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Marine bacteria: A Pandora box against cancer

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Abstract
Due to their exceptional biocompatibility, bioavailability, safety and stability marine natural pigments have recently become a potent alternative in the food, cosmetic, and pharmaceutical industries. Numerous studies have demonstrated that marine pigments like chlorophyll, carotenoids, phycobiliprotein, melanin having an array of biological and biomedical applications, are frequently isolated from bacteria, fungi, algae and seaweed. The role of these potent pharmaceutical derivatives are seen to have antioxidant, antibacterial, anticancer as well as anti-inflammatory characteristics. Substantial reports over the last few decades have centralized on isolating and identifying new marine chemicals for their purpose as anti-cancer drug therapies. Because of their extraordinary antioxidant nature besides antibacterial activities, these therapeutic potential bacterial pigments can be harnessed and can be seen as a newer addition to prevalent anticancer drugs. A number of erstwhile reports have thrown much light regarding marine pigments that includes -carotene, fucoxanthin, astaxanthin, violaxanthin, halocynthiaxanthin, lutein, zeaxanthin, canthaxanthin, peridinin, and phycocyanin derivatives which exhibited potent anti-proliferative effects against breast and colon cancer cell lines by inducing apoptosis, fragmenting DNA, and arresting the cell cycle. Thus this review concentrates on these microbial pigments that can open newer avenues against the curse of cancer.

Keywords: Marine pigments, anticancer, anti-inflammatory, antioxidant

Introduction
Majority of the marine bacteria are known for their association with the wide variety of pharmaceutical functions (Dewapriya *et al*. 2014) [1]. The marine biological system increasingly acknowledged as a source of potential natural compounds (Abdelhamid *et al*. 2020) [2]. These pigments are produced on standard microbial growth conditions. The quorum-sensing system appears to be a mediator in the production of these pigments by micro-organisms. The need for new sources of environmentally benign natural goods, such bacterial pigments, for various biomedical and industrial uses has recently expanded as a result of research on natural products and microbial ecology science. Carotenes are polyunsaturated hydrocarbons which can have 30, 40, or 50 carbon atoms in a single molecule. Melanins are polyphenolic colors that are created by the processes of hydroxylation, oxidation, and polymerization from phenolic compounds. Quinones are aromatic chemicals having ring structures that range in color from yellow to red. Tambjamines are yellow-colored alkaloid substances (Ramesh *et al*. 2019) [3]. Violacein a marine pigment produced by *Chromobacterium violaceum*, can be cited as an important pigment having noted pharmacological properties (Williams *et al*. 2009) [4]. A stable free radical called 1, 1-diphenyl-2-picrylhydrazyl (DPPH) was used to assess the reactivity with oxygen and nitrogen reactive species.]. The anti-microtubule medicines dolastatin A and curacin A, which entered preclinical and clinical trials and served as lead structures for the creation of a variety of synthetic analogues with substantial anticancer activity, are prominent examples of chemicals derived from cyanobacteria (Williams *et al*. 2009) [4]. Prodigiosin is distinguished by its alluring crimson hue. It is made by a variety of microorganisms, including *Serratia spp*. It is a tripyrrole-structured pigment that is cell-associated. As a result, it is regarded as a versatile secondary metabolite. Additionally, it can be utilized as a dye in the textile industry (Pérez *et al*. 2016 & Metwally *et al*. 2021) [6, 5].

In response to ecological pressures including competition for space, predation, and tide changes, marine organisms develop complex secondary metabolites. Developing alternative antimicrobial medications that are less expensive, less toxic, and not susceptible to the microbial defense mechanisms of traditionally used therapeutics is being driven by the emergence of drug-resistant microorganisms, meeting various priorities being antioxidant, anti- inflammatory, anticancer compounds (Gomes *et al*. 2022) [7].

