

# MARINE-DERIVED NATURAL PRODUCTS: A NOVEL SOURCE OF POTENTIAL ANTICANCER DRUGS IN THE OCEAN

## Abstract

Cancer continues to rank among the deadliest diseases in the world. Living organisms have been studied for potential cancer treatments due to the need for new drugs. By using molecular modelling and chemical synthesis, it has been discovered that the marine environment is a rich source of chemicals with unique chemical properties that can be applied to improve the specificity, effectiveness of cutting-edge medications. Many unique bioactive metabolites with various chemical structures have been found in marine populations. This overview includes information on marine plants, bacteria, algae, sponges, fungi, soft coral, and actinomycetes, with an emphasis on the last two. Studies on marine natural products' capacity to fight cancer as well as their effectiveness in suppressing tumors, compound-induced apoptosis, and cytotoxicity were initially studied in connection to in vitro and in vivo research. It is also covered how the biological effects are supported by molecular processes. In this book chapter, we highlighted the variety of marine species, as well as the inventiveness of chemical structures and chemical property space. The usage of components obtained from marine sources, treatment methods, and discussions of their potential future uses as anticancer drugs are also included.

**Keywords:** Anticancer drugs, marine-derived products, Microorganism, Antioxidants

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## I. INTRODUCTION

One of the worst diseases in the world is still cancer[1]. The planet's surface is covered by water on a 70%+ basis. The oceans are the most beautiful area on Earth, they are home to a wide diversity of marine and freshwater organisms, as well as more natural and biochemical mixing [1]. On the other hand, several FDA-approved medications have been obtained via terrestrial means. Nonetheless, increased marine sources have recently yielded a slew of complexes, anticancer drug candidates, and a slew of significant metabolites. There are about 30,000 natural resource blends of marine origin. Each year since 2008, more than 1,000 complexes have been erected. In addition, structural categorization breakthroughs, randomness, and diversity are frequently used to characterize these complexes [2]. Obtaining vital drugs to treat various cancers and diseases requires access to marine sources. Researchers scoured the seas and oceans for aquatic organisms that created mixes that may be used in clinical and therapeutic settings. Seaweeds, enormous mangroves, sponges, and microbes are among the aquatic life species that have joined them [3]. Anticancer drugs and natural substances derived from the sea have a variety of applications in the treatment of different malignancies as well as cancer itself. MNPs can be used to revive important pharmacological mediators, such as naturally occurring immune agents, chemically produced combinations, or chemical complexes [4]. Cancer death rates remain high despite a lack of focus on significant research initiatives, including fresh clinical ideas employing cutting-edge therapeutics[5]. The majority of anticancer pharmaceutical markets around the world rely on natural resource-derived components and metabolites generated by engineering processes, which include mixes derived from organisms living in the marine environment [6]. As a result of advances in biology and immunotherapy research, as well as significant advancements in current medication design and production, cancer cure research has become a viable goal. [7].

Lymphomas, testicular cancer, and juvenile lymphoblastic leukemia are only a few of the human cancers that have been cured or have had their survival durations prolonged [8–10]. Despite substantial breakthroughs in existing therapies [11,12], chemotherapy has been associated with several side effects [13], spurring a search for a more effective solution with fewer side effects [14]. Natural products have the potential to be exploited in the development of new drugs, drug candidates, and chemical entities [15,16]. Bioactive natural products are used in around 80% of licensed chemotherapeutic treatments [17], while bioactive natural products are used in more than half of all drugs [18]. Natural products are used to treat 87 percent of human ailments, including cancer. [19], which is widespread. Natural bioactive compounds that target cancer-causing macromolecules, such as those implicated in oncogenic signal transduction pathways, have been shown to induce cancer [20–22] In the late 1800s, the term "marine" first appeared. Biotechnology evolved after 1980 into a science that focused marine research on applications such as medical development[23]. This investigation is still being conducted, and cutting-edge technology is being used. [24]. There is growing interest in using the variety and complexity of marine natural product scaffolds, given their tremendous potential, to create intelligent medications. We discussed marine-derived compounds that may have anticancer properties.

