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Marine drugs: A secret of wealth and a novel epoch in cancer treatment

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ABSTRACT

Cancer remains one of the most lethal diseases in worldwide. Significant research has been done for new anticancer medicine from natural sources, including plants, microorganisms, and marine organisms, because there is an urgent need for drugs with novel mechanisms of action. Over 90% of the oceans biomass is made up of marine flora, including bacteria, actinobacteria, cyanobacteria, fungi, microalgae, seaweed, mangroves, and other halophytes. The various types of marine drugs are highlighted in this review, with a focus on marine plants, algae, bacteria, actinomycetes, fungi, sponges, and soft corals. Over 80% of the biodiversity on earth is found in marine ecosystems, and many of these animals have acquired special adaptations that allow them to survive in a variety of difficult settings.

KEYWORDS: marine plant, microorganism, antitumor, anticancer

INTRODUCTION

Ocean acts as a source of a vast range of organisms because of the varying conditions that are offered by the several marine zones. Since ancient times, people have made use of the sea's abundant natural resources, including preparations prepared from algae as well as fish and other marine animals for food and medicine. Fish oils are a prevalent illustration. Oceans are home to more than 80% of all known plant and animal species. Molluscs, echinoderms, bryozoans, prawns, shells, and marine microbes are sources of bioactive substances (i.e., oils and cosmetics) that come from marine organisms like sponges, tunicates, fish, soft corals, nudibranchs & sea hares derived product use since prehistoric time [1].

Each of these marine bio products has a significant potential market value, making the ocean an abundant supply of novel molecules with considerable promise as pharmaceuticals, dietary supplements, cosmetics, agrichemicals, and enzymes. Numerous compounds with novel antibacterial, anticancer, and anti-inflammatory activities have been discovered, many of which are structurally and pharmacologically significant. Natural products frequently offer chemicals that can be used as clinical or commercial medicine or as biochemical instruments to show how certain disease-related pathways are involved and how they

might be targeted for drug development. 60 and 75 p% respectively, the novel medicine for cancer and infectious diseases are obtained from natural sources.

More than 22,000 microbial secondary metabolites are known, with actinomycetes producing 70% of them, fungi 20%, Bacillus species 7%, and other bacteria 1-2%. 10% of all known biologically active natural compounds are typically derived from microorganisms. Several marine antineoplastic drugs have been found to reach the clinical trial phase. Bryostatin 1, ET-743, and dolastatin 10, for instance. Recently, a phase II clinical trial for bryostatin 1 against melanoma, non-lymphoma, Hodgkin's kidney cancer, and colorectal cancer was initiated. The biological action of bryostatin 1 is mediated by the encouragement of regular bone marrow progenitor cell development [2].

Marine Anticancer Drugs

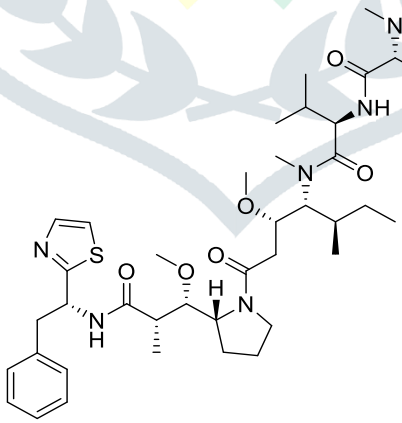
1. ***Dolabella auricularia***

Synonym: Wedge sea hare

Biological Source: *Dolabella auricularia* was isolated from sea hare lipophilic extract of the marine *cyanaobacterium* in Palau.

Family: Aplysiidae

Chemical constituents: 90% moisture, 2.044%, ash , 5.324% crude fat , 0.75% protein , 0.25% phosphorous, potassium , sodium , calcium , magnesium , iron , zinc.



Dolabella auricularia

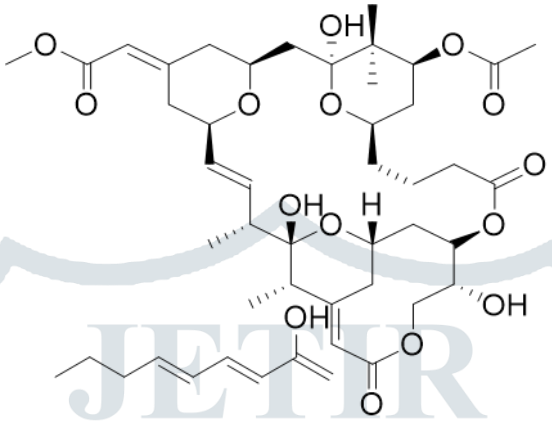
Uses: Dolabella auricularia is used as an anticancer drug. It is sometimes used by the keepers of large marine aquaria to limit algal growth in the tank. [3, 4]

