1 Marine Biotechnology: A Frontier for the Discovery of Nutraceuticals, Energy, and Its Role in Meeting Twenty-First Century Food Demands

Imran Khan, Khodzori Fikri Akmal, Wei Sheng Chong, Balu Alagar Venmathi Maran, and Muhammad Dawood Shah

Abstract

One of the most underutilized biological resources in the world is the marine environment, which makes up nearly three-quarters of the Earth's surface. A variety of organisms with unique biological systems and features can be found in the marine environment. They have evolved special characteristics that allow them to survive in a variety of hostile environments. By applying a wide variety of screening tools, extracts and purified compounds of these organisms can be studied for food processing, biological activities, and bioenergy production. Biomolecules derived from marine organisms have a wide range of applications in the food industry, including colorants, preservatives, and flavor enhancers. Some of the most useful marine-derived food ingredients are pigments, polyunsaturated fatty acids, sterols, polysaccharides, proteins, and enzymes. Among the therapeutics, more than 60 % of the active pharmaceutical formulations come from natural products or their derivatives, which have been reported to possess biological activities (anticancer, anti-inflammatory, antioxidant, antimicrobial, etc.). Using marine resources to produce biodiesel is one of the hottest areas for renewable energy. International cooperation, novel biotechnological tools, mass production of marine organisms, integration of biotechnology with other sectors, etc., will be necessary to fully explore the potential of marine sources.

I. Khan
Department of Biotechnology, Abdul Wali Khan University Mardan, Khyber Pakhtunkhwa, Pakistan

K. F. Akmal · W. S. Chong · B. A. Venmathi Maran · M. D. Shah (✉)
Borneo Marine Research Institute, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
e-mail: dawoodshah@ums.edu.my

M. D. Shah et al. (eds.), *Marine Biotechnology: Applications in Food, Drugs and Energy*, https://doi.org/10.1007/978-981-99-0624-6_1

1.1 Introduction

Despite covering around three-quarters of the Earth's surface, the marine environment is one of the world's least utilized biological resources. The marine environment is home to a wide variety of organisms (Fig. 1.1), each with its own set of biological systems and characteristics. For example, marine algae, sponges, corals, fish, and microbes have evolved specific characteristics that allow them to flourish in a variety of hostile environments such as salinity, pressure, temperature, and darkness (Rasmussen and Morrissey 2007).

Marine organisms hold useful industrial products. About 230,000 species have been estimated to be dwelling in the marine environment. However, many species

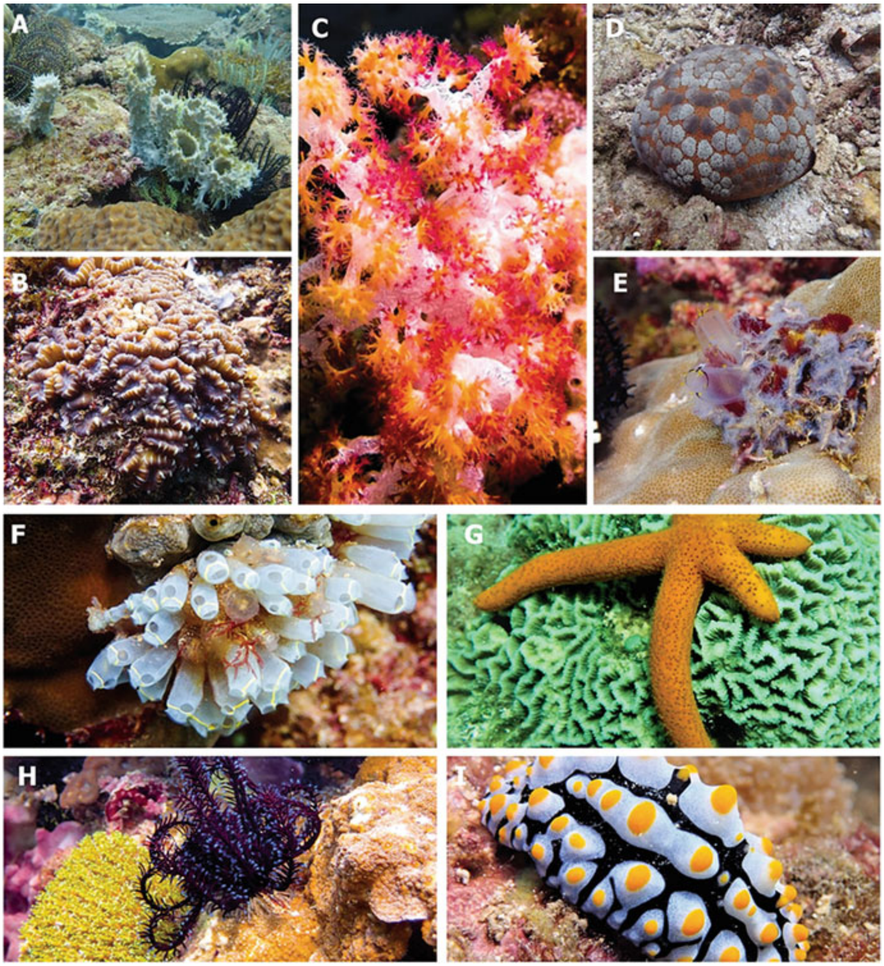

Fig. 1.1 Some of the marine invertebrates. (**a**) Sponge, (**b**) hard coral, (**c**) soft coral, (**d**) cushion star, (**e**) ascidian, (**f**) tunicate, (**g**) star fish, (**h**) feather star, (**i**) nudibranch

have yet to be discovered and characterized. Marine organisms produce a wide variety of metabolites (primary and secondary) which have remarkable biological applications. The integration of modern tools into marine research is unmasking the hidden potential and fast-tracking marine research for the discovery of novel products, characterization of marine resources, and exploitation of these resources for human welfare. According to the Dictionary of Marine Natural Products and MarinLit database (http://pubs.rsc.org/marinlit/), over 39,000 compounds have been identified so far in the marine environment, and approximately 38,700 articles have been published on marine products. According to the record of the PubMed database, there has been a consistent and steady increase in the research work carried out on marine products and marine biotechnology (Fig. 1.2).

To address the current and future challenges from the perspective of the marine environment, marine (blue) biotechnology has been developed to modernize the established tools and engineer new technologies for the efficient utilization of marine resources. Marine biotechnology thrives to discover, exploit, and utilize the potential of marine resources (including organisms and the environment) for the prosperity of humanity while maintaining the natural ecosystem of the marine environment. Not only for humanity's benefit, but marine technologies are also innovating new ways and harnessing modern technological tools for the welfare of marine life. From a wider perspective, marine biotechnology involves the use of marine organisms or their components to produce goods or services and exploit marine resources for ubiquitous applications in the fields of medicine (particularly drug discovery), cosmetics, environmental remediation, food, feed supply and processing, and energy production (Freitas et al. 2012; Baerga-Ortiz 2009; Tramper et al. 2003). Like other types of biotechnology, marine biotechnology also utilizes and innovates the tools of molecular and cellular biology, genetics, chemistry, OMICS, and bioinformatics. Advances in these fields have facilitated the application of marine biotechnology, in which marine organisms and their compounds are explored and useful components are identified, obtained, and characterized for use in a variety of fields such as food and feed, pharmaceutical, and biomedical industries (Rotter et al. 2021).