## II. MARINE-DERIVED NATURAL PRODUCTS AND THEIR CLASSIFICATION

Up until 2008, marine invertebrates were the primary source of new compounds discovered in marine creatures; Marine invertebrates of the phylum Porifera (mostly sponges) and Coelenterate provided more than 75% of these chemicals (mostly coral). This percentage stayed the same between 1985 and 2008. [25]. As coral grows in the tropical ocean, which has the highest biodiversity, and sponges are found in the most diverse environments worldwide, the majority of new compounds have been found in coral and sponges. The world's oceans are vast, and marine creatures serve as the foundation for both a vast array of chemical component clusters and innovative anticancer medicines. The separation and blending of various chemical combinations of marine origin for cancer therapy is done utilizing developed techniques. [26]. Marine natural products can be divided into seven groups based on their chemical composition: Alkaloids, strigolactones, ethers (including ketals), phenols (including quinones), terpenoids, steroids (including steroidal saponins), and peptides [27]. In any case, marine sources for anticancer drugs remain underutilized. The most noteworthy MNPs include a variety of created classes of marine alkaloids, terpenes with a wide range of structural diversity, peptides from various marine creatures, polyketides with unique biological properties, and high molecular weight organic sugars (Table 1). All of these types of MNPs are essential in the development of anticancer drugs because of their strong natural defenses against potentially lethal infections. of MNPs are crucial in the creation of anticancer medicines [28,29].

## III. MECHANISMS FOR THE ANTICANCER ACTIVITY OF MARINE PLANTS

A global search for cutting-edge drugs that are deadly to cancer cells but innocuous to healthy cells has been prompted by the expansion of cancer registries. In addition to the tumor cells, the normal cells in the area of the body where the cancer had grown were also relatively dangerously affected by the anticancer treatments previously used. These days, the search for new anticancer drugs uses both terrestrial and marine habitats. [30]. DNA repair enzymes are able to undo the bulk of the harm. Age increases the risk of cancer and oxidative DNA damage [31].

**1. Antioxidants:** Marine creatures that are continually exposed to environmental stresses and changes need on antioxidant molecules to maintain cellular redox equilibrium and to survive. [32]. By oxidizing specific intracellular chemical moieties, antioxidants can lead to genetic changes and the activation of metabolic pathways that encourage proliferation and neoplastic transformation. [33]. As a result of their differing oxidant targets or cellular compartmentalization, several defenses work best together [34]. Under normal conditions, large levels of SOD prevent the formation of peroxy nitrite. Additionally, glutathione levels are decreased by the antioxidant (GSH). GSH is composed of amino acids containing sulfhydryl groups and is required for intermediate antioxidant metabolism [35]. The right kind of nourishment supports the body's built-in enzymatic defenses against free radicals. These enzymes' structure and catalytic activity are affected by a number of essential minerals, including manganese, selenium, zinc, and copper [36]. Vitamin E has not been linked to any enzyme system's functionality, in contrast to other vitamins [37]. The only known function of this compound is that of an antioxidant and free radical scavenger, which makes it a superb lipid and phospholipid membrane defender [38]. Gene expression is regulated by vitamin E, and it also lessens

inflammatory responses, among other effects. It has been demonstrated that ascorbate is a potent ROS scavenger for singlet oxygen, hydroxyl radicals, hydrogen peroxide, and superoxide radical anion. [39,40]. Vitamin C also protects target molecules from nitrosation by scavenging reactive nitrogen oxide species [41]. By absorbing another hydrogen atom, the ascorbyl free radical can be reduced to ascorbate or further oxidized to dehydroascorbate[42]. A recycling system for vitamin C has been developed as a result and works similarly to the vitamin E system. Free radicals are produced during tissue metabolism, but they can only do so much damage before being neutralized by the cell's antioxidant defenses and repair mechanisms. If a person is healthy and gets enough nutrients, there won't be much tissue damage since metabolically active tissue cells are more likely to repair any damage that does occur. [43]. Despite the fact that many different types of marine plants are employed in food and pharmaceuticals, their antioxidant and anticancer properties have yet to be investigated [44].

