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A Potential Source of Anti-Cancer Drugs: Marine Raw Materials

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Review Article

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Abstract

Marine populations serve as a repository for novel bioactive metabolites with a wide range of chemical configurations. The influence of marine species is highlighted in this review, with a focus on marine plants, algae, bacteria, actinomycetes, fungi, sponges, and soft corals. Disease ailment patterns are shifting, and new diseases are arising as a result of changing settings. The massive increase in the world's population has put a strain on the available drug resources. As a result, drug companies are constantly on the search for fresh resources to help them develop effective and safe drugs to meet the growing demands of the global population. The marine environment contains an abundance of various materials for developing novel medications to treat important diseases such as cancer. Cancer is still one of the deadliest diseases on the planet. New medications with novel modes of action are desperately needed, thus much research has been done on new anticancer treatments derived from natural sources, including plants, microorganisms, and marine organisms. The anti-cancer benefits of marine natural products in in vitro and in vivo research were initially discussed, as well as their activity in tumor prevention and associated compound-induced apoptosis and cytotoxicities.

Keywords: Marine Environment; Anti-Cancer Products; Biochemicals

Introduction

Cancer is still one of the deadliest diseases on the planet. Globally, about 1,000,000 new cases and 65,000 deaths are expected, with men having a two-fold higher incidence rate than women. In North America, Australia, and New Zealand, the countries with the greatest incidence rates in men and women, respectively, non-melanoma skin cancer (NMSC) is the most commonly diagnosed cancer. Increased risk is linked to age and an unhealthy lifestyle, with the highest incidence rates observed. Cancer is becoming more common as a result of environmental changes and modern lifestyles. Lung and breast cancers are the most often diagnosed cancers in men and women, and they are the main causes of cancer-related death. Meanwhile, cancer predisposition factors can be both external (tobacco, chemicals, radiation, and infectious organisms) and internal (genetic predispositions, immune conditions). The discovery of a cancer cure has become a realistic goal as to advances in biology and immunotherapy research, as well as substantial developments in current pharmaceutical design and production. Lymphomas, testicular cancer, and juvenile lymphoblastic leukaemia are only a few of the human cancers that have been cured or given a longer life expectancy. Despite the major breakthroughs in current medicines, chemotherapy has been linked to a number of adverse effects, prompting the hunt for a more effective cure with fewer side effects.

Natural products can be used to develop new medications, drug candidates, and chemical entities.

Bioactive natural materials are used in approximately 80% of approved chemotherapeutic medications and more than half of all drugs. Natural products are used to treat 80% of human disorders, including cancer. The molecular mechanisms that underpin the biological consequences are also discussed. Marine invertebrates, algae, and bacteria create biochemicals that are quite distinct from those produced by similar terrestrial creatures, and thus have a lot of potential as novel types of medications. Natural bioactive compounds cause cytotoxicity by targeting macromolecules produced by cancer cells, such as those found in oncogenic signaling pathways. *In vitro, in vivo* models, and in cancer clinical trials, a number of marine-derived metabolites work as anticancer medicines by inhibiting the development of human tumor cells. A new generation of anticancer medications has been discovered thanks to advanced technology and extensive research on marine natural ingredients. They are currently being tested in clinical trials.

From Marine Organisms to Anti-Cancer Drugs

Actinomycetes create 70% of known microbial secondary metabolites, fungi make 20%, Bacillus spp. produce 7%, and other bacteria produce 1–2%. It's worth noting that microbial products account for roughly 10% of all biologically active natural compounds currently known [1-6]. There are only a few examples of marine anticancer drugs that have progressed to the clinical stage [7]. Bryostatin 1, and dolastatin 10 are examples. Phase II clinical trial for bryostatin 1 against melanoma, non-lymphoma, Hodgkin's kidney cancer, and colorectal cancer has recently begun. The biological impact of bryostatin 1 is mediated by its ability to promote normal bone marrow progenitor cell development [5,8]. A vast number of highly effective agents have emerged from the marine environment. These compounds can stop human cancer cells from growing and have other anticancer properties such as antimitotic activity, apoptosis, and autophagy induction [9]. Some are known to have the ability to stop cancer cells from migrating, invading, or spreading.

Cyanobacteria that target histone deacetylase, transcription enzymes, and practically all biological activities involving chromatins were also discovered [10]. So far, more than 20,000 new compounds have been discovered in marine sources, and the number is growing every year. Cytarabine, Ziconotide, Trabectidin, Eribulin, and Brentuximabvendotin are cancer medications derived from marine sources that have been approved for human use and have been on the market for a long time [11,12]. Furthermore, a huge range of anti-cancer medications are being researched to see if they can help people with cancer pain or work as an adjuvant in immunological therapy. Single-celled organisms ranging from eubacteria to eukaryotes like fungi and protists make up the majority of marine-derived agents. The marine blue-green algae, once renowned for producing dangerous toxins, are now emerging as a major source of anticancer medications.