By the year 2025, it is predicted that the global market for marine biotechnology will reach $6.4 billion, covering a wide range of commercial objectives for the pharmaceutical, chemical, and biofuel industries (Hurst et al. 2016; Vierros et al. 2016). Another report has recently projected the marine biotechnology market value at $7.3 billion by 2026 (IndustryARC 2020). Due to the potential of blue growth, marine biotechnology is progressively making its way into economic-driven policies. Biotechnology holds the potential to play at the forefront and apply the capabilities of marine organisms in the economic, food, and therapeutic sectors. Marine organisms are a major source of a variety of molecules (of biomedical and industrial value) as they have evolved to dwell in the extreme conditions of chemistry, pressure, temperature, and darkness (Poli et al. 2010). One of the many ways to get exclusive benefits from these resources is through the "marine genetic resources" (MGRs) which offer genetic materials of potential value and economic benefits (United Nations 1992). We presume that strong cooperation between academics could enhance the utilization of marine resources in the form of detecting, isolating,

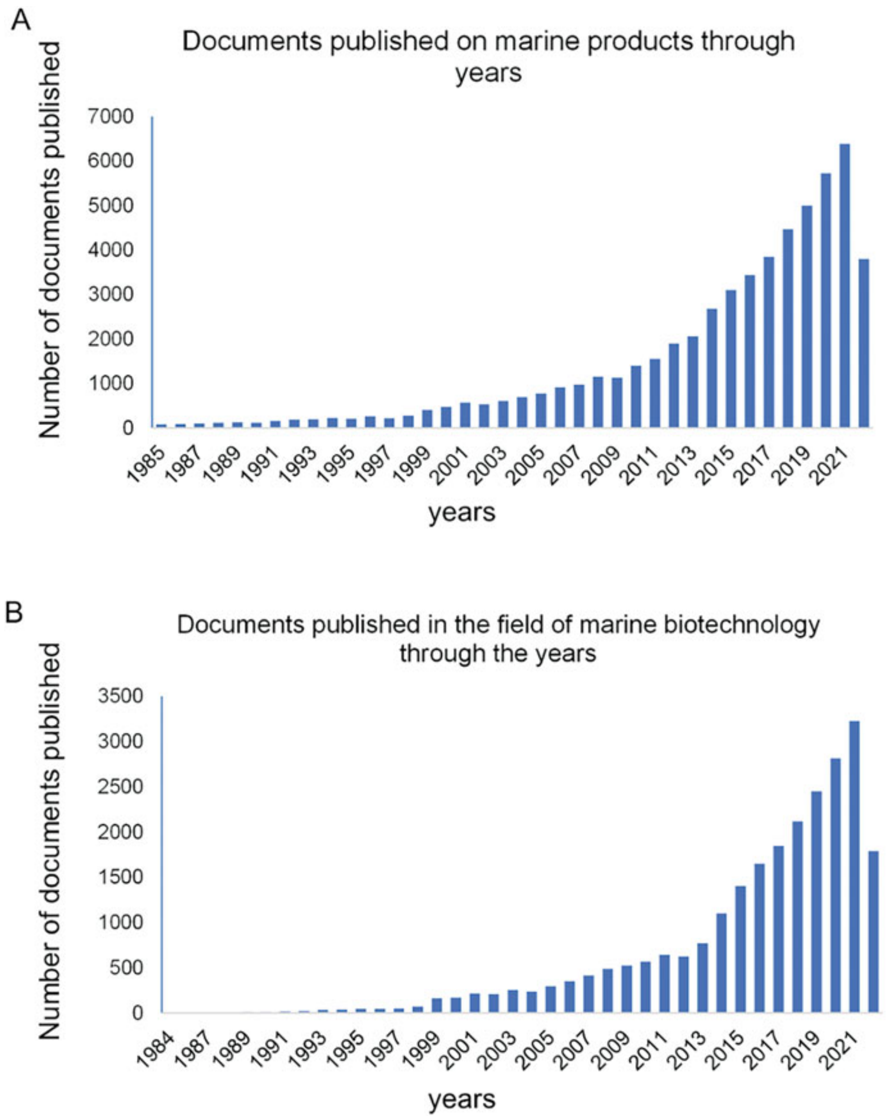

Fig. 1.2 Number of documents published on marine products (**a**) and marine biotechnology (**b**). The PubMed database was accessed for this information on the 15th of July 2022

and classifying marine organisms (such as bacteria, marine invertebrates, fungi, and microalgae) and characterizing them for bringing their products to industries.

By applying a wide variety of screening tools, extracts and purified compounds of these organisms can be studied for food processing, therapeutically, and industrially significant biological activities, including anticancer, anti-inflammatory, antiviral, antibacterial, and anticoagulant activities, as well as for ion channel/receptor

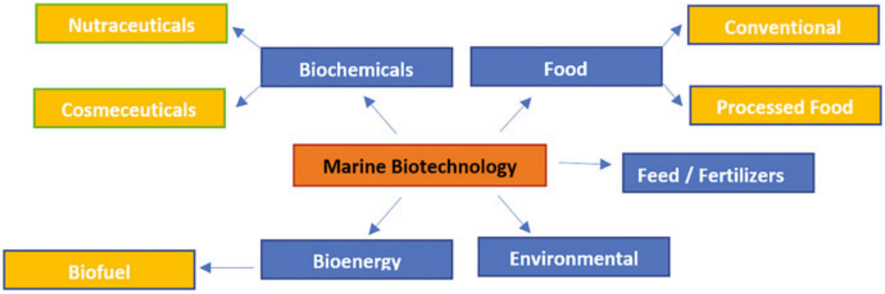

Fig. 1.3 Marine biotechnology's role in food, energy, and nutraceutical production

modulation and plant growth regulation (Shah et al. 2022; Kijjoa and Sawangwong 2004; Abdelnasser et al. 2017; Pech-Puch et al. 2020).

Marine biotechnology's important role in food, nutraceuticals, and energy production has been discussed below in Fig. 1.3.

1.2 Food

Biomolecules derived from marine organisms have a wide range of applications in the food industry, including food production at high temperatures and pressures, coloring agents, preservatives, and flavor enhancers. Some of the most useful marine-derived food ingredients include photosynthetic pigments, polyunsaturated fatty acids (PUFAs), sterols, polysaccharides, proteins, and enzymes (Rasmussen and Morrissey 2007).

Marine-based food ingredients obtained from marine algae (macroalgae and microalgae) (Figs. 1.4 and 1.5) are an important source of nutrients. Algae are inhibited all over the world, a rich source of bioactive compounds and nutritional compounds including calcium, sodium, magnesium, iodine, phosphorus, potassium, iron, and zinc (Ścieszka and Klewicka 2019). The usage of algae in the biotechnology industry has extensively grown since the chemical composition and bioactive substances identified in algae are suitable to be used in various fields, especially in the food industry. Polysaccharides originating from algae, such as algins, carrageenans, and agar, are widely utilized in a range of foods for their capacity to form gels and function as thickeners and stabilizers (Rasmussen and Morrissey 2007). Algae have largely been used in meat and bakery products to improve their quality and safety. The presence of *Porphyra umbilicalis*, *Undaria pinnatifida*, *Enteromorpha*, and *Himanthalia elongata* algae altered the antioxidative capacity of meat and cereal-based products (Gupta and Abu-Ghannam 2011).

Macroalgae, according to their color are divided into three groups: brown algae from the family Phaeophyceae (which gets its brown or yellow-brown color from fucoxanthin), red algae from the family Rhodophyceae (which contains phycoerythrin and phycocyanin), and green algae from the family Chlorophyceae (dominating

Fig. 1.4 Macroalgae, (**a**) *Pyrodinium bahamense*, (**b**) *Akashiwo sanguinea*

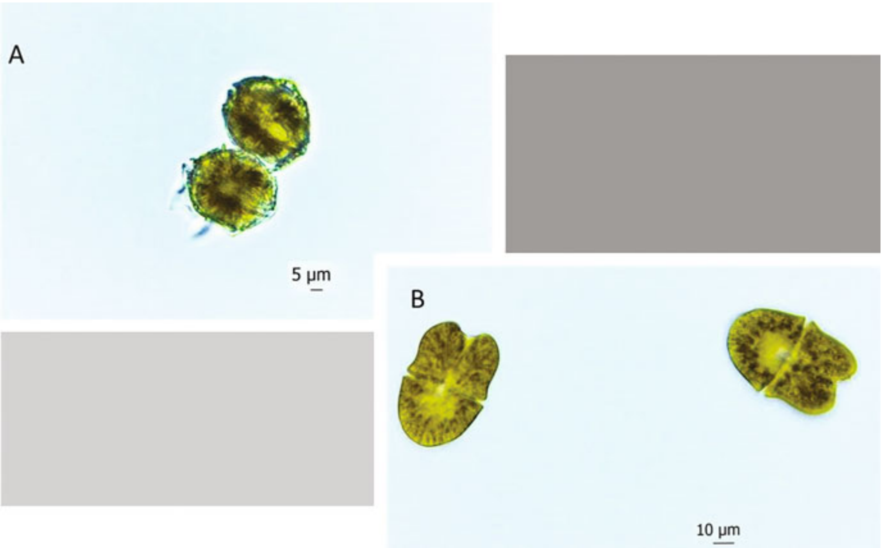

Fig. 1.5 Microalgae, (**a**) *Pyrodinium bahamense*, (**b**) *Akashiwo sanguinea*

chlorophyll a and chlorophyll b) (Shah et al. 2022; Domínguez 2013). Macroalgae are predominant producers in the sea and coastal areas. A major amount of their biomass is driven away to the deep sea and sediment (Ortega et al. 2019). Macroalgae is added to dairy products such as milk desserts, cheese, ice cream, yoghurt, cottage cheese, and processed cheese to improve their nutritional values. Brown algae, for example, *Laminaria*, is added to dairy products to make them iodine-rich. Green algae *Chlorella* and brown algae *Undaria pinnatifida* are added to

Fig. 1.6 Sea cucumber *Pearsonothuria graeffei*

increase the quality of the cheese during storage. Fermented foods with a high concentration of lactic acid bacteria incorporated with algae, which have biologically active metabolites of natural origin, improve product quality and develop a completely new category of fermented foods. For instance, calcium is trapped in casein in cheese, which prevents those without the necessary enzymes from absorbing calcium from those products. As a result, the inclusion of calcium-rich algae might boost the amount of the element in dairy products and aid in the treatment of hypocalcemia (Ścieszka and Klewicka 2019).