Researchers are invited to present recent findings and novel research on a wide range of topics related to the evolution of emergent marine antioxidant biosynthesis, the functional and ecological roles of these molecules in the ocean, biotechnological production, and potential applications of these molecules as new medications, dietary supplements, and healthcare products in this Special Issue.[32].According to epidemiological research, consuming a lot of plant-based foods that are rich in antioxidants may help prevent cancer. Many antioxidants, both natural and synthetic, have been shown to slow the chemical carcinogenesis in test animals. In addition to a diet high in vegetables and fruits, some prospective research on the effects of supplemental antioxidants, such as vitamin E, vitamin C, selenium, and carotenoids, might be proposed for the maintenance of health and the prevention of disease. [45].

- 2. Immunomodulation and Apoptosis:** Since they specifically target tumor cells, tumor neovasculature, and host negative immunoregulatory components, MAbs have become effective immunotherapeutic agents against cancer (checkpoints). However, to effectively use anticancer vaccines that actively modulate the immune response, it will be necessary to identify the proper tumor-rejection antigens, enhance interactions between peptides, antigen-presenting cells, and T cells, and block any adverse immunological checkpoints that obstruct a productive immune response. [46]. Apoptosis is a multi-step process in which dying cells undergo a number of changes. Several signaling pathways are involved. When the balance of anti- and proapoptotic proteins shifts, the apoptotic machinery is activated. Antiapoptotic proteins are upregulated, proapoptotic proteins are downregulated, and caspase synthesis is lowered, all of which can limit apoptosis [47]. In cancer-causing conditions marked by a lack of apoptosis, dysregulation of apoptotic signaling may be involved [48]. Activating the mitochondrial apoptosis pathway and acting as a death receptor, caspase 8 is also responsible for Cytochrome C emission. An example of an effector caspase is caspase 3, which destroys proteins necessary for cell survival to kill cells [49]. Inducing apoptosis is one of the most effective ways to halt cancer cells from reproducing. Radiation and apoptosis-inducing medicines, such as tamoxifen, have been used to treat cancer [50,51]. Apoptosis is a process through which several chemopreventive medications work to prevent cancer [52]. Plant extracts may induce apoptosis by increasing the number of macrophages, enhancing immune surveillance, and turning on signal complexes that trigger death [53]. Phytochemicals from the sea can also activate macrophages, causing them to perish. Fucoidan, an

immunomodulator derived from *Laminaria japonica*, acts directly on macrophages and T cells, restoring immunological function in immunocompromised mice [54]. It may also aid in the recovery of immune function in irradiated mice [55,56]. Fucoidan may boost the *in vitro* synthesis of interferon and interleukin-1 (IL-1) (IFN) [57]. The percentage of murine cytotoxic T cells increases when high-weight fucoidan produced from Okinawa mozuku is used. [58].) [59]. This might cause macrophage polarization to shift from M2 to M1, which might then cause H<sub>2</sub>O<sub>2</sub> to regenerate and increase the IMSN nanozyme's catalytic activity. Both *in vivo* CT26-tumor-bearing mouse models and *in vitro* multicellular tumor spheroids were used (MCTS), the anticancer impact of IMSN-PEG-powerful TI has been demonstrated. A potential method to eradicate cancer cells is the tumor treatment method based on nanozymes with immunomodulation enhancement [60].

