical applications. Brown algae as biosensors are exceedingly delicate and reproducible. This strategy is more solid and regularly usable as compared to other explanatory methods. Diatom shells, in addition, contain unique 3D shapes and are used to make nanoparticles for medical and biomolecule delivery. Medicate stacking and discharge from DENPs appear to be improved by unique shape and functionalisation. Several studies have looked into modified DENPs for drug delivery (DOX, camptothecin, paclitaxel) in the treatment of colon and breast cancer, with promising results. Hereditarily adjusted biosensors are demonstrated to be more straightforward, dependable, quick and exact. Biosensors are successful but have a few impediments, since within the field condition, diverse variables create numerous impacts on their action. Encouragement and research work is required to make a viable biosensor.

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