Microalgae can carry out photosynthesis and they are classified according to their cytological and morphological characteristics, pigments, type of reserve metabolites, and components of the cell wall. Marine diatoms are golden-brown due to xanthophyll pigments, and blue-green algae possess chlorophyll a, and blue phycocyanins (Domínguez 2013). Microalgae are fast-growing algae species that can double their biomass more than once in 24 h. It is estimated that the microalgae can yield 20 kg/m^2/year (Varshney et al. 2015). Microalgal biomass (defatted) holds application in the feed industry for carnivorous fish. It is reported that defatted *Nannochloropsis oceania* biomass could be used as a replacement for fishmeal as it has shown a positive impact on the growth, feed intake, and health of Atlantic salmon (Sørensen et al. 2017). Further, the addition of *Nannochloropsis* spp. biomass as a feed additive to the diet of Pacific white shrimp enhanced its resilience toward temperature change and improved its level of reactive oxygen species (Guimarães et al. 2021).

Sea cucumbers (Fig. 1.6) are marine invertebrates and are characterized by leathery skin, a soft body, and a single-branched gonad. So far, about 1716 species have been identified and classified. These organisms live in a hostile marine environment (Pangestuti and Arifin 2018). Sea cucumbers have been traditionally used

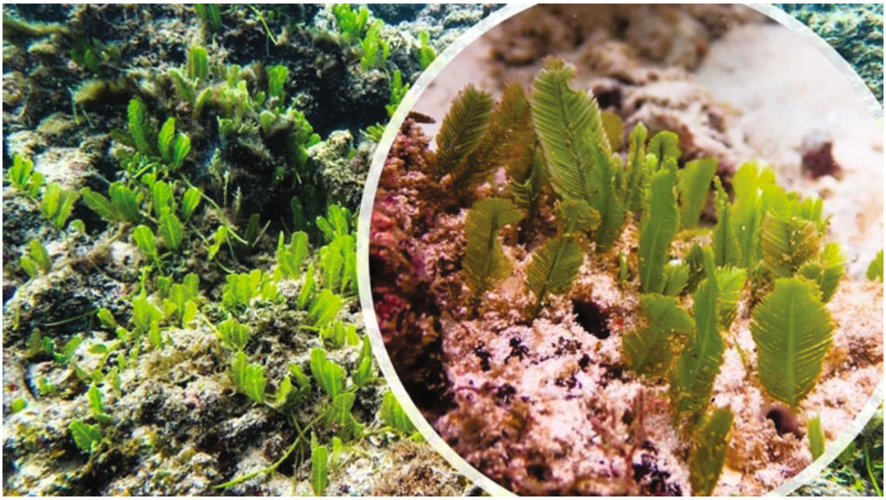

Fig. 1.7 Seagrass *Halophila ovalis*

as food and medicine in Asia. They could be used in soups, pickled food items, or stir-fried foods. In Indonesia, sea cucumbers are known as "teripang" or "trepang" and "beche-de-mer" in France. According to the Ming dynasty literature, sea cucumbers possessed similar therapeutic abilities as herbal ginseng and they are known as "haishen", which means "ocean ginseng" (Bahrami et al. 2014). Sea cucumbers are an ideal tonic food, as these organisms are rich in protein and interestingly, the lipid level is lower. They are collagen-rich and contain an elevated level of gelatin content (Pangestuti and Arifin 2018). *Holothuria poli* is a type of sea cucumber and is ubiquitous in the Mediterranean Sea, Canary Islands Sea, and the northern Red Sea. *Holothuria poli* has been extensively examined for the presence of secondary metabolites (Ismail et al. 2008). *Pearsonothuria graeffei* is another sea cucumber with a good source of triterpene glycosides, which can act as a functional food (Zhao et al. 2012).

Seagrasses are types of plants (also known as angiosperms) that live in marine environments and contribute to the sustainability of coastal ecosystems (Fig. 1.7) (Grignon-Dubois and Rezzonico 2013). In addition to being a source of animal feed, seagrasses have been utilized for centuries as food, medicine, and fertilizer. Seagrasses may be used as a functional food since it is an important source of protein, carbohydrate, lipids, fiber, phenol, flavonoids, and tannin. Seagrasses also contain essential elements (carbon, hydrogen, and nitrogen) as well as photosynthetic pigments (chlorophyll a, chlorophyll b, total chlorophyll, and carotenoid) (Rengasamy et al. 2013).

Fish is a vital source of protein and most people on earth still largely catch fish from the wild, with significant negative effects (Fig. 1.8). Aquaculture development is one of the most significant biotechnology applications in marine research. Producing fish species that have a faster growth rate, higher adaptability and

Fig. 1.8 Aquaculture facilities

survivability, and better fish yield has always been the major goal of the aquaculture sector (Uddin and Islam 2019).

The ocean's fisheries are becoming more stressed due to heavy expenditures on fishing fleets and technology as well as constantly rising yields. Numerous fishing areas are currently so overfished that their further viability is in jeopardy (Shakouri et al. 2010). Food security can be greatly aided by using biotechnology in sustainable aquaculture and fisheries. In this regard, fish that have been genetically modified (GM) have the potential to significantly boost fish farm yields, but they have also raised significant environmental concerns in the US and Europe over potential effects on wild species. To allay these worries and address public resistance to biotechnology, it is crucial to establish a solid, trustworthy, and widely recognized technique for calculating the potential for harm caused by GM fish escaping into the wild. To explore the impact of the transgenic itself on wild populations, a novel technique based on population genetics has just been devised; however, it has limitations (Muir 2004). Gene transfer technology was employed to promote fish growth. In China, a developed gene containing the promoter gene of antifreeze protein and salmon growth hormone cDNA was introduced into the red sea bream fish genome by the technique of electroporation and significant results were obtained in terms of cold tolerance and an increment in body weight (Zhang et al. 1998). In Malaysia, a new type of grouper known as the hybrid grouper (TGGG) has been produced by researchers by crossing sperm of *Epinephelus lanceolatus* with eggs of the *Epinephelus fuscoguttaus* grouper species (Fig. 1.9). *Epinephelus lanceolatus*, also known as Giant grouper, lives in marine, brackish, and reef-associated environments, whereas *E. fuscoguttaus*, also known as Tiger grouper, is an Indo-specific species that live primarily on coral reefs and lagoon pinnacles (Ching and Senoo 2008; Pears et al. 2006; Othman et al. 2015; Shapawi et al. 2019). Hybrid

Fig. 1.9 Hybrid grouper (*Epinephelus lanceolatus x Epinephelus fuscoguttaus*)

groupers reach maturity more quickly and consume feed more efficiently, implying a decrease in the cost of feed for commercial farming compared to nonhybrid parents. It can also survive a wide range of climatic conditions due to its genetic improvement (Ching and Senoo 2008; Shapawi et al. 2019).

1.3 Nutraceuticals

Many potently active compounds worthy of therapeutic use have been found via research into the pharmacological characteristics of marine natural materials. The marine environment is a remarkable source of bioactive natural products, many of which have chemical and structural characteristics that are not present in terrestrial natural products (Kong et al. 2010). Among the therapeutics, more than 60 % of active pharmaceutical formulations come from natural products or their derivatives (Cragg and Newman 2013). Secondary metabolites from marine resources have vast and profound applications in the pharmaceutical industry. These compounds have evolved from millions of years of natural selection. Due to the intrinsic abilities of marine natural products, these molecules can identify and attach to macromolecules, disturb their function, and affect their biological activities (Mayer et al. 2010).