- 3. Nutritional Values and Anticancer Effects:** Because it provides vital ecological services, marine biodiversity is an important resource for human society. In one of the strangest ecosystems, this web supports hundreds of unique species of bacteria, fungi, and viruses that participate in a variety of ecological and biochemical processes. Because the marine ecology is so diverse, every drop of ocean water contains nine out of ten microorganisms that we don't know about. [61]. The needs of humans for food, nutrition, and the treatment of ailments are all met in large part by marine plants. Diets for cancer prevention primarily consist of plant-based foods. The risk of cancer has been linked to increased consumption of a wide range of plant foods. There is evidence that certain cancers can be prevented by eating non-starchy vegetables and fruits. [62]. Seaweeds are consumed by humans and have been used traditionally to treat a number of disorders. They include a wide range of intriguing components (arthritis, tuberculosis, influenza, colds, cancer, etc.). The majority of people inadvertently ingest seaweed products every day in the form of processed foods like fruit, meat, and dairy as well as household goods like cosmetics, paint, solid air fresheners, toothpaste and other similar items. Vitamins B1, B12, A, C, E, and D, niacin, riboflavin, folic acid 3, 4, pantothenic acid, and minerals Na, Ca, K, and P are all abundant in seaweeds. The majority of the essential amino acids for life and welfare are present in them, providing a well-balanced amino acid profile. They contain far more trace elements than vegetables and other terrestrial plants, including over 54 essential for human physiological activities [63,64]. With their favorable physiological effects, therapeutic qualities, and additional health benefits like anticancer or anti-inflammatory activity, the potential for marine-derived minerals and other marine bioactive components as functional food additives is enormous [65]. Appropriate animal models must be employed for the investigation in order to show how these chemicals work. The sea cucumber is a top candidate for drug discovery since it is a rich source of bioactive chemicals, even if much more research is required in this area. The majority of the time, isolated drugs have only been evaluated in extremely modest concentrations and in conjunction with different substances [66].

#### IV. NATURE AND CANCER CHEMOTHERAPY

Natural goods have been enormously successful in contemporary civilization. Because secondary metabolites from plants and microbes were used, our life expectancy more than doubled in the 20th century. By enabling organ transplantation, they have revolutionized medicine by easing suffering and anguish. Since the chemical variety of a region depends on its biological and geographical richness, researchers look at the entire

globe while bioprospecting. [67]. Many organic substances derived from plants and marine microorganisms have been shown to be beneficial in the treatment and prevention of cancer over the past 50 years (Table 1). [68,69]. Invertebrates, terrestrial bacteria, animals, plants, and plants all contribute to the development of anticancer drugs. Taxol, an antineoplastic therapy derived from the bark of the Western Yew tree, has been discovered to be effective in the treatment of breast cancer when combined with the active complex alkaloid medications Vinblastine and Vinorelbine [70]. They have been shown to be useful in the treatment of juvenile leukemia, Hodgkin's disease (lymphocytic cancer), and choriocarcinoma [71]. The National Cancer Institute gives scientists the resources they need to learn more about how diet and nutrition affect cancer prevention, but research into cancer chemoprevention using marine natural compounds is still in its infancy [72,73] has not been adequately examined, and there is a dearth of preclinical and clinical evidence on this method [74]. Anticancer chemicals have been discovered and developed using plants, microorganisms, and marine animals. As a consequence, numerous natural products are now being researched in preclinical studies, and 14 natural products originating from osanic creatures are undergoing clinical trials at different stages, demonstrating the promise of marine natural chemicals [75]. Using marine resources, a concentrated, combinatorial strategy has been suggested as a means to accelerate the creation of novel anti-cancer medications with higher efficacy and fewer adverse effects [76,77]. Finding novel medicines continues to rank highly in the priority list for cancer therapy due to the rapid rise in chemotherapeutic drug resistance. The demand for innovative anti-tumor drugs that work against incurable malignancies and have therapeutic efficacy while having fewer side effects or less toxic adverse effects is further increased by the high toxicity frequently associated with existing cancer chemotherapeutic therapies [78].

**Table 1: List of marine-derived substances that may have anticancer properties follows.**

Compound Name/Class	Source	Cancer type	Mechanism	Ref.
Apratoxin A/Peptide	Bacteria, <i>lyngbyaboulloni</i>	Cervical cancer	Cell cycle inhibition IC <sub>50</sub> = 2.2 nM	[79]
Brugine/Alkaloid	Plants, <i>bruguierasexangula</i>	Lewis and Sarcoma 180	not disclosed	[64]
Fucoidan/Polysaccharides	Algae, <i>ascophyllum nodosum</i>	Colon cancer	At conc. of 80 to 100 µg/mL prevent the growth of arterial smooth muscle cells.	[80]
Lyngbyabellin B/Peptide	Bacteria, <i>lyngbya majuscula</i>	Burkitt lymphoma cancer	Suppression of cell growth IC <sub>50</sub> = 0.02 µM	[81]
Sansalvamide A/Peptide	Marine fungi	Pancreatic, breast, colon, and prostate cancers	Hinders the synthesis of protein complexes	[81]