2. Bryostatin

Synonym: Bryostatin

Biological source: Bryostatin are the group of macrolide lactones from the marine organism *Bugula neritina*. It is the Macrocyclic lactones

Chemical constituent: Acetate, ester, methyl ester, enoate ester, organic heterocyclic compound secondary alcohol



Bryostatin

Uses: Bryostatin is used as an anticancer agent; it is anti AIDS/HIV agents, Alzheimers disease. [5, 3]

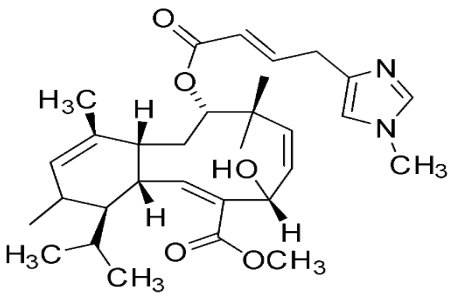
3. Sarcodictyin

Synonym: Sarcastic

Biological source: It is found in paraphaerasclera aurea and *erythropodium caribaeorum*.

Family: Sarcoidosis

Chemical constituent: dimethyl, limettin, scoparone, methyl-hydroxy-8, 7-methoxy, 5-prenyloxy coumarin.



Sarcodictyin

Uses: It is used as an anticancer drug, anti-inflammatory, anti-biotic, cytotoxic effect. [6]

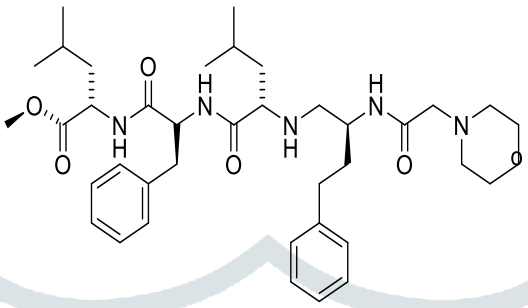
4. Carfilzomib

Synonym: Bortezomib

Biological Source: Carfilzomib is derived from epoxomicin.

Family: Epoxyketone [28]

Chemical constituent: Morpholin-4-acety, 2- amino- 4- phenylbutanoyl



Carfilzomib

Uses: It is used as an anticancer activity, also used to treat multiple myeloma. [7, 8]

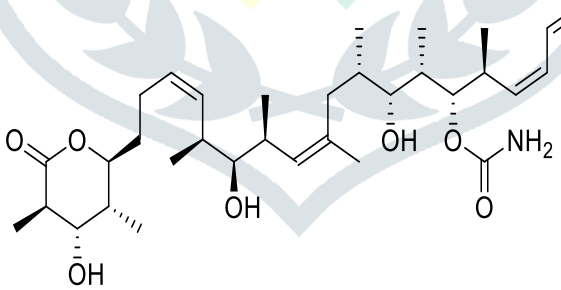
5. Discodermolide

Synonym: Disermolid

Biological Source: Discodermolide is isolated from the caribean deep sea sponge.

Family: Corallistidae

Chemical constituent: keto aldehyde, acetylene



Discodermolide

Uses: It is immunosuppressive agent, anticancer agent; it is also use to proliferative. [9, 10]

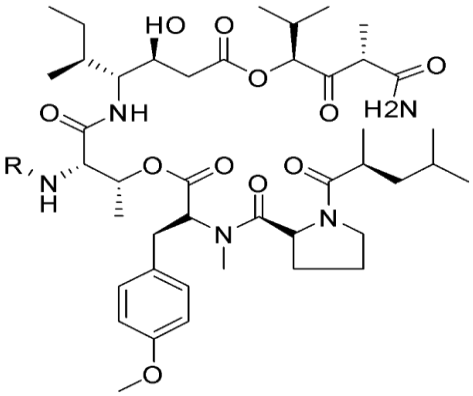
6. Didemnins

Synonym: Didemnin

Biological source: Didemnins is isolated from a tunicate of the genus trididemnum.