The horizon of marine bioactive compound discovery has exponentially expanded. For instance, in the 1960s, researchers could access and study shallow-water subtidal creatures down to a depth of around 40 m. Whereas scientists have recently gained access to an array of undiscovered marine settings and habitats through the acquisition of advanced tools, such as manned submersibles and remotely operated vehicles, which are currently making it possible to visit depths of 5000 m and deeper (Miyake et al. 2011).

For functions like communication, reproduction, and defense against predation, competition, and infection, marine species have evolved biochemical and physiological systems that involve the creation of bioactive compounds. According to a comparison study by Kong et al. (2010), marine natural products have a higher level of chemical novelty than terrestrial natural products. Nearly every class of marine organisms shows a diversity of molecules with distinctive structural characteristics because of the physical and chemical circumstances in the marine environment. But in addition to its incredible chemical diversity, marine water also offers a remarkable variety of life. About 32 of the 34 basic phyla of life are found in marine waters, whereas 17 are found on land (with some overlap). The ocean is far more diversified from a basic point of view, making it the ideal area to start the development of a natural pharmacy (Kijjoa and Sawangwong 2004). Moreover, the utilization of modern computational tools could also help to find effective synergies of two or more compounds for enhanced therapeutic properties (Harakeh et al. 2015). In some cases, the immobilization of medicinal products (such as lactoperoxidase) into silver nanoparticles could enhance their medicinal efficacy (Sheikh et al. 2018).

Many marine-derived compounds are important to the nutraceutical industry. Nutraceuticals are bioactive chemicals having medical properties or additional health advantages, such as anticancer, anti-inflammatory, antioxidant, and antimicrobial activity, and many marine-based food components come under this category (Rasmussen and Morrissey 2007; Hamed et al. 2015; Kijjoa and Sawangwong 2004). Nutraceutical fortification of foods has become a popular means of offering nutritious food products to health-conscious customers. Consumer awareness of marine-based nutraceuticals has grown as a result of publications on their numerous health advantages, such as increased antioxidant activity and immunity (Ohr 2005). Currently marketed marine nutraceuticals include omega-3-rich fish and algal oils, chitin and chitosan, shark liver oil, marine enzymes and chondroitin from shark cartilage, sea cucumbers, and mussels (Rasmussen and Morrissey 2007). Chondroitin (a component of cartilage) has been shown to possess anti-inflammatory and anticancer properties, whereas omega-3 fatty acids are well-known for their wide range of health benefits, such as a reduced risk of cardiovascular disease and enhanced brain development in babies (Rasmussen and Morrissey 2007). Marine-based dietary components and nutraceuticals can be derived from a variety of sources, such as marine plants, microorganisms, and sponges, each of which has its own set of biomolecules that allow it to survive in its particular habitat (Rasmussen and Morrissey 2007) (Fig. 1.10).

As previously stated, several marine-derived compounds have been shown to have nutraceutical benefits. It is also commonly believed that marine resources provide the chance to uncover unique chemical diversity with exciting pharmacologically active molecules that could be utilized to treat bacterial, inflammation, cancer, parasitic infections, and several other ailments (Fajarningsih 2013).

Sponge extracts have bioactive compounds that are antiviral, anti-inflammatory, antibiotic, antifouling, antimalarial, anticancer, immunosuppressive or neurosuppressive (Sipkema et al. 2005). About 5000 therapeutically important compounds have been detected in sponges and about 15,000 or more marine organisms have been documented as possessing bioactive compounds (Sipkema et al. 2005). In addition to sponges, ascidians and gorgonian marine creatures have been also shown to exhibit antiviral and antiproliferative properties. In research, a

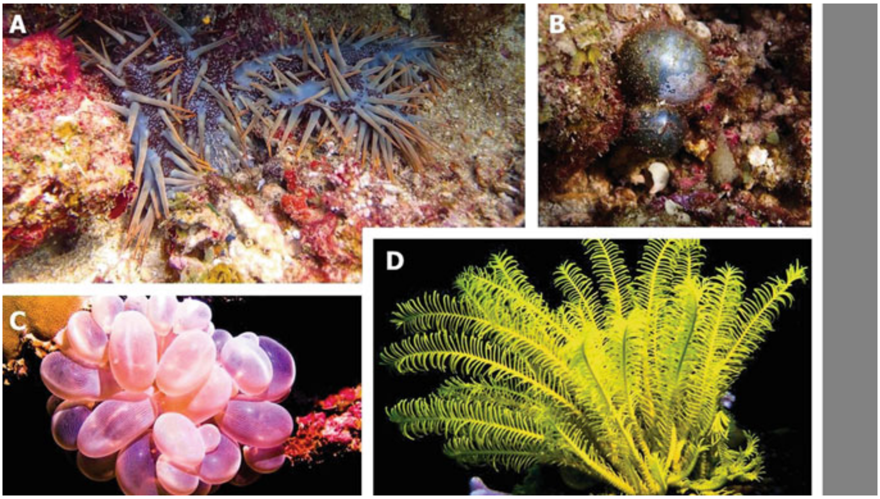

Fig. 1.10 Some marine invertebrates: (**a**) crown-of-thorns starfish, (**b**) bubble algae, (**c**) hard coral, (**d**) feather star

total of 65 marine species were collected off the coast of Mexico's Yucatan Peninsula, including 51 sponges from the phylum Porifera, 13 ascidians from the phylum Chordata, and one gorgonian from the phylum Cnidaria. They were chosen based on chemotaxonomical parameters. Each extract was tested in vitro for antiviral and antiproliferative activities against human adenovirus and five human tumor cell lines, including hepatocyte carcinoma, breast cancer adenocarcinoma, human lung carcinoma, pancreatic carcinoma, and human skin melanoma. In plaque tests, they were removed using organic solvents. Antiviral activity was found in 11 extracts from ten sponges, including *Ircinia felix*, *Ectyoplasia* sp., *Chondrilla* sp., *Myrmekioderma gyroderma*, *Agelas citrina*, *Monanchora arbuscula*, *Dysidea* sp., *Cinachyrella kuekenthali*, *Aaptos* sp., *and Spongia tubulifera*, *and Spongia tubulifera*, *Dysidea* sp., *Agelas citrina*, *Chondrilla* sp., and *Monanchora arbuscula* extracts demonstrated the strongest antiviral activity. The extract's IC_{50} values were lower than those reported for cidofovir (a drug used to treat human adenovirus infections) (Pech-Puch et al. 2020).

To date, antiproliferative activity has been demonstrated by four ascidians (*Trididemnum solidum*, *Polysyncraton* sp., *Clavelina* sp., and *Eudistoma amanitum*) and 21 sponges (*Tethya* sp., *Agelas citrina*, *Leucetta floridana*, *Forma hermatypica*, *Chondrilla caribensis*, *Dysidea* sp., *Myrmekioderma gyroderma*, *Clathria (Clathria) gomezae*, *Amphimedon compressa*, *Cinachyrella kuekenthali, Cliona varians*, *Monanchora arbuscula*, *Mycale laevis*, *Spongia tubulifera*, *Plakinastrella onkodes*, *Aaptos* sp., *Haliclona (Rhizoniera) curacaoensis*, *Aiolochroia crassa*, and *Scopalina ruetzleri*). The ascidian *Eudistoma amanitum* and the sponge *Haliclona (Rhizoniera) curacaoensis* had the most potent antiproliferative activity. In addition, greater than 50% of the extracts exhibited antiproliferative activity against the hepatocyte cancer cell line (Pech-Puch et al. 2020).

In addition to marine invertebrates and sponges, algae, sea cucumber, seagrasses, etc., also contribute as the source of drug production. Macroalgae including *Sargassum polycystum*, *Halymenia durvillaei*, *Caulerpa lentillifera*, *Caulerpa racemosa*, *Dictyota dichotoma*, *Kappaphycus alvarezii*, etc. have been shown to have anti-inflammatory, antioxidant, antibacterial, and anticancer properties. Several different nutraceutical compounds have been reported in these seaweeds. For instance, *S. polycystum* contains lutein, neophytadiene, and cis-vaccenic acid. *H. durvillaei* contains eucalyptol, oleic acid, and pentadecane. *C. lentillifera* contains canthaxanthin, oleic acid, and eicosane, *C. racemose* has monocaprin pseudoephedrine, and palmitic acid, *D. dichotoma* has squalene, saringosterol, and fucosterol, while *K. alvarezii* contains phthalic anhydride, 2-pentylthiophene, and furoic acid (Shah et al. 2022). The marine dinoflagellate *Gambierdiscus toxicus* has produced a series of new polyether antibiotics, gambieric acids, which are the most effective antifungal drugs yet to be discovered. For example, Gambieric acid A is 2000 times more active than amphotericin B, a therapeutically relevant antifungal drug with very mild toxicity in mice and cultured human cells (Nagai et al. 1992).