Phlorofucofuroecol A/Polyphenol	Brown seaweeds	Cancer	not disclosed	[82]
Phloroglucinol/polyphenol	Brown seaweed	Colon cancer	Cause cell death at 300 $\mu$ M and DNA damage	[83]
Chondroitin-4-sulphate/Polysaccharides	Sea cucumber, <i>Cucumaria frondosa</i> ,		Not disclosed	[64,84]
Chondroitin-6-sulphate/Polysaccharides	Sea cucumber, <i>Cucumaria frondosa</i> ,		Not disclosed	[64,84]

## V. ANTICANCER BIOACTIVE ANTIBIOTICS DERIVED FROM MARINE SOURCES

Biologically active substances with a variety of modes of action, including antiproliferative, antioxidant, and antimicrotubule properties, have been created, in particular, by sea algae and cyanobacteria. Due to the finding of their secondary metabolites in sponges, ascidians, tunicates, and mollusks, peptides from marine animal sources have recently attracted interest [85], antibiotics with bioactive anticancer agents. This product was made with marine resources. The majority of these medications focus on elements of universal signal transduction pathways [86]. Antitumor antibiotics, such as anthracyclines, 26/64 actinomycin, and aureolic acid, are among the most commonly used cancer chemotherapeutic medicines [87,88]. Actinomycin D may target numerous tumour metabolic regulators as a new anti-glioma strategy by targeting peptididolides, dactinomycin, and other clinically useful agents from these families, which were discovered to downregulate a number of glioma metabolic enzymes of glycolysis, glutaminolysis, and lipogenesis (Figure 3, Figure 8, and Table 2) [89]. Antitumor antibiotics that block topoisomerase II are among the most commonly used [90–92]. Geldanamycin is a naturally occurring benzoquinone ansamycin fermentation product that inhibits HSP90 in HeLa cells and causes cytotoxicity [93,94]. The trabectedin complex's mode of action was aided by the three fused tetrahydroisoquinoline rings. The chemical structure, according to the researchers [95], interacts directly with transcription factors like SP-1 to impede important links between DNA and transcription by binding covalently to DNA's minor groove. Bryostatin is another chemotherapeutic drug that modifies the paclitaxel-induced protein kinase C inhibitor (PKC) [96]. The anticancer medication bryostatin 1, produced from the bryozoan *Bugula neritina*, can trigger Bcl-2 ubiquitination and proteasome breakdown, allowing lymphoblastic leukemia bone marrow progenitor cells to grow [97]. Bryostatins are protein kinase C (PKC) activators that regulate cell proliferation, differentiation, and activation [98]. Cell cycle arrest, protein synthesis inhibition, and antiangiogenic activity similar to didemnin B and aplidine are all proposed mechanisms [99,100]. Plinabulin (NPI-2358), a highly selective and powerful vascular disrupting agent (VDA) derived from a marine fungus extract, is now in phase II clinical studies [101] owing to its efficacy against multidrug-resistant human tumour cell lines. [102]. Antileukemic activities have been shown for the penicillium *chrysogenum* alkaloid sorbicillactone-A, which is found in the marine sponge *Ircinia fasciculata* [103]. Depsipeptide (NSC 630176), a bicyclic peptide derived from *Chromobacterium violaceum*, inhibited a histone deacetylase and reduced c-MYC expression, causing cell cycle arrest in the G0-G1 phase. [104]. In recent years, lead compounds identified for various pharmaceutical uses have

been largely sourced from marine sources. It's interesting to note that marine microorganisms continue to be the source of several crucial and little-known bioactive metabolites. Microorganisms occupy an extensive stretch of the biosphere, ranging from the shallow water along the beach to the abysmal seaward regions that cover 70% of it. [105]