Family: Didemnidae

Chemical constituent: Protein, cyclic peptide, polyketide, peptide



Didemnins

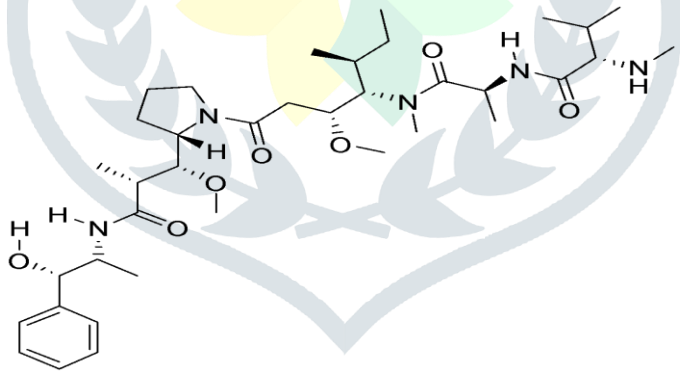
Uses: Didemnins is used as an antiviral, antitumor, and immunosuppressant activities [11].

7. Brentuximab vedotin

Synonym: Adcetris, Brentuximab vedotin

Biological source: Brentuximab vedotin it's obtained from gastropod mollusk *Dolabella auricularia.* **Family:** Didemnidae [28]

Chemical constituent: Nucleosides, Polysaccharides, Peptides, Alkaloids, Polyphenols, Diketopiperazines, Terpenoides, Polyketides.



Bretuximab vedotin

Uses: It is used as an antineoplastic agent, used in the treatment of Hodgkins lymphoma and systemic anaplastic large cell lymphoma. [12]

Extraction of marine anticancer drug

A] Extraction processes

Two extracts must be made in order to obtain anti-cancer chemicals from the above-ground marine specimen.

(1) Centrifugation is used to perform aqueous extraction.

(2) The organic solvent mixture DCM/MeOH is used to re-extract the drymarc (1:1).

B] Aqueous extraction by centrifugation

After the grinding and after all the dry ice has sublimated from the specimen, an aqueous extraction of a ground marine specimen is performed three to four days later. The ground specimen bag is taken out of the freezer, its contents transferred into a 4 L beaker, and enough milli-Q high purity water is added to create a mixture of roughly 3:1. Since being collected, the marine specimen has never been left unfrozen until now. Using a mechanical tool like the ConTorque motorized paddle stirrer, mixing is done inside a refrigerator at roughly 4°C for about 45 minutes, or until homogenous, ice-free aqueous slurry is achieved. It is necessary to prepare the centrifuge rotor by lining it with a strip of pre-cut Whatman 3 mm chromatography paper. The paper will stick to the rotor wall without bubbles or folds when it is firmly pressed against the rotor walls and saturated with high quality water. The aqueous slurry is slowly fed to the middle of the basket rotor while the rotor is spinning at 1200 to 1500 rpm and a 4 L flask in wet ice is prepared to receive the filtrate coming via the draining hose from the rotor catch-basin. The filtering process can be sped up by increasing the rotor speed, however speeds beyond 2000 rpm are rarely necessary and could compress the filter cake, reducing the flow rate. Set the rotor speed for this kind of rotor over 2500 rpm. Aqueous extracts, which are typically 3 to 5 L for a 1 kg specimen, are put into stainless steel trays that can be used for freezing and freeze-drying and are labelled with a barcode. The filter paper with the compressed tissue attached is taken out of the rotor and placed in a dish with the appropriate label. The aqueous-soluble extract and marc plus paper are lyophilized after being frozen in -40°C "sharp" freezers. When the ice cake is 3 cm thick, freeze-drying of marine aqueous extracts and marcs normally takes 5 to 7 days. The aqueous Extract is weighed after being freeze-dried and transferred into borosilicate bottles, and an aliquot is obtained for screening. Additionally weighed, the drymarc is extracted again using DCM/MeOH. The extraction of an organic solvent for screening. During centrifugation, a number of issues could arise, including ripped paper, clogged paper, and marc material getting into the receiving flask. A new filter paper is then put in the rotor, centrifugation is restarted, and the aqueous fraction is passed through the filter paper a second time after the torn paper and marc have been removed and placed in a dish with a label. Scraping a blocked paper is frequently an efficient approach to restore filtrate flow, although caution must be exercised to avoid tearing the filter paper. With practice, one may be able to predict clogging issues based on the slurry's consistency (i.e., a challenging holothurian) and attempt to prevent them by using a filter assist (i.e. Celite). Some challenging, slimy materials can be filtered using a coarse pre-filter made of fibre glass that is placed on top of the paper filter inside the basket rotor. Sometimes nothing works, so the entire sample is lyophilized and frozen. In any event, all additional weights that have been added to the marc and will persist after lyophilization are recorded such as paper, fibre glass, Celite, etc., These aqueous extracts have salt in them, and saltwater is particularly corrosive to metal parts, therefore washing the equipment thoroughly and frequently is crucial. Cleaning and drying the basket rotor should be done carefully, being sure to get all of the residue out from under the rim. After finishing each specimen, the centrifuge's interior is rinsed and dried. After being emptied, glassware is promptly and thoroughly cleansed. Prior to being stored, all goods are thoroughly cleansed with high purity water.[13]