The sea cucumber is an abundant source of compounds with therapeutic properties, including amino acids, minerals, carotenoids, triterpene glycosides, chondroitin sulfates, bioactive peptides, vitamins, collagen, fatty acids, and gelatin. These compounds have exhibited therapeutic activities such as anticancer, antimicrobial, wound healing, anticoagulant, neuroprotective, and antioxidant. The most commonly known and used sea cucumber species include *Holothuria fuccogilva*, *Stichopus hermanni*, *Actinopyga mauritiana*, *Thelenota ananas*, and *Thelenota anax* (Pangestuti and Arifin 2018).

Seagrasses may contain bioactive compounds with industrial applications (Grignon-Dubois and Rezzonico 2013). Seagrasses, for example, have a high concentration of secondary metabolites (flavonoids, polyphenols, and fatty acids) that act as a defense mechanism against abiotic stresses (Custódio et al. 2016). Benito-González et al. (2019) report that *Halodule unnerves* and *Posidonia oceanica* extracts exhibit antifungal, antioxidant, and antiviral properties. In seagrass tissues, agents such as luteolin, chrysoeriol, and diosmetin are frequently found (Guan et al. 2017). Zosteric acid, which is found in the genus *Zostera* and has antifouling properties, is another agent (Vilas-Boas et al. 2017). However, a comprehensive evaluation of the biological roles of these metabolites is required due to the presence of hazardous chemicals. For instance, pyrrolizidine alkaloids are present in the grass subfamily *Pooideae (Poaceae)*, which has been used for a variety of biological purposes; nevertheless, it was recently discovered that this substance might cause hepatotoxicity in rats (Li et al. 2018).

Several aquatic vertebrates are also employed as model species in biomedical research. One such example is Zebrafish, which have been employed in more than 40,000 biomedical research investigations. Genetics, toxicology, drug development, pathobiology of human diseases, and cellular and developmental biology have all been transformed using transgenic fluorescent zebrafish lines. Due to the synthesis of fluorescent proteins in intracellular organelles, cells, and molecules of interest, these structures can be viewed and monitored instantaneously and in vivo. (Choe et al. 2021).

Despite the abundance of great biological activity and high potential of marine natural products, their advancement as medicinal agents has been slowed down as a result of several circumstances, such as the availability of low active molecules, a high level of chemical complexity and in certain situations, their high toxicity at therapeutic doses. To overcome some of the aforementioned challenges and advance some of the more promising compounds closer to the clinic and the market, many commercial companies have been established specifically to apply the ethos of biotechnology to the production of marine drugs. (Baerga-Ortiz 2009). Many potent new compounds derived from marine natural products are candidates for clinical trials. For example, aplidine is a cyclic depsipeptide which is isolated from the marine tunicate *Aplidium albicans*. The bioactive compound is in the trial against a patient with a solid tumor (Maroun et al. 2006). Bryostatins are produced by the marine invertebrate *Bugula neritina*, with several types being isolated from various populations of the same species, over 13 structurally related compounds have been obtained. The tumor-promoting phorbol esters are negatively impacted by bryostatin-1, a protein kinase C (PKC) activator. Additionally, bryostatin-1 modulates the immune system, causes myeloid and lymphoid cell lines to differentiate, produces platelet aggregation, and encourages hematopoiesis. It has shown considerable anticancer action in preclinical models against a variety of cell types and has also been proven to increase the antitumor effects of different chemotherapeutic drugs, including, vincristine, cytosine arabinoside, paclitaxel, etc. (Amador et al. 2003). The Phase II study of Bryostatin 1 in combination with the chemotherapy medication Vincristine in select patients for aggressive non-Hodgkin's lymphoma has been effective (Barr et al. 2009). Kahalalide F, cyclic depsipeptides, is isolated from a sacoglossan mollusc, *Elysia rufescens*. It is also obtained from a green alga, *Bryopsis* sp. Indeed, *E. rufescens* consumes *Bryopsis* sp. which shows that Kahalalide F is a part of the green alga it was consuming. Clinical studies for the potent anticancer agent have progressed to phase II for a variety of cancer types. The bioactive compound modifies the lysosomal and mitochondrial membranes and causes oncosis, which results in cell death (Piel 2010).

Additionally, several pharmaceutical firms, including Nereus Pharmaceuticals (San Diego, USA) and PharmaMar (Madrid, Spain) have developed strategies to locate cultivable marine microbes to maximize their growth, boost the production of bioactive compounds, and enhance chemical diversity through synthetic modification to produce marine drugs, Currently, Nereus Pharmaceuticals, a biotech firm focused on the development of marine drugs, is presently undertaking Phase I clinical studies for the proteasome inhibitor salinosporamide A (isolated directly from the fermentation of the marine actinomycete *Salinispora tropica*) for the treatment of solid tumors, lymphomas, and multiple myeloma (Baerga-Ortiz 2009; Fenical et al. 2009). PharmaMar, another biotech firm, manufactures and markets trabectedin (Yondelis®), a natural anticancer agent, which is developed through a semi-synthetic process that involves chemically modifying a naturally occurring fermentation product from *Pseudomonas fluorescens* to create the finished product (Baerga-Ortiz 2009; Cuevas and Francesch 2009). These advancements proved the crucial role of marine biotechnology in the production of drugs.

1.4 Bioenergy

Since the dawn of human civilization, carbon-based fuel has been the main source of energy. Due to expanding commercial businesses and the global population, there is a rising need for energy, which is squeezing fossil fuel resources and also adversely affecting our environment and posing dangerous consequences in the form of rising sea levels, harmful gases, rising temperatures, and declining biodiversity. Searching for and developing alternative energy sources that are also environmentally friendly is required to meet increasing energy demands.

One of the hot sectors for renewable energy is the manufacturing of biofuel from renewable biomass sources as a substitute strategy. Compared to fossil fuels, biofuel is affordable, environmentally beneficial, and holds the potential to substitute fossil fuels (Hossain and Jahan 2021). The development of cutting-edge technologies is expected to provide human civilization with renewable energy, particularly biofuels, on an affordable and sustainable scale (Hossain and Jahan 2021). Biofuels like biodiesel, bioalcohol, bio-oil, biogas, and syngas are produced from the biomass of living or dead organisms. Biomass contains carbon, which is used for biofuel production. Microalgae and macroalgae are marine resources that are used for biofuel production. Marine biomaterials are considered a good source of energy production. Marine biomaterials that are used for fuel production should be composed of a high level of lipids (ranging from simple polymers to complex polysaccharides) (Ali et al. 2020).

Fortunately, macro and microalgae have high lipid levels, which can produce a high amount of energy, and they have a fast growth rate that makes them suitable for biofuel production (Gosch et al. 2012; Ali et al. 2020). For example, water hyacinth can accumulate great biomass in a short time due to its fast growth rate, which makes it a potential renewable energy source that may substitute conventional fossil fuels. Besides, the research found that dried water hyacinth biomass can be manufactured into briquettes that can replace coal as the co-firing agent in power plants (Rezania et al. 2015). Marine resources, particularly algae, can be a potential and stable biomass source because the ocean contains a massive untapped algal resource that could reduce land costs and efficiently synthesize organic carbon through photosynthesis (Pogson et al. 2013; Hossain and Jahan 2021).

As well as being an energy source, algae can also contribute to the fixation of greenhouse gases (CO_2) by consuming them during the process of photosynthesis (Chen et al. 2015). The typical photosynthetic efficiency for algae is 6–8% which is significantly higher than the 1.8–2.2% of terrestrial plants (Chen et al. 2015; Aresta et al. 2005). Algal biomass can be converted into biofuels such as biogas, bioethanol, biodiesel, and bio-oils through anaerobic digestion, fermentation, transesterification, liquefaction, and pyrolysis (Chen et al. 2015). Microalgae appear to be the only biodiesel source with the ability to replace fossil fuels. Microalgae, unlike other oil crops, develop extraordinarily quickly and constitute rich oil content. Within 24 h, microalgae often quadruple their biomass. During exponential growth, biomass doubling durations can be as quick as 3.5 h. Microalgae can have an oil concentration of up to 80% by weight of dry biomass (Chisti 2007). In this context, marine algae might be a feasible and dependable source of biomass, as the ocean holds an untapped enormous algal resource that could reduce land expenses while simultaneously successfully synthesizing organic carbon via photosynthesis. (Chen et al. 2015). Biofuels from marine resources are cost-effective and reduce greenhouse gases, sulfur oxide, and hazardous matter emissions from the shipping industry (Tan et al. 2021).