- 1. Polysaccharides:** More and more commonly, polysaccharides are being employed as building blocks for the development of nanoscale drug delivery systems. This is accounted for by the exceptional qualities of polysaccharides, such as their biodegradability, biocompatibility, low toxicity, and low cost [106]. Another prominent chemical family found in many marine species is polysaccharides, which include alginates, agar, and carrageenans[64]. (Figure 5; Table 1). Polysaccharide cytotoxicity is predominantly mediated by innate immune system stimulation [107], it causes the creation of tumor-crushing cytokines, the activation of natural killer cells and macrophages, and their migration to the target site[108,109]. Internally sulfated glycosaminoglycans caused the death of mice melanoma cells by changing their transcription [110,111] This effect was discovered to be caused by caspase-3 activation and subsequent downregulation of the kinase pathway [112,113] Many different types of polysaccharides found in sea creatures have intriguing biological traits with human GAGs. Fucoidans and their LMW forms, among other algal polysaccharides, may serve as one of the primary sources of polysaccharides for cell therapy and regenerative medicine in the future. [114].
- 2. Alkaloids:** There are four different categories of marine alkaloids: indoles, phenylethylamines, halogenated indoles, and other alkaloids. (Figure 6; Table 1), most of which are phenylethylamines and indoles [64,115] Alkaloids such as brugine, acanthicifolin, and benzoquinones are found in *Bruguierasexangula*, *Acanthus illicifolius*, and *Kandeliacandel*. [64]. The alkaloid "rhizophorine" is found in *Rhizophora mucronata* and *Rhizophora stylosa*, two mangrove species found on the beaches and river banks of East Africa and the Indo-Pacific region. A range of cancer cell types has been demonstrated to be inhibited by these compounds.
- 3. Polyphenols:** Polyphenols include catechin, phenolic acids, tannins, flavonoids, anthocyanidins, gallic acid, epicatechin gallate, epigallate, and gallic acid, in addition to lignin, epigallocatechin gallate, epicatechin gallate, gallic acid, and epigallate (Table 1)[116]. It has been demonstrated that polyphenolic substances lower cellular protein levels and the mitotic index, both of which are necessary for the proliferation and colony formation of cancer cells. Because of its cytotoxic properties, scutellarein 4'-methyl ether, for instance, has anticancer activity both in vitro and in animals. Along with having anticancer properties, phenols also have anti-inflammatory, antiviral, and antiplatelet aggregation inhibitory actions [117]. These polyphenols impeded the metabolism of xenobiotic-metabolizing enzymes, resulting in a shift in the telophase mitotic process and, as a result, cell division disruption [118].
- 4. Peptides:** Peptides of various types have been detected in a wide spectrum of marine flora. Nearly 2500 novel peptides with anti-proliferative action have been found in the recent decade [119] Cytotoxicity was induced in human HeLa cervical cancer cells by the cyclic depsipeptide apratoxin A, which inhibited cell cycle 35/64. Coibamide A [120], a cyclic depsipeptide isolated from *Leptolyngbya* sp., and lyngbyabellin B, a cyclic



depsipeptide obtained from *Lyngbya majuscula*, show a similar mechanistic effect.[121]. Peptides produced by *Lyngbya* spp. and *Notoc* spp. can inhibit cell growth via microfilament breakdown, secretory route blockage, and other intracellular processes. [122]. *Scopulariopsis brevicaulis* produces spulularide A and B, two new cyclodepsipeptides that inhibit colon and pancreatic cancer cell proliferation significantly. Sansalvamide A, a cyclic depsipeptide, was synthesised from a variety of marine mushrooms. A mammalian cell line has discovered a connection between a heat shock protein (HSP90) and a cancer protein client, despite the fact that the precise mechanism of this depsipeptide is unknown. Sansalvamide A, an anti-tumor medication, binds to the N-middle domain of HSP90 to stop the formation of protein complexes [81].

