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# Potential of Marine Compound's as an Anticancer Activity

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**ABSTRACT**

A number of novel compounds, which are produced in the marine environment, have been found to exhibit the anticancer effects

Some marine organisms cytarabine, eribulin mesylate, brentuximab vedotin, and trabectidine have proved to be important producers of chemically active compounds with valuable bioactive properties, including anticancer. Thus, the ocean has proved to be a huge source of bioactive compounds, making the discovery and study of these compounds a growing area.

Cancer remains one of the most lethal diseases worldwide. There is an urgent need for new drugs with novel modes of action and thus considerable research has been conducted for new anticancer drugs from natural sources, especially plants, microbes and marine organisms. Marine populations represent reservoirs of novel bioactive metabolites with diverse groups of chemical structures.

This review highlights the impact of marine organisms, with particular emphasis on marine plants, algae, bacteria, actinomycetes, fungi, sponges.

**Keywords:**marine,microorganism,anticancer,clinical trial, eribulin mesylate, fucoxanthin.

## INTRODUCTION

Cancer is one of the most devastating and deadly diseases in the World. In 2020, more than 19 million new cases of cancer were reported globally, resulting in approximately 10 million deaths. The high rates of cancer incidence have been reported with the increased risk of age and lifestyle changes, which are becoming less and less healthy.[1,2]

The struggle for existence in a natural environment occasionally makes a species develop its own unique weapons such as speed, power, or even toxins. As these toxins possess biologically potent activity and unique modes of actions, these natural products have been regarded as a robust platform for further medicinal research.[3,4] Thus far, marine natural products have been particularly highlighted for their extraordinary bioactivity under highly diluted conditions.[5,6] marine natural products could have the powerful potential for drug discovery, there are also a few obstacles associated with them. First, it is rather difficult to secure a sufficient amount of these products for further study.[7] In most cases, the medicinal study of natural products requires a substantial number of test samples for elucidation of target protein/receptor and following signaling pathway.

Over the past decades, a large number of marine-derived compounds have been screened, and a wide range of activities, such as antiviral, antibacterial, antitumor, antidiabetic, and anti-inflammatory, have been reported.[8] According to the data of National Institutes of Health, the anti-tumor activity rate of marine compounds is far greater than that of terrestrial compounds.[9] To our best knowledge, cytarabine, eribulin mesylate, brentuximab vedotin, and trabectidine are marine-based drugs used against cancer. [10,11]

In terms of incidence and mortality, breast and lung cancers are the most common and are each responsible for more than 2 million diagnoses in 2020. The more frequent cancers in men are lung, prostate, and colorectum cancers, and lung cancer is responsible for more deaths (more than 1 million), followed by colorectum cancer. In women, breast cancer is the most frequent, followed by colorectum and lung cancers. In women, breast cancer has the highest mortality, with approximately 600,000 deaths. [12]

Furthermore, it is estimated that in 2040 the number of new cancer cases in the globe will reach 28 million, with mortality beyond 16 million. [13]

Cancer treatment can involve different therapies, such as surgery, chemotherapy, radiation therapy, and even immunotherapy.[14,15]

Currently, the development of drugs for the treatment of cancer has been widely studied.

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One of the primary sources of these drugs are natural compounds from plants and marine organisms.[16,17]
several natural products derived from marine sources have also been used in the prevention and treatment of various cancers, including leuckemia, metastatic breast cancer, soft tissue sarcoma and ovarian cancer.[18,19]

**Marine-derived natural products and their classification**

Oceans are vast and marine animals are the beginning of novel anticancer therapeutics for an enhanced cure and colossal chemical compound cluster assortment. Different chemical mixes from marine origin are isolated and amalgamated by manufactured methodology for cancer therapy.[20] In any case, marine sources are, as it were, unexplored for anticancer therapeutic drugs. Despite the way that various classes have been built up, thinking about their compound structures, the most outstanding MNPs incorporate different engineered classes of alkaloids from the marine algae, terpenes having varied structural diversity, peptides from assorted marine animals, polyketides with fascinating biological properties, and high molecular weight organic sugars. All these sorts of MNPs assume a primary job in the blend of anticancer medications dependent on their critical natural functions against unending lethal infections.[21]