From Marine Plants

Algae make for over 90% of all marine plant species. Because maritime plants, such as marine algae and mangroves, contain such a wide chemical diversity, compounds isolated from them have been demonstrated to have antibacterial, antifungal, analgesic, anti-inflammatory, cytotoxic, hypotensive, and spasmogenic properties [12,13].

Macroalgae Seaweed

Because seaweeds are good providers of protein, iodine, vitamins, and minerals, their metabolites have demonstrated remarkable anti-cancer properties. Polyphenols like catechin, epicatechin, epigallo-catechingallate, and gallic acid are abundant in the seaweeds. Many scientists have studied the antioxidant, anticancer, and immunomodulating properties of seaweeds over the last three decades [14].

Palmariapalmata Red Algae/Dulse: This edible seaweed has been demonstrated to be a powerful antioxidant that can stop cancer cells from multiplying. The anti-proliferative effects of dulse extracts in this study are most likely due to the polyphenol concentration of these extracts' bioactivity [15,16].

Acanthophoraspicifera: On cancer cells grown in mice, the alcoholic extract of the red alga Acanthophoraspicifera has tumoricidal activity comparable to the conventional medication 5-flurouracil. The rise in mean survival time, decrease in tumor volume, and increase in viable cell count are all indications of this [17,18].

Ascophyllumnodosum: In comparison to fibroblasts, fucoidan, isolated from Ascophyllumnodosum, had an anti-proliferative effect on sigmoid colon cancer cells. The low-molecular-weight fucoidan extracted from Ascophyllumnodosum has an anti-proliferative effect on fibroblasts, sigmoid colon cancer cells, and smooth muscle cells, among other normal and malignant cells. In mice, fucoidans have antitumor, anticancer, antimetastatic, and fibrinolytic effects [19,20].

Microalgae

Cyanobacteria, often known as blue-green algae, are rich in over 400 new metabolites, including unique, physiologically active peptide and polyketide metabolites that can kill cancer cells by triggering apoptosis or influence cell signaling by activating the protein kinase c family. Approximately half

of the 41 cyanobacteria strains tested showed the capacity to kill cancer cells. Dolastatin 10 and curacin A, two anti-microtubule medicines produced from cyanobacteria, have been clinically tested for cancer treatment [21,22].

Calothrix Cyanobacteria: Cyanobacteria, often known as blue-green algae, produce over 400 new compounds, some of which are effective at killing cancer cells by inducing apoptosis or affecting cell signaling. Calothrixins A and B are anticancer proteins that have significant anticancer effect against human cancer cells. Scytonemin can be found in the extracellular sheaths of a variety of blue-green algae species, both aquatic and terrestrial. This chemical inhibits the proliferation of human fibroblasts and endothelial cells while also regulating mitotic spindle formation [23,24].

From Marine Bacteria

Lactobacilli and Noctilucascintillans: Lactobacilli and Noctilucascintillans, respectively, showed chemopreventive benefits in vivo against colon cancer and melanoma cancer. Lactobacilli has the ability to reduce the activities of the enzymes azoreductase, nitroreductase, and β-glucuronidase, and these dietary components were able to reduce the standard level of enzymes in the intestinal tract, suggesting that Lactobacilli could reduce the risk of colon cancer development. Anticancer chemicals are produced by probiotic bacteria such as Lactobacilli and Bifidobacteria [25,26]. Only a few marine bacteria can be isolated under laboratory settings, thus new culture techniques to isolate slow-growing bacteria and bacteria that are distinctive in the synthesis of novel natural products are urgently needed [27,28].

From Marine Actinomycetes

Dietzia, Rhodococcus, Streptomyces, Salinispora, and Marinispora are examples of marine actinomycetes. Actinomycetes are by far the most prolific makers of secondary metabolites among marine bacteria.

Streptomyces Species: Gutingimycin is a Streptomyces species' highly polar trioxacarcin derivative. In addition to the known trioxacarcins A–C, the same Streptomyces species also produces trioxacarcins D–F. Marine actinomycetes of the Micromonosporaceae family are among the most promising antibiotic-producing bacteria. Anticancer compounds that target proteosome function have been discovered in these microorganisms, and their industrial potential has been proven by multiple medications [29,30].