1.5 Cultivation and Sustainable Collection Methods

The increasing number of species being introduced into in-vitro culture are directly related to the productive exploration of bioactive marine compounds. A well-regulated and controlled maintenance system for marine organisms is in high demand to ensure sustainable exploitation for industrial applications. Several photosynthetic marine organisms are heterotrophic. The bioactive compounds produced by marine organisms are markedly influenced by the type of growth nutrients and abundance of the organisms in the culture. Therefore, a sophisticated system is required to ensure the production of desired bioactive compounds in a cost-effective manner (Eriksen 2008).

To understand and harness the potential of marine organisms, it is crucial to develop and maintain pure cultures using preservation methods for biotechnological applications. To do so, it is vital to comprehend and replicate the naturally occurring environmental conditions for a particular organism (Joint et al. 2010; Khan et al. 2019; Ullah et al. 2017). After obtaining a pure culture, genetic screening and contaminant elimination are important to avoid biases in the result and the growth of a competitor organism in the same culture. For instance, the algal samples obtained from nature are often accompanied by zooplankton that could feed and eventually kill algae. One more thing that needs to be taken into consideration is timing. Some species die quickly and therefore, an adequate medium should be supplied so that the organism can multiply and lead to a sustainable pure culture.

One of the revolutionary techniques that have been recently developed is the Laser-Induced Forward Transfer Technique (LIFT). This system has allowed researchers to isolate single cells from a complex system, such as the ocean, to study the biodiversity of the environment and evaluate the physiology, genome, gene expression, and functions of an organism (Fig. 1.11). Interestingly, the system can be coupled with other microscopic approaches (e.g., fluorescent and Raman microscopy) to examine single microorganisms with particular functions, unmasking their activities in the natural reservoir. More details about the system have been explained elsewhere (Peng et al. 2022).

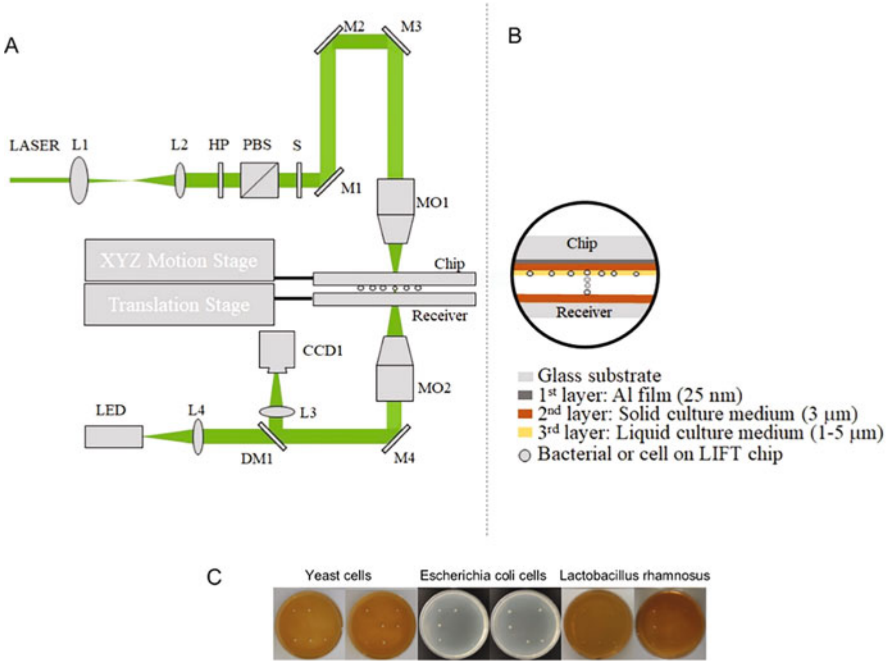

Fig. 1.11 Graphical illustration of the laser-induced forward transfer (LIFT) system. (**a**) This plot shows the mechanistic inner side of the system for sorting single cells out of the complex samples. (**b**) A three-layer structure is used for the isolation of a cell. (**c**) An example of the cells sorted and isolated by the LIFT system to the growth media

1.6 Recommendations

1. International partners are needed for joint expeditions to explore marine resources.
2. Novel culturing tools should be designed to bring uncultivable marine organisms into lab conditions.
3. Marine organisms' in-vitro cultivation for the mass production of industrially important products.
4. Since intraspecific changes cause variation in compounds and their concentrations in different marine environments, we recommended a wider exploration of marine organisms in different geological sites. This will help in cataloging the marine organisms at various sites and will help with their future characterization.
5. More investment and education should be brought to marine potential to promote and harvest the potential of marine biotechnology, which is a better tool for the holistic management of complex marine social-ecological systems.

6. Marine biotechnology should be integrated with other disciplines for a better understanding of the ocean system complexity, generate enough data for comprehension of the ocean capacity, and design pragmatic approaches that are solution-oriented, realistic, and practical.
7. Efficient biotechnological tools are required for bioactive compound identification, characterization, and isolation. Maintainable cultivation is required to bring promising organisms into the lab and manipulate their potential for selected compounds. In addition, sensitive biosensors are demanded to monitor the production of target compounds in the culture.

1.7 Conclusion

The marine environment is home to marine organisms that can be harvested and used in the medicinal, nutraceutical, and cosmeceutical industries due to their variety of primary and secondary metabolites due to their adaptability in harsh marine conditions. Current and future concerns, such as the exploitation of marine resources, climate change, and IUU fishing, among others, can be addressed while simultaneously improving humanity's quality of life by applying marine biotechnology to advance the discovery and characterization of novel marine pharmaceuticals. Doing so may reduce the pressure on the exploitation of marine resources while at the same time offering economic opportunities within the industries.

Funding This research work has been funded by the Skim Penyelidikan Lantikan Baharu (SLB2232) from the Universiti Malaysia Sabah to MDS.

References

Abdelnasser SM, Yahya SMM, Mohamed WF, Asker MMS, Abu Shady HM, Mahmoud MG, Gadallah MA (2017) Antitumor exopolysaccharides derived from novel marine *Bacillus*: isolation, characterization aspect and biological activity. Asian Pac J Cancer Prev 18(7): 1847–1854. https://doi.org/10.22034/APJCP.2017.18.7.1847

Ali MK, Mir SH, Hyder MKMZ, Yang W (2020) Harvesting of bioenergy and biomaterials from marine resources. In: Encyclopedia of marine biotechnology. Wiley, Hoboken, NJ, pp 711–736. https://doi.org/10.1002/9781119143802.ch27

Amador ML, Jimeno J, Paz-Ares L, Cortes-Funes H, Hidalgo M (2003) Progress in the development and acquisition of anticancer agents from marine sources. Ann Oncol 14(11):1607–1615. https://doi.org/10.1093/annonc/mdg443

Aresta M, Dibenedetto A, Barberio G (2005) Utilization of macro-algae for enhanced CO2 fixation and biofuels production: development of a computing software for an LCA study. Fuel Process Technol 86(14–15):1679–1693. https://doi.org/10.1016/j.fuproc.2005.01.016

Baerga-Ortiz A (2009) Biotechnology and biochemistry of marine natural products. P R Health Sci J 28(3):251–257

Bahrami Y, Zhang W, Franco C (2014) Discovery of novel saponins from the viscera of the sea cucumber *Holothuria lessoni*. Mar Drugs 12(5):2633–2667. https://doi.org/10.3390/md12052633

