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THE ROLE OF MARINE COMPOUNDS IN IMMUNOMODULATION

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Abstract
Marine animals have a wealth of biologically active compounds that can be used to cure and prevent a variety of illnesses, including cancer, inflammation, immune system problems, and others. One advantage of studying marine life is that it can show a vast array of biodiversity and the chemical diversity of marine natural products. Numerous investigations have concentrated on marine substances that may have pharmacological uses, such as immunomodulators, for the treatment of immune-mediated illnesses and cancer.Immune system modulation is any change in the immune response that could result in the induction, expression, amplification, or inhibition of any immune response phase. Studies frequently focus on the impact of chemicals produced from marine sources on macrophages and lymphocytes by monitoring the release of mediators (cytokines) using the immunological technique enzyme-linked immunosorbent assay (ELISA), Western blot, immunofluorescence, and real-time PCR. The main sources are fish, mollusks, sponges, bacteria, microalgae, macroalgae, and corals. The compounds originating from marine sources that have been discovered as possible immunomodulatory medications within the past three years are the main topic of this review.
Keywords: marine organisms, immunomodulatory activity, inflammation

1. INTRODUCTION

Seventy percent of the earth's surface is made up of the sea, which is known for its vast variety in terms of species and the natural resources it may offer [1]. There are between one million and 700,000 species in the world's oceans, according to recent reports, yet just a small portion of all marine organisms are now being examined for their possible bioactivities. It has been demonstrated that a wide variety of molecules for natural defense and communication, as well as possible bioactivities against human illnesses, are produced by marine species[2]. Compared to molecules having terrestrial origins, marine-derived products have a significantly higher biodiversity. Many researchers and businesses interested in preventing and treating human diseases have taken notice of this. The food, cosmetic, pharmaceutical, and aquaculture sectors already make use of marine chemicals. Applications for biomaterials and bioenergy have also seen recent advancements [10]. Since the action mechanisms of chemotherapy and radiation therapy can occasionally be non-specific and cause side effects in patients, it is necessary to search for novel, non-toxic substances from natural sources for the treatment of cancer. In the past ten years, a variety of diseases, including cancer, have been prevented and treated with innate and adaptive immune-stimulating agents[4].

Anticancer medications made from marine sources are used commercially, and numerous others are undergoing clinical studies. Immunomodulation is the term for procedures used to modify and/or control the immune response for medical reasons[6]. Immunomodulators are chemicals that affect the immune system; they are basically categorized as immunostimulants and immunosuppressants[8]. Epidemiological data from around the world indicate that the estimated prevalence of immunological diseases has gone up. By 2026, it is anticipated that the current 4.1-billion-dollar global market for autoimmune disease diagnosis would have grown to 6.3 billion dollars[9]. This has sped up the search for a class of chemicals, usually immunomodulatory, that can either strengthen or weaken the immune response in immunologically mediated diseases[3]. Because they draw and encourage additional cells to the afflicted location, activated macrophages produce cytokines that promote inflammatory responses and are crucial for the host's defence against tumor cells and infectious illnesses. Conversely, uncontrolled and persistent inflammatory reactions harm the host and contribute to the emergence of nearly all inflammatory illnesses, including metabolic diseases[11].

2. REVIEW OF LITERATURE

Investigations have been carried out by measuring the cytokine expression level of TNF-α and interleukins, and macrophages have been utilized extensively to evaluate the immunomodulatory activity of bioactive natural products. Most typically, experiments examine how sea-derived substances affect macrophages and lymphocytes, and they quantify the release of mediators (cytokines) using Western blot, immunofluorescence, real-time PCR. Scientists can estimate the expression of a particular transcript by using PCR alone, but they are unable to determine if the transcript is being translated into protein.Therefore, using a range of techniques to further identify the immunomodulation process is crucial[12]. Numerous research studies and projects have been conducted to find novel immunomodulatory actions, and numerous articles [15]. 2019 saw the publication of both reviews. Because of the scientific community's interest in the topic, numerous new investigations have been carried out after the reviews were published. Gathering current data on marine creatures' immunomodulatory activity, including observations of both pure substances, is the aim of the current review. Finally, our overview discusses emerging research areas and trends[14].

Fungi are often said to produce anti-inflammatory chemicals. It has been demonstrated that some fungi promote immunity, have anticancer effects, and fortify the immune system after chemotherapy and radiation have weakened it. Polysaccharides, which are substances that are increasingly being acknowledged for their probiotic qualities and for the therapy of immunological problems, have also been shown to be found in fungi[16]. YCP, an α-D-glucan found in the mushroom mycelium, has a wide range of immunomodulatory effects via affecting T cells and dendritic cells in vitro, activating macrophages in vitro, and increasing phagocytotic activity in vitro and in vivo[18]. YCP was recently administered orally to mice that had acute colitis caused by dextran sodium sulphate (DSS). At seven days, the YCP was effective in restoring mucosal damage, lowering intestinal immunological homeostasis, and alleviating the clinical signs and symptoms of colitis in mice. Additionally, DSS caused the colon to overexpress the pro-inflammatory cytokines IL-1β, IL-6, and TNF-α; however, the YCP stopped this from occurring.