## VI. MANGROVES AND OTHER COASTAL PLANTS

Mangroves are known to have secondary metabolites that are effective cancer preventives. Although having abundant chemically loaded resources, the mangrove flora has not been extensively researched for anticancer substances[123]. Anticancer medications could be based on seventeen different mangrove species (**Table 2**). The alkaloid 1,2, dithiolane (Brugin), derived from *Bruguiera sexangular* sulfide, exhibits anti-Sarcoma-180 and anti-Lewis lung cancer antibodies. Tannins from a similar material have been shown to be anticancer in lung cancer cases [124]. Tetranor triterpenoids (xylogranatins A to D) are poisonous to a variety of deadly tumour cell lines, in contrast to limonoid forms such granaxylocarpins A and B, which are cytotoxic to P-388 leukaemia [125]. Tetranor triterpenoids are anticancer mixtures derived from the mangrove *Xylocarpus granatum*, popularly known as the cannonball mangrove. A marina is cytotoxic to many cancerous tumour cell lines, including K562 and HeLa. Large cell lines like KB and NCI-H187 respond similarly to compound cardenolide glycoside groups produced from *Cerbera odollam* seeds, including 2'-O-acetyl cerleaside A, 17b-neriifoline, and cerberin [123].

**Table 2: Anticancer properties of marine floral compounds**

Marine flora	Chemical	Biological activity	Ref.
<b>Microbial flora</b>			
Microcystis aeruginosa	Siatoxin, Microviridin Toxin BE-4	Anticancer, antibiotics	[126,127]
Streptomyces peucetius	Daunorubicin	Acute myeloid and acute lymphocytic leukemia anticancer interventions	[128]
<b>Algal flora</b>			
Cyanobacteria Nostoc linckia and Nostoc spongiaeforme var. tenue	Borophycin	Human colorectal adenocarcinoma activity and cytotoxicity against human epidermoid carcinoma (LoVo)	[129]
Cyanobacteria	Apratoxins	The inhibition of certain cancer cell lines	[130]
Nostoc linckia	Cytophycin 1	Human solid tumors and tumor cell lines: cytotoxicity	[131]
Nostoc spongiaeforme	Cryptophycin 8	Greater in vivo therapeutic effectiveness and less toxicity compared to cryptophycin 14	[132]
Chondria sp.	Condriamide A	Cytotoxicity	[133]
Caulerpa sp.	Caulerpenyne	Anticancer, antitumour, anticancer, and antiproliferating activity	[134-136]
Cystophora sp.	Meroterpenes and Usneoidone	Antitumour	[137]
Symploca sp.	Largazole	Antiproliferative activity	[138]
Leptolyngbya sp.	coibamide A	cytotoxicity against mouse neuro-2a and NCIH460 lung cells	[120]
Palmarispalmata	Phloroglucinol and its polymers, including deckol, 8,8'-bieckol, dieckol, phlorofucofu roeckol A (a pentamer)	Phlorotannins' antioxidant action	[139]
Sargassum thunbergii	Crude	Inhibition of tumor metastasis and antitumor activity in rat mammary adeno carcinoma cells	[140,141]

## VII. CONCLUSION AND FUTURE PERSPECTIVES

Marine creatures have emerged as an intriguing source of both known and unknown substances with the potential to provide long-term economic and human advantages in recent decades. Many of these substances have shown tremendous promise as therapeutics, with specific and robust effects against a variety of disorders, including cancer. The current pipeline has demonstrated its potential as a source of anticancer medicines. Six of the nine drugs now available are used to treat cancer, and other chemicals derived from or produced from marine organisms are currently undergoing clinical studies to see if they may also cure cancer. Yet, compared to the overall number of identified compounds with anticancer potential, the number of substances in use or undergoing clinical studies is small. Many tumor cell lines have been shown to have in vitro anticancer activity, including those derived from

cancers of the lung, kidney, prostate, melanoma, bladder, osteosarcoma, breast, and lymphoid. Apoptosis, necrosis, and lysis of tumor cells are thought to be the main pathways through which marine materials inhibit tumor growth both in vitro and in vivo, according to the majority of studies on the topic. Technological advancements and scientific breakthroughs established a foundation for studying a wide range of chemically distinct, physiologically active, and taxonomically diverse marine floras. Successful marine-derived compounds such as trabectedin, eribulin, brentuximab vedotin, and cytarabine have been demonstrated to be extremely beneficial in pre-clinical and clinical research for preventing oxidative DNA damage, inducing apoptosis, decreasing carcinogenesis, and activating macrophages. Lastly, therapy strategies and the current use of marine-derived components are explored, as well as their future direction and clinical trials as anticancer drugs.

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