Barr PM, Lazarus HM, Cooper BW, Schluchter MD, Panneerselvam A, Jacobberger JW, Hsu JW, Janakiraman N, Simic A, Dowlati A, Remick SC (2009) Phase II study of bryostatin 1 and vincristine for aggressive non-Hodgkin lymphoma relapsing after an autologous stem cell transplant. Am J Hematol 84(8):484–487. https://doi.org/10.1002/ajh.21449
Benito-González I, López-Rubio A, Martínez-Abad A, Ballester A-R, Falcó I, González-Candelas L, Sánchez G, Lozano-Sánchez J, Borrás-Linares I, Segura-Carretero A (2019) In-depth characterization of bioactive extracts from *Posidonia oceanica* waste biomass. Mar Drugs 17(7):409
Chen H, Zhou D, Luo G, Zhang S, Chen J (2015) Macroalgae for biofuels production: progress and perspectives. Renew Sust Energ Rev 47:427–437. https://doi.org/10.1016/j.rser.2015.03.086
Ching CL, Senoo S (2008) Egg and larval development of a new hybrid grouper, tiger grouper *Epinephelus fuscoguttatus* giant grouper *E. lanceolatus*. Aquac Sci 56(4):505–512
Chisti Y (2007) Biodiesel from microalgae. Biotechnol Adv 25(3):294–306. https://doi.org/10.1016/j.biotechadv.2007.02.001
Choe CP, Choi S-Y, Kee Y, Kim MJ, Kim S-H, Lee Y, Park H-C, Ro H (2021) Transgenic fluorescent zebrafish lines that have revolutionized biomedical research. Lab Anim Res 37(1): 26. https://doi.org/10.1186/s42826-021-00103-2
Cragg GM, Newman DJ (2013) Natural products: a continuing source of novel drug leads. Biochim Biophys Acta 1830(6):3670–3695. https://doi.org/10.1016/j.bbagen.2013.02.008
Cuevas C, Francesch A (2009) Development of Yondelis® (trabectedin, ET-743). A semisynthetic process solves the supply problem. Nat Prod Rep 26(3):322. https://doi.org/10.1039/b808331m
Custódio L, Laukaityte S, Engelen AH, Rodrigues MJ, Pereira H, Vizetto-Duarte C, Barreira L, Rodríguez H, Alberício F, Varela J (2016) A comparative evaluation of biological activities and bioactive compounds of the seagrasses *Zostera marina* and *Zostera noltei* from southern Portugal. Nat Prod Res 30(6):724–728
Domínguez H (2013) Algae as a source of biologically active ingredients for the formulation of functional foods and nutraceuticals. In: Functional ingredients from algae for foods and nutraceuticals. Elsevier, Burlington, pp 1–19. https://doi.org/10.1533/9780857098689.1
Eriksen NT (2008) The technology of microalgal culturing. Biotechnol Lett 30(9):1525–1536. https://doi.org/10.1007/s10529-008-9740-3
Fajarningsih ND (2013) An emerging marine biotechnology: marine drug discovery. Squalen Bull Mar Fish Postharvest Biotechnol 7(2):89. https://doi.org/10.15578/squalen.v7i2.19
Fenical W, Jensen PR, Palladino MA, Lam KS, Lloyd GK, Potts BC (2009) Discovery and development of the anticancer agent salinosporamide A (NPI-0052). Bioorg Med Chem 17(6):2175–2180. https://doi.org/10.1016/j.bmc.2008.10.075
Freitas AC, Rodrigues D, Rocha-Santos TAP, Gomes AMP, Duarte AC (2012) Marine biotechnology advances towards applications in new functional foods. Biotechnol Adv 30(6):1506–1515. https://doi.org/10.1016/j.biotechadv.2012.03.006
Gosch BJ, Magnusson M, Paul NA, de Nys R (2012) Total lipid and fatty acid composition of seaweeds for the selection of species for oil-based biofuel and bioproducts. GCB Bioenergy 4(6):919–930. https://doi.org/10.1111/j.1757-1707.2012.01175.x
Grignon-Dubois M, Rezzonico B (2013) The economic potential of beach-cast seagrass–*Cymodocea nodosa*: a promising renewable source of chicoric acid. Bot Mar 56(4):303–311
Guan C, Parrot D, Wiese J, Sönnichsen FD, Saha M, Tasdemir D, Weinberger F (2017) Identification of rosmarinic acid and sulfated flavonoids as inhibitors of microfouling on the surface of eelgrass *Zostera marina*. Biofouling 33(10):867–880
Guimarães AM, Guertler C, do Vale Pereira G, da Rosa Coelho J, Costa Rezende P, Nóbrega RO, do Nascimento Vieira F (2021) *Nannochloropsis* spp. as feed additive for the pacific white shrimp: effect on midgut microbiology, thermal shock resistance and immunology. Animals 11(1):150. https://doi.org/10.3390/ani11010150
Gupta S, Abu-Ghannam N (2011) Recent developments in the application of seaweeds or seaweed extracts as a means for enhancing the safety and quality attributes of foods. Innovative Food Sci Emerg Technol 12(4):600–609

Hamed I, Özogul F, Özogul Y, Regenstein JM (2015) Marine bioactive compounds and their health benefits: a review. Compr Rev Food Sci Food Saf 14(4):446–465. https://doi.org/10.1111/1541-4337.12136

Harakeh SM, Khan I, Kumosani T, Barbour E, Almasaudi SB, Azhar EI, Rath M, Niedzweicki A (2015) The role of nutrients and phyto-compounds in the modulation of antimicrobial resistance. Front Cell Infect Microbiol 5(Jun). https://doi.org/10.3389/fcimb.2015.00053

Hossain J, Jahan R (2021) Biofuel: marine biotechnology securing alternative sources of renewable energy. Springer, Singapore, pp 161–194. https://doi.org/10.1007/978-981-15-8999-7_7

Hurst D, Børresen T, Almesjö L, De Raedemaecker F, Bergseth S (2016) Marine biotechnology strategic research and innovation roadmap: insights to the future direction of European marine biotechnology. Marine Biotechnology ERA-NET

IndustryARC (2020) Marine biotechnology market—forecast (2023–2028). Accessed on October 2022. https://www.industryarc.com/Report/16110/marine-biotechnology-market.html

Ismail H, Lemriss S, Ben Aoun Z, Mhadhebi L, Dellai A, Kacem Y, Boiron P, Bouraoui A (2008) Antifungal activity of aqueous and methanolic extracts from the Mediterranean sea cucumber, *Holothuria polii*. J Mycol Méd 18(1):23–26. https://doi.org/10.1016/j.mycmed.2008.01.002

Joint I, Mühling M, Querellou J (2010) Culturing marine bacteria—an essential prerequisite for biodiscovery. Microb Biotechnol 3(5):564–575. https://doi.org/10.1111/j.1751-7915.2010.00188.x

Khan I, Yasir M, Farman M, Kumosani T, Albasri SF, Bajouh OS, Azhar EI (2019) Evaluation of gut bacterial community composition and antimicrobial resistome in pregnant and non-pregnant women from Saudi population. Infect Drug Resist 12:1749–1761. https://doi.org/10.2147/IDR.S200213

Kijjoa A, Sawangwong P (2004) Drugs and cosmetics from the sea. Mar Drugs 2(2):73–82. https://doi.org/10.3390/md202073

Kong D-X, Jiang Y-Y, Zhang H-Y (2010) Marine natural products as sources of novel scaffolds: achievement and concern. Drug Discov Today 15(21–22):884–886. https://doi.org/10.1016/j.drudis.2010.09.002

Li YH, Tai WCS, Khan I, Lu C, Lu Y, Wong WY, Chan WY, Wendy Hsiao WL, Lin G (2018) Toxicoproteomic assessment of liver responses to acute pyrrolizidine alkaloid intoxication in rats. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev 36(2):65–83. https://doi.org/10.1080/10590501.2018.1450186

Maroun JA, Belanger K, Seymour L, Matthews S, Roach J, Dionne J, Soulieres D, Stewart D, Goel R, Charpentier D, Goss G, Tomiak E, Yau J, Jimeno J, Chiritescu G (2006) Phase I study of Aplidine in a daily × 5 one-hour infusion every 3 weeks in patients with solid tumors refractory to standard therapy. A National Cancer Institute of Canada Clinical Trials Group study: NCIC CTG IND 115. Ann Oncol 17(9):1371–1378. https://doi.org/10.1093/annonc/mdl165

Mayer AMS, Glaser KB, Cuevas C, Jacobs RS, Kem W, Little RD, McIntosh JM, Newman DJ, Potts BC, Shuster DE (2010) The odyssey of marine pharmaceuticals: a current pipeline perspective. Trends Pharmacol Sci 31(6):255–265. https://doi.org/10.1016/j.tips.2010.02.005

Miyake H, Shibata H, Furushima Y (2011) Deep-sea litter study using deep-sea observation tools. In: Interdisciplinary studies on environmental chemistry, pp 261–269. Retrieved from https://www.researchgate.net/publication/266245893

Muir WM (2004) The threats and benefits of GM fish. EMBO Rep 5(7):654–659. https://doi.org/10.1038/sj.embor.7400197

Nagai H, Murata M, Torigoe K, Satake M, Yasumoto T (1992) Gambieric acids, new potent antifungal substances with unprecedented polyether structures from a marine dinoflagellate *Gambierdiscus toxicus*. J Org Chem 57(20):5448–5453. https://doi.org/10.1021/jo00046a029