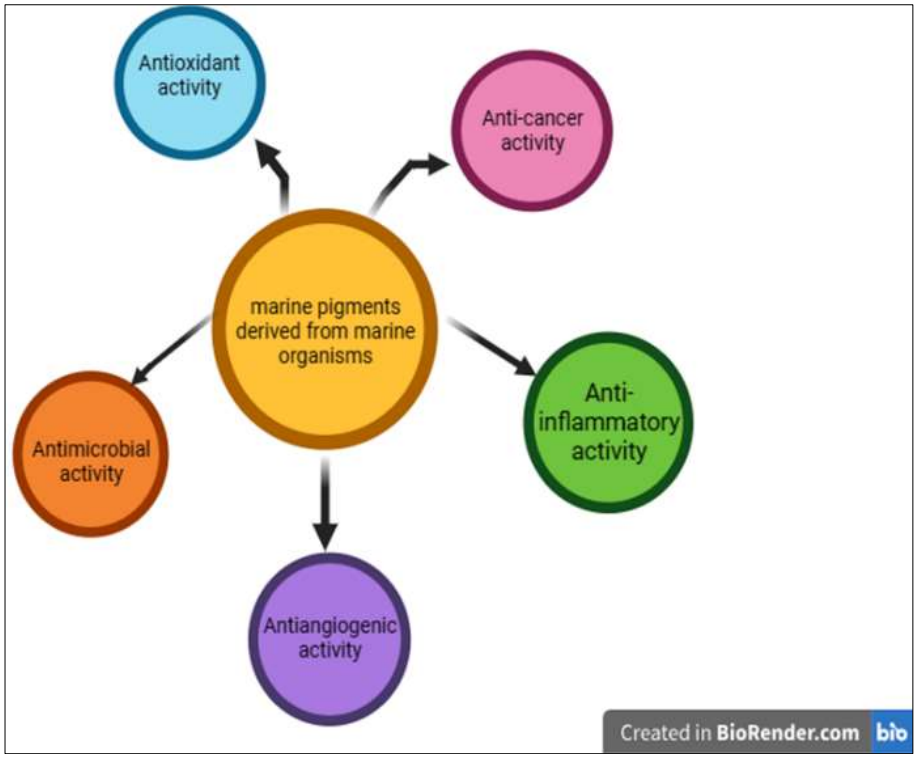

Fig 1: Varied properties of pigments obtained from marine bacteria (Image created through Biorender)

Marine Bacteria derived pigments: A hub of pharmaceutical agents

Free radicals are created during the oxidation process, which also involves the exchange of oxygen or hydrogen atoms or electrons and tissue damage. In general, free radicals have unpaired electrons and are reactive chemical entities (Atoms, molecules, or ions). They are either formed exogenously as a result of stimulation by pollutants, heavy metals, tobacco, pharmaceuticals, radiation, etc., or endogenously as a result of metabolism in living cells. Any substance that prevents the oxidation process by stifling a free radical reaction is an antioxidant. Antioxidants work by neutralizing excess free radicals in the body to protect biological systems from the harmful side effects caused by metabolism, such as highly reactive free radicals. It is evident that a wide variety of marine microorganisms like seaweeds, cucumbers, fishes, and invertebrates-sponges, soft corals, crabs, and crustaceans and micro-organisms like microalgae, bacteria, and fungus may produce compounds with antioxidant activity (Vladkova *et al*. 2022) [8]. An array of marine microalgal species is still left to fully explore in search of brand-new medicinal chemicals (Manochkumar *et al*. 2022) [9]. Astaxanthin,β -carotene, lutein, and lycopene are the most significant carotenoids on the worldwide market out of the more than 1000 natural carotenoids that have been discovered to date. Numerous studies have shown that astaxanthin has better antioxidant activity than other carotenoids. Additionally ketocarotenoids, in particular hydroxylated astaxanthins, have antioxidant effects on both human and animal health. Many astaxanthin-producing bacteria, including *Brevundimonas* sp. strain SD212, *Paracoccus bogoriensis*, and *Agrobacterium aurantiacum*, have been identified from natural habitats (Liu *et al*. 2020) [10]. Actinomycetes are a group of marine bacteria that are particularly good at producing bioactive substances with a variety of biological activities, including anticancer, antibiotic, immunosuppressive, antioxidant, antiviral, and enzyme inhibitory characteristics (Shyam *et al*. 2021 & Fahmy *et al*. 2021) [11, 12].

Marine organism fighters against cancer

A wide variety of marine organisms produces a number of pigments that have marked anti-inflammatory which has gained wide spread prominence for their use as anticancer agents. Examples can be cited of *Chromobacterium* derived violacein, a blue coloured pigment well known for their cytotoxic behaviour against cancerous cells (Konzen *et al*. 2006) [13]. Melanin is a polymeric pigment of natural origin that is widely distributed among many living organisms through its excellent biocompatible nature along with other properties like anti-inflammatory, rich anti-oxidant and anti-proliferative activities. (Marcovici *et al*. 2022) [14]. Chemotherapy, phototherapy, immunotherapy, and gene therapy are among the cancer treatments that make use of naturally occurring melanin and melanin (Mavridi-Printezi *et al*. 2023) [15]. The anticancer capabilities of melanins had been reported from various sources. Breast cancer (BC) is the most common cancer in women diagnosed globally, and it is also the leading cause of cancer-related deaths in women. The high frequency and mortality of BC, as well as the shortcomings of current preventative and therapeutic strategies, increase the urgency and need for the

development of innovative medications. Chemotherapy resistance results in cancer growth and metastasis, making it one of the biggest management problems for cancer and a leading cause of cancer-related mortality. Different secondary metabolites found in sponges are thought to have anti-tumour properties. Stylisin has been isolated from the genus *Stylissa* and has been shown to have antioxidant qualities as well as cancer cell cidal activities. Human Immunodeficiency Virus Type 1 (HIV-1) is inhibited by Compounds like debromohymenialdisine (DBH), hymenialdisine (HD), and oroidin that were isolated from *S. carteri* are seen to inhibit HIV Type 1. Human glioma and neuroblastoma cells are killed by the *Scopalina ruetzleri* ethyl acetate fraction (Bashari *et al*. 2019) [16].

Antioxidant properties of marine pigments

Because of the intramolecular non-covalent electrons, which are easily able to interact with free radicals like melanin is a potent antioxidant. It has been demonstrated that melanin considerably elevates the functional potential of antioxidant enzymes that could alter the release of lipofuscin in the central nervous system delaying the onset of aging (Ghattavi *et al*. 2022) [17]. Natural marine pigments with significant antioxidant capabilities include carotenoids, chlorophylls, and phycobiliproteins. Pheophorbide A, a chlorophyll derivative from the green seaweed species *Enteromorpha prolifera*, has been shown to exhibit antioxidant characteristics. It possesses significant radical scavenging of hydroxyl ions, DPPH like radicals thus making it a good antioxidantIt has been hypothesized that the majority of phycocyanin's antioxidative action is caused by phycocyanobilin, which may excel as a potent antioxidant in the living system. (Manivasagan *et al*. 2018) [18].

Conclusion

In this article, several therapeutic properties of a wide array of marine species producing primary secondary metabolites possess potent antioxidant, anti-inflammatory, anti-cancer, anti-angiogenic, and antimicrobial activities which can be widely used in medicinal and therapeutic purpose. Fatal diseases can be cured by this various marine derived compounds, with their respective mechanism of actions. These marine natural pigments, carotenoids, lipids, polysaccharides which are efficient to combat with the various prevalent forms of cancer in the colon, stomach, liver, cervical, prostrate, breast, lung cancers. Pigments derived from seaweed, sponges, algae derived pigments and metabolites which have a strong anti-inflammatory properties as well. These pigments can therefore be an alternative choice over the conventional use of chemotherapeutic drugs to mitigate the chance of side-effects and to be a cost effective drug strategy.

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