**Marine natural products and origins of anticancer drugs**

A broad spectrum of pharmaceutically related bioactivities is demonstrated by MNPs. Marine microorganisms such as sponges, algae or corals and particularly marine bacteria and fungi have been shown to produce novel secondary metabolites (SMs) with unique and diverse chemical structures that can beessential to the production of anticancer drugs.[22]Anticancer drugs from the marine sources include prokaryotes, specifically marine bacteria such as Lactobacilli and Noctiluca scintillans, algae (seaweeds) that produce secondary anticancer metabolites, mangroves with anticancer metabolites and least explored flora for anticancer compounds, and other sorts of marine living things that retain moderately more than 70 % of the globe. Likewise, The biodiversity of the marine microflora and microalgae is widespread in the world's oceans, making up to an area of 90 % sea biomass.[23]Notwithstanding, a wide variety of bioactivities have been identified to evoke several MNPs and appear to be a fertile conduit for the generation of new cancer treatment drugs or drug leads.

| Chemical class | Compounds included | Pharmaceutical/Biological activity | Anticancer chemicals | Anticancer chemicals | Ref |
|---|---|---|---|---|---|
| Alkaloids | Pyridoacrines ; indoles; | anticancer; antimalarial& antimicrobial | Topsentin; tambjamine D, discorhabdines | Sponges; tunicates; | 9 |
| Polyketides | Macrolides; aromatic; compounds | Antibiotic; anticancer; antifungal; antiparasitic | Haloroquinone; | Sponges; ascidians; soft coralsand symbiotic bacteria | 24 |
| Polyphenols | Phenolic acids; flavonoids; anthocyanidins; tannins& gallic acid | Antioxidant; anticancer, antiviral; anti-inflammatory; inhibit human platelet aggregation; metal chelators | Scutellarein 4′ -methyl ether; phloroglucinal; ecol; phlorofucofuroecol A; diecol, and 8,8′ -Biecol | seaweeds; seagrass, and mangroves | 25 |
| Terpenes | Monoterpenes; sesquiterpene | Cytotoxic; antiproliferative; antimicrobial; | Caulerpenyne; usneoidols Z and E | Soft coral and sponges | 26 |

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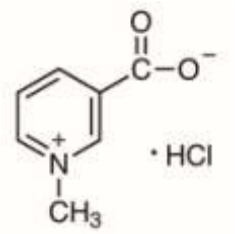
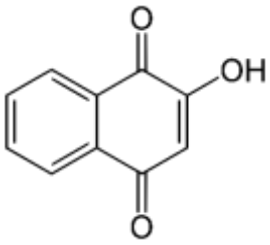
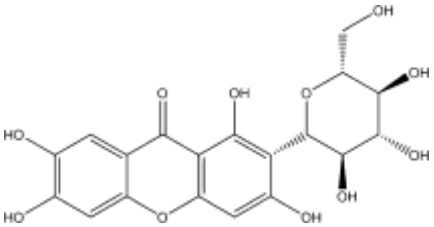
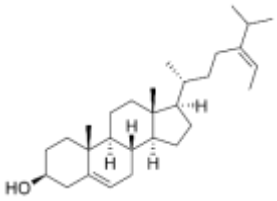
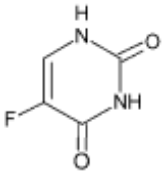
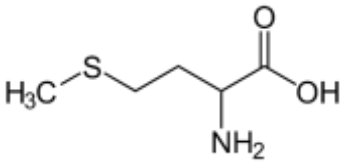
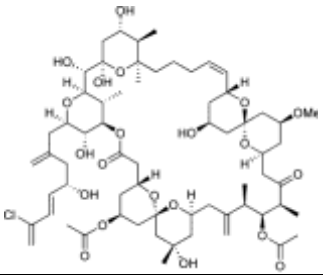
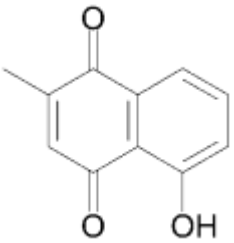
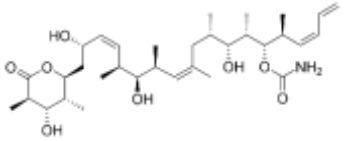
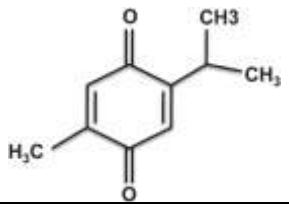
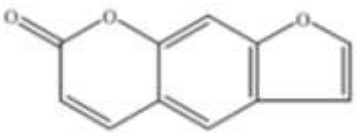
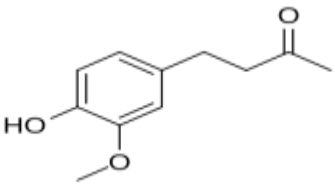
| | | | | | |
|---|---|---|---|---|---|
| | s; diterpenes; sesterterpenes | anticancer | | | |