C] Drymarc is re-extracted by organic solvent

Immediately after being removed from the freeze dryer, lyophilized marine marcs are set up for extraction with an organic solvent; if this is not possible, they are then stored under vacuum. Spicules are not the potential irritants, but marcs that contain them can be quite harsh on the skin, similar to coarse fiber glass. In this extraction lab, handling marine marcs while wearing thick rubber gloves, a lab coat with sleeves fastened and a hood is regular procedure. It is also highly advised for anyone else who might be involved in the process. The dry weights of the aqueous extract and marc are necessary in order to determine the possible yield that could be achieved from one of these Extracts, even though the wet-frozen weight of each Specimen had already been recorded in an earlier phase. As a result, the gross weight of the lyophilized marc in its container is determined by setting it on a balance. Then the marc is put into a percolator along with the filter paper. Returning the empty jar to the scale and subtracting its weight. The lyophilized weight of the marine tissue itself is calculated by subtracting the weight of the filter papers and/or filter aids from the gross weight. This weight is then recorded in the database. It is possible to estimate the weight that would have been obtained if the full, original wet-frozen specimen had been lyophilized by adding this weight to the weight of the lyophilized aqueous extract. From this, an estimate of the yield per kg from the initial collection and an estimate of the yield of an interest molecule from either a water extract or an organic extract can be determined. Any significant Marc clumps are broken up into smaller pieces and compressed inside the percolator to reduce the amount of solvent used.. Enough Add 1:1 DCM/Me OH to provide at least one inch of solvent coverage for the marc. In organic solvent, marine marcs often do not swell. The organic solvent is removed from the percolator after an overnight soak, and the marc is then coated once more, but this time with pure Me OH. The Me OH has been emptied and the organic solvent extracts have been evaporated to produce a Concentrate extract after another half-hour of soaking. Marine marcs extracted with organic solvents dry quickly without foaming. The concentrate is put into the proper storage bottles or vessel, where it is dried further using a high vacuum dryer. It is then weighed, and the weights of the recording of this dry extract. [13]

Marketed product of Marine Anticancer Drugs

Drugs approved as anti-cancer compounds and derived from marine compounds. [14]

Compound	Marine organisms	Chemical classes	Therapeutic use	References
Lurbinectedin	Tunicate	Alkaloid	Solid tumors	[15]
Trabectedin	Tunicate	Alkaloid	Solid tumors	[16]
Midostaurin	Tunicate/Actinobacteria	Indolocarbazole	Leukemia's	[17]
Plitidepsin	Tunicate	Peptide	Multiple myeloma	[18]
Belantama mafodotin	Mollusk/cyanobacteria	ADC/peptide	Multiple myeloma	[19]

Enfortumab vedotin	Mollusk/cyanobacteria	ADC/peptide	Solid tumors	[20]
Polatuzumab vedotin	Mollusk/cyanobacteria	ADC/peptide	Lymphomas	[21]
Brentuximab vedotin	Mollusk/cyanobacteria	ADC/peptide	Lymphomas	[22]
Eribulin mesylate	Sponge	Macrolide polyketide	Solid tumors	[23]
Fludarabine phosphate	Sponge	Nucleoside	Leukemia's, lymphomas	[24]
Cytarabine	Sponge	Nucleoside	Leukemias, lymphomas	[25]
Nelarabine	Sponge	Nucleoside	Leukemias lymphomas	[26]

Table no.1 Marketed Preparation Marine Anticancer Drugs

CONCLUSION

On a variety of tumour cell lines, including those generated from kidney, lung, prostate, bladder, melanoma, osteosarcoma, mammary, and lymphoid cancers, it has been discovered that a number of marine natural products have anticancer activity in vitro. Marine flora, which includes microalgae, fungi, seaweed, mangroves, bacteria, cyanobacteria, actinobacteria, and halophytes, is a crucial component of the ocean's ecosystem. To demonstrate the medicinally potent chemicals linked to the discovery of new anti-cancer treatments, reports on the bioactive molecules combating a variety of tumour cells, including those from the prostate, bladder, renal, lung, mammary, melanoma, bone, and blood cancers, were discussed here.

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