Micromonospora Marina: Thiocoraline is a new bioactive depsipeptide that suppresses RNA production and was obtained from Micromonospora marina, a marine organism. Lung and colon cancer cell lines, as well as melanoma, are all selectively cytotoxic by the bioactive chemical. Surprisingly, the chemical has antiproliferative properties in colon cancer cell lines [31,32].

From Marine Fungi

Fungi derived from the sea are a rich and potential source of new anticancer drugs. Marine habitats produced physiologically active principal chemicals from higher fungus (basidiomycetes), endophytic fungi, and filamentous fungi. Aspergiolide A, obtained from the marine filamentous fungus Aspergillus glaucus, contributed to cytotoxicity against cell lines, while alkaloids isolated from Penicillium sp. generated from deep-ocean sediment had anticancer properties [25,33].

From Marine Sponges

Tethyacrypta: The discovery and identification of spongothymidine and spongouridine from this sponge is one successful example. These molecules were discovered to have antiviral properties, which led to the creation of cytosine arabinoside as a clinically effective anticancer drug. Cytarabine prevents DNA synthesis. Its mode of action is based on its capacity to quickly convert into cytarabine triphosphate, which causes DNA damage during synthesis. As a result, cancer cells that divide quickly are the most vulnerable [34-36].

From Soft Corals

Sarcophyton is one of the most extensively distributed soft coral genera in the tropical and subtropical oceans, with roughly 30 species collected and examined for the presence of bioactive secondary metabolites, i.e., fatty acids that demonstrated dose-dependent cytotoxic activity against brine shrimp [37,38]. Cembranoids, which are found in large numbers in soft coral, are one of the most significant components (up to 5 percent dry weight). Cembranoids have biological effects, including as cytotoxicity, anti-inflammatory action, and antagonistic activity. Furano-cembranoids and decaryiol derived from Nephthea sp. and Sarcophytoncherbonnieri are effective against numerous tumor cell lines, according to in vitro cytotoxicity studies [39,40].

Extraction of Anti-Cancer Agents from Marine World

Collection of Specimens

- Marine specimens, both animals and plants, having anti-cancer activity, were obtained.
- For ex. the sponges were collected at 10-35 m depths by scuba diving.
- One of the most important properties of marine

specimens is fast degradation; therefore, these samples are quickly frozen with dry ice and stored frozen at −20°C until they are processed.

- In determining anti-cancer activity, more than one extracts from different parts of single marine animal or plant show a "positive" anti-cancer activity [41,42].

Grinding Procedure

Marine frozen tissue pieces and dry ice pellets are slowly added into the grinder. The amount and speed of sample addition is dependent upon the specimen's characteristics. Approximately, double the volume of dry ice is added to the specimen to keep the mechanism and housing cold during grinding [43,44].

Extraction and Isolation

This grounded tissue was soaked in an organic solvent (methanol) for 24 hrs. The specimen does not tend to swell in organic solvent. After soaking overnight, the organic solvent is drained from the percolator and the tissue was covered again with pure methanol. After soaking another half-hour, the methanol was drained and the organic solvent extracts are evaporated to give a concentrate extract [45,46].

Storage

Organic solvent extracts of marine specimen dry quickly. The concentrate is transferred into an appropriate storage bottles or a vessel and further dried by applying a high vacuum dryer and stored at −20°C until use [47,48].

Screening

After adding extract to human cancer cell culture, cells were incubated for 24 h under 5% CO2 at 37°C. Then, the cells were observed under a microscope to evaluate cytotoxicity of the extracts [49] (Table 1).

Sr. No.	Compound	Sources	Reference
1	Citarabin	Sponge	[50]
2	Sorbicillactone-A	Sponge	[51]
3	Halicondrin B	Sponge	[52]
4	Aplidine	Tunicate	[53]
5	Bryostatin 1	Bryozoan	[54]
6	Plinabulin	Algae	[50,55]
7	Soblidotin	Bacterium	[56]
8	Didemnin B	Tunicate	[57]
9	Discodermolide	Sponge	[58]
10	Depsipeptide	Cyanobacteria	[59]

Table 1: Marine Derived Anti-Cancer Compounds with Sources.

Conclusion

To date, marine-derived medications have included an antibiotic obtained from fungi, two closely similar chemicals derived from a sponge that cure cancer and the herpes virus, and a neurotoxin derived from a snail that is 10,000 times more effective than morphine without the side effects. The diversity of marine creatures, as well as innovative chemical structures and chemical property space, are highlighted in this paper. Finally, therapeutic techniques and the current utilization of marine-derived components are explored, as well as their future direction and constraints.

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