**Structure of marine natural product:**

| | | |
|---|---|---|
| Trigonelline HCL  | Lawsone  | Mangiferin  |
| Fucosterol  | 5- flurouracil  | methionine  |
| spongistatin  | Plumbagin  | Discodermolide  |
| thymoquinone  | Psoralen  | Zingerone  |

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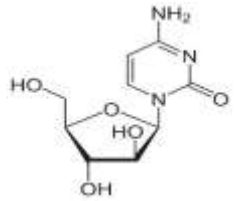
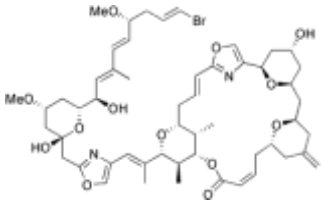
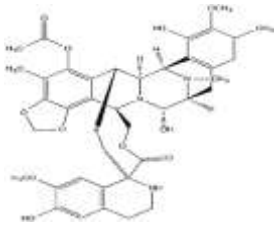
| Cytarabine | phorboxazole A | Trabectedin |
|---|---|---|
|  |  |  |

The highly complex structure of marine natural products frequently makes it very difficult to modify or synthesize them on a large scale.[27,28]In order to improve the biological activity of these products, both chemical modification and related structure-activity relationship (SAR) study of marine natural products are necessary.[29]
However, their highly complex structure hampers efficient modifications and any subsequent systematic research.[30]

**Eribulin mesylate :-**

Eribulin mesylate (E7389) is a microtubule inhibitor with a unique mechanism of action. Eribulin is a simplified synthetic analog of the marine natural macrolide halichondrin B. Halichondrin B, which has demonstrated antitumor activity, was first isolated from the rare Japanese sponge Halichondriaokadai.[31,32] Pharmaceutical production and clinical development of halichodrin B was initially limited by its natural availability.

**Drug summary:**

**Drug name** - Eribulin mesylate

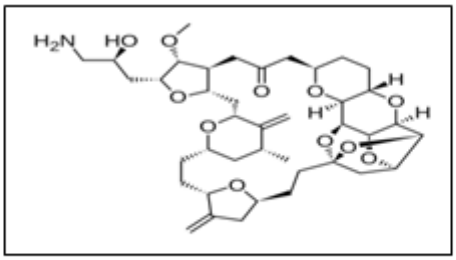
**Phase**- preregistration

**Indication**- Breast cancer

**Pharmacological description**- tubulin antagonist , Cell cycle inhibitor

**Route of administration** – parentral ,Intravenous

**Chemical structure-**



**Pharmacodynamics of Eribulin mesylate**

Most tubulin binding agents including the taxanes, epothilones and vinca alkaloids, inhibit both the shortening and growth phases of microtubule dynamic instability. By contrast, eribulin is thought to work mainly through an end-poisoning mechanism that inhibits microtubule growth without affecting microtubule shortening. This results in sequestration of tubulin into nonfunctional aggregates and ultimate formation of abnormal mitotic spindle that is unable to continue mitosis.[33,34,35]