Ohr LM (2005) Riding the nutraceuticals wave. Food Technol 59(8):95–96. Retrieved from https://agris.fao.org/agris-search/search.do?recordID=US201301029582

Ortega A, Geraldi NR, Alam I, Kamau AA, Acinas SG, Logares R, Gasol JM, Massana R, Krause-Jensen D, Duarte CM (2019) Important contribution of macroalgae to oceanic carbon sequestration. Nat Geosci 12(9):748–754

Othman AR, Kawamura G, Senoo S, Fui CF (2015) Effects of different salinities on growth, feeding performance and plasma cortisol level in hybrid TGGG (Tiger grouper, *Epinephelus fuscoguttatus* x giant grouper, *Epinephelus lanceolatus*) juveniles. Int Res J Biol Sci 4(3):15–20

Pangestuti R, Arifin Z (2018) Medicinal and health benefit effects of functional sea cucumbers. J Tradit Complement Med 8(3):341–351. https://doi.org/10.1016/j.jtcme.2017.06.007

Pears RJ, Choat JH, Mapstone BD, Begg GA (2006) Demography of a large grouper, *Epinephelus fuscoguttatus*, from Australia's Great Barrier Reef: implications for fishery management. Mar Ecol Prog Ser 307:259–272. https://doi.org/10.3354/meps307259

Pech-Puch D, Berastegui-Cabrera J, Pérez-Povedano M, Villegas-Hernández H, Guillén-Hernández S, Cautain B, Reyes F, Pachón J, Gómez P, Rodríguez J, Jiménez C, Sánchez-Céspedes J (2020) Antiviral and antiproliferative potential of marine organisms from the Yucatan Peninsula, Mexico. Front Mar Sci 7:607. https://doi.org/10.3389/fmars.2020.00607

Peng L, Bo L, Yun W, Kunxiang L, Yinping Z, Huang WE, Bei L, Haruyuki A (2022) Isolation and culture of single microbial cells by laser ejection sorting technology. Appl Environ Microbiol 88(3):e01165–e01121. https://doi.org/10.1128/aem.01165-21

Piel J (2010) The chemistry of symbiotic interactions. In: Comprehensive natural products II: chemistry and biology, vol 2. Elsevier, Oxford, pp 475–510. https://doi.org/10.1016/b978-008045382-8.00049-6

Pogson M, Hastings A, Smith P (2013) How does bioenergy compare with other land-based renewable energy sources globally? GCB Bioenergy 5(5):513–524. https://doi.org/10.1111/gcbb.12013

Poli A, Anzelmo G, Nicolaus B (2010) Bacterial exopolysaccharides from extreme marine habitats: production, characterization and biological activities. Mar Drugs 8(6):1779–1802. https://doi.org/10.3390/md8061779

Rasmussen RS, Morrissey MT (2007) Marine biotechnology for production of food ingredients. Adv Food Nutr Res 52:237–292. https://doi.org/10.1016/S1043-4526(06)52005-4

Rengasamy RRK, Radjassegarin A, Perumal A (2013) Seagrasses as potential source of medicinal food ingredients: Nutritional analysis and multivariate approach. Biomed Prev Nutr 3(4):375–380.

Rezania S, Ponraj M, Din MFM, Songip AR, Sairan FM, Chelliapan S (2015) The diverse applications of water hyacinth with main focus on sustainable energy and production for new era: an overview. Renew Sustain Energy Rev 41:943–954. https://doi.org/10.1016/j.rser.2014.09.006

Rotter A, Barbier M, Bertoni F, Bones AM, Cancela ML, Carlsson J, Carvalho MF, Cegłowska M, Chirivella-Martorell J, Conk Dalay M, Cueto M, Dailianis T, Deniz I, Díaz-Marrero AR, Drakulovic D, Dubnika A, Edwards C, Einarsson H, Erdoğan A et al (2021) The essentials of marine biotechnology. Front Mar Sci 8:158. https://doi.org/10.3389/fmars.2021.629629

Ścieszka S, Klewicka E (2019) Algae in food: a general review. Crit Rev Food Sci Nutr 59(21):3538–3547. https://doi.org/10.1080/10408398.2018.1496319

Shah MD, Venmathi Maran BA, Shaleh SRM, Zuldin WH, Gnanaraj C, Yong YS (2022) Therapeutic potential and nutraceutical profiling of North Bornean seaweeds: a review. Mar Drugs 20(2):101. https://doi.org/10.3390/md20020101

Shakouri B, Yazdi SK, Fashandi A (2010) Overfishing. In: 2010 2nd international conference on chemical, biological and environmental engineering, pp 229–234. https://doi.org/10.1109/ICBEE.2010.5649533

Shapawi R, Ching FF, Senoo S, Mustafa S (2019) Nutrition, growth and resilience of tiger grouper *(Epinephelus fuscoguttatus)* × giant grouper *(Epinephelus lanceolatus)* hybrid- a review. Rev Aquac 11(4):1285–1296

Sheikh IA, Yasir M, Khan I, Khan SB, Azum N, Jiffri EH, Kamal MA, Ashraf GM, Beg MA (2018) Lactoperoxidase immobilization on silver nanoparticles enhances its antimicrobial activity. J Dairy Res 85(4):460–464. https://doi.org/10.1017/S0022029918000730

Sipkema D, Franssen MCR, Osinga R, Tramper J, Wijffels RH (2005) Marine sponges as pharmacy. Mar Biotechnol (NY) 7(3):142–162. https://doi.org/10.1007/S10126-004-0405-5

Sørensen M, Gong Y, Bjarnason F, Vasanth GK, Dahle D, Huntley M, Kiron V (2017) Nannochloropsis oceania-derived defatted meal as an alternative to fishmeal in Atlantic salmon feeds. PLoS One 12(7):e0179907

Tan ECD, Hawkins TR, Lee U, Tao L, Meyer PA, Wang M, Thompson T (2021) Biofuel options for marine applications: technoeconomic and life-cycle analyses. Environ Sci Technol 55(11): 7561–7570. https://doi.org/10.1021/acs.est.0c06141

Tramper J, Battershill C, Brandenburg W, Burgess G, Hill R, Luiten E, Müller W, Osinga R, Rorrer G, Tredici M, Uriz M, Wright P, Wijffels R (2003) What to do in marine biotechnology? Biomol Eng 20(4–6):467–471. https://doi.org/10.1016/S1389-0344(03)00077-7

Uddin SA, Islam MM (2019) Blue biotechnology, renewable energy, unconventional resources and products as emerging frontiers at Sea. J Ocean Coast Econ 6(2):8. https://doi.org/10.15351/2373-8456.1100

Ullah R, Yasir M, Khan I, Bibi F, Sohrab SS, Al-Ansari A, Al-Abbasi F, Al-Sofyani AA, Daur I, Lee S-W, Azhar EI (2017) Comparative bacterial community analysis in relatively pristine and anthropogenically influenced mangrove ecosystems on the Red Sea. Can J Microbiol 63(8). https://doi.org/10.1139/cjm-2016-0587

United Nations (1992) Convention on biological diversity, concluded at Rio de Janeiro on 5 June 1992. In United Nations–Treaty Series No 30619

Varshney P, Mikulic P, Vonshak A, Beardall J, Wangikar PP (2015) Extremophilic micro-algae and their potential contribution in biotechnology. Bioresour Technol 184:363–372. https://doi.org/10.1016/j.biortech.2014.11.040

Vierros M, Suttle CA, Harden-Davies H, Burton G (2016) Who owns the ocean? Policy issues surrounding marine genetic resources. Limnol Oceanogr Bull 25(2):29–35

Vilas-Boas C, Sousa E, Pinto M, Correia-da-Silva M (2017) An antifouling model from the sea: a review of 25 years of zosteric acid studies. Biofouling 33(10):927–942

Zhang P, Xu Y, Liu Z, Xiang Y, Du S, Hew CL (1998) Gene transfer in red sea bream (*Pagrosomus Major*). In: New developments in marine biotechnology. Springer US, Boston, pp 15–18. https://doi.org/10.1007/978-1-4757-5983-9_4

Zhao Q, Xue Y, Wang JF, Li H, Long TT, Li Z, Wang YM, Dong P, Xue CH (2012) In vitro and in vivo anti-tumour activities of echinoside A and ds-echinoside A from *Pearsonothuria graeffei*. J Sci Food Agric 92(4):965–974. https://doi.org/10.1002/jsfa.4678