The injured tissues were restored as a result of the substantial increase in tissue concentrations of IL-10 and IL-22. All things considered, the marine fungus YS4108's α-D-glucan YCP may be used as a treatment for ulcerative colitis. promoting the growth of human mesenchymal stem cells (hMSCs) by bioprospecting a vast library of extracts from Irish deep-sea species using high-throughput drug screening technologies.

3. MATERIALS AND METHODS

The library also contained filamentous fungus, which at 6.8% reduced the inflammation caused by activated macrophages. The extracts have actually considerably decreased the synthesis of pro-inflammatory cytokines such as TNFα and IL-1β, and they might be helpful in the hunt for anti-inflammatory medications. The misuse of antibiotics, antiseptics, and anticancer medications has led to the development of multidrug-resistant microorganisms, which is a major environmental problem [5]. The accumulation of chemical and antibiotic residues in the environment is upsetting the natural balance between plants and animals. Probiotic bacterial strains have been shown to exhibit antibacterial action against a range of infections. One such strain is a novel marine bacterial isolate that has been identified as a probiotic candidate for promoting environmental adaptability and host immune system stimulation against disease, both of which can be measured using murine macrophages. According to the World Health Organization, probiotics are live bacteria that, when consumed in sufficient quantities, offer health advantages such increased immunity, illness prevention, stress tolerance, better digestion, and improved absorption of nutrients. Their broad evolutionary and adaptive diversification into a variety of conditions and harsh habitats, along with their ease of collection and reference culture, making them particularly attractive targets for the search for immunomodulating chemicals to be novel drugs.

Furthermore, it has been observed that a variety of microalgae have immunomodulatory properties in both animal and human models. Specifically, it has been demonstrated time and over again that marine microalgae

polysaccharides have a strong immune-boosting effect. Because polysaccharides are highly bioactive compounds that often exhibit little toxicity, they have attracted special attention. It has been discovered that marine microorganisms, especially microalgae, are good environmentally sustainable producers of polysaccharides. have additionally shown a correlation between the molecular weight of the polysaccharides and their immunomodulatory properties. [13]. For instance, it was demonstrated that the microalga's low-molecular-weight exopolysaccharides and extracellular polysaccharides exhibited superior immunomodulatory properties. In the watery media, the microalgae release exopolysaccharides. A ccording to a 2022 in silico study employing molecular docking. The researchers' objectives were to look into the immunomodulatory properties of microalgal pigments and provide an initial indication of how they affect the human immune system. Van der Waals contact is the main mechanism by which the pigments adhere to the protein.

Consequently, these associations suggest that there is interaction between the protein and its receptor. When the binding energy is reduced, the ligand-protein binding is more beneficial. Researchers discovered that β-carotene has the lowest binding energy with IL-6, with a binding energy of -7.9 Kcal/mol. Dysregulation of IL-6 can lead to autoimmune disease and chronic inflammation. Finding compounds that can immunomodulate and inhibit the NF-kB pathway will come from research on natural compounds that can inhibit NIK. Similarly, the pigment found in microalgae may help control the immune system and prevent or reduce chronic inflammation. Recently, the effects of β-glucans isolated from the microalga Sphaerodactylus tirocinium have been evaluated after being administered as nutritional supplements to seabream Sparus juveniles. A fish species that is widely prized for aquaculture in Europe, and a marine diatom that is rich in numerous health-promoting compounds, such as β-glucans [7]. These polysaccharides can also act as prebiotics by binding particular cell receptors, which promotes the growth of the commensal microbiota and directly activates the innate immune system. These recurring patterns, known as pathogen-associated microbial patterns (PAMPs), are detectable by host-cell pattern-recognition receptors (PRRs) and are conserved with bacterial lipopolysaccharides (LPS). Once identified, they have the ability to trigger inflammation and start the host's innate immune cells to become active. High-intensity fish farming increases the risk of opportunistic bacterial infections, which can lead to a disease that compromises immune function.As previously documented in other research where β-glucans were given orally, young sea bream Sparus aurata were recently fed β-glucans generated from microalgae for two weeks, which increased their immunological parameters and resistance to infections.

The majority of these microalgal compounds boost the immune system by activating APCs, which serves as a vaccine adjuvant. Overall, the species of microalgae that produce immunomodulating molecules are still poorly understood and need more research.

4. RESULT AND DISCUSSION

The current included the latest immunomodulatory chemical compounds that were isolated from marine microorganisms. Numerous investigations into the identification and isolation of marine-derived chemicals with biological—more specifically, immunomodulatory—activity have been carried out in recent years. Fish, corals, bivalve mollusks, and other sea creatures are among of the most well-researched active animals of the past few years. These marine species are occasionally used as food, and it is frequently demonstrated that certain peptides that are isolated have anti-inflammatory and immunomodulatory properties. It is claimed that all of these peptides produced from diet exhibit immunoregulating effects on the immune response.It has also been shown that marine invertebrates, including sponges, echinoderms, and bivalve mollusks, are a significant source can be used to treat cancer, immunodeficiencies, and infections [17].

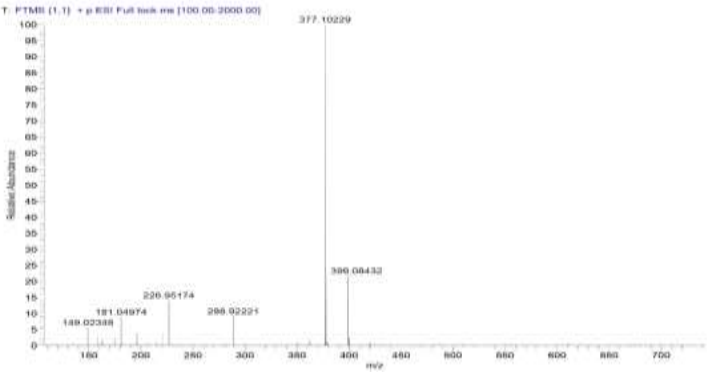
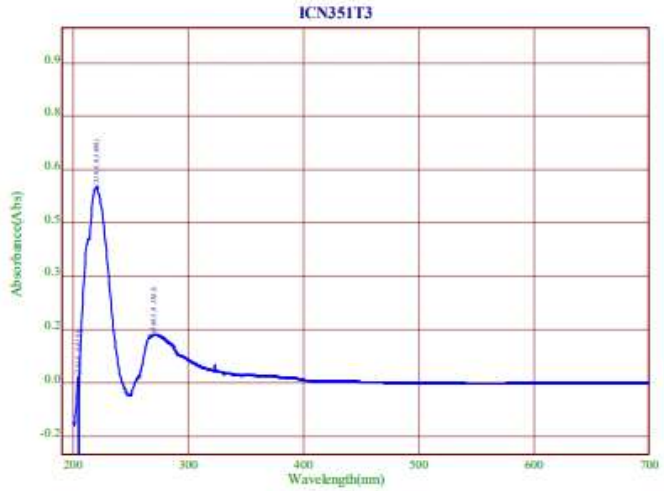


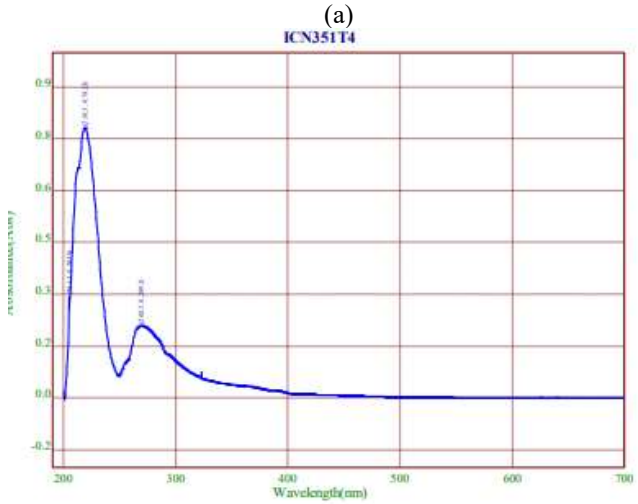
Figure 1: Electro spray ionization high resolution mass spectra

Due to its high nutritional value, oysters, a marine bivalve mollusc that lives along the coast, are frequently consumed as food. In this work, they assessed how oyster peptides (OPs) regulated the immunity of intestinal microbiota and mucosa in immunosuppressed mice that were given the anticancer medication cyclophosphamide (Cy). The body's first line of defense against potential environmental damage is the immune system of the intestinal mucosa, which is made up of lymphocytes, macrophages, and plasma cells. Most significantly,

cyclophosphamide reduces sIgA levels, which are essential for intestinal homeostasis and immunological balance, while also destroying intestinal mucosa and bacteria. The most common bacteria in the intestinal flora, Firmicutes, are responsible for producing the short-chain fatty acids (SCFAs) acetic acid, propionic acid, butyric acid, and acid valeric acid. Metabolites called SFCAs may help the immune system develop normally.



(a)



(b)

Figure 2: UV spectrum of purified compounds

Additionally, it was specifically observed that animals injected with Cy and whose faces were given OP showed. Biochemical examination of the mollusks has led to the isolation of a large number of bioactive metabolites that are either produced by the symbionts, consumed through their meal, or produced by the mollusks themselves. Corals also contain compounds that affect the immune system. Throughout the second half of the 20th century, a great deal of research has been done on the chemical composition of coral mucus, the primary excretory product of hard (Scleractinia) and soft (Alcyonacea) corals. It is made up