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**Pharmacokinetics and metabolism of Eribulin mesylate**

Eribulin has been shown to demonstrate triphasic elimination with a slow to moderate clearance and a slow elimination. The terminal half-life of eribulin ranges in studies from 36 to 48 h. Pharmacokinetics seems linear and dose-proportional. Eribulin has a rapid distribution phase with a mean distribution half-life of ~ 0.43 h. Urinary elimination is minimal. Plasma area under the concentration--time curve and maximum plasma concentration were found to increase linearly over various dose ranges studied.[36,37]

**Fucoxanthin:-**

Fucoxanthin, a natural xanthophyll carotenoid, is generally found in edible brown seaweeds. This compound, together with β-carotene, is considered as one of the most abundant carotenoids in nature. This compound is a marine carotenoid exhibiting several health benefits.[38] Fucoxanthin has remarkable biological properties for human health.[39] It is known that fucoxanthin has antioxidant activity[40,41], antiobesity[42], antidiabetic[43], anti-inflammatory[44], anti-acne[45], neuroprotective[46], and anticancer activities.[47,48]

**Drug summary:**

**Drug name** - fucoxanthin

**Molecular Formula**

- $C_{42}H_{58}O_6$

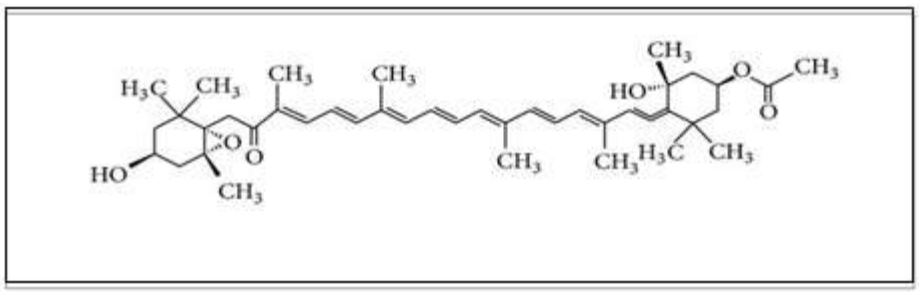
**Synonyms**

- Fucoxanthin
- all-trans-Fucoxanthin

**Molecular Weight**

658.9 g/mol

**Chemical structure**



**Fucoxanthin and its sources**

Fucoxanthin is a major marine carotenoid found in edible brown seaweeds such as Undariapinnatifida[49], Sargassum duplicatum and Sargassum binderi[50], Sargassum fulvellum[51], Fucus evanescens[52], Fucoxanthin is one of the most abundant carotenoids, and contributes more than 10% of the estimated total production of carotenoids in nature[53], especially in the marine environment[54].

Currently, the most common method for extracting the compound from a natural source is by liquid solvent extraction using hexane, petroleum ether, or toluene. For example, fucoxanthin has been extracted from Laminaria japonica using dimethyl sulfoxide[55] and ethanol[56], Undaria pinnatifida using acetone[57], chloroform/ methanol[58], and ethanol[59], Hijikia fusiformis[60], Eisenia bicyclis using acetone[61], Ishigeokamurae using methanol/chloroform[62], Sargassum hemiphyllum using ethanol[63], Sargassum binderi, Sargassum plagyofillum, Turbinaria turbinata and Padina australis using hexane/acetone.[40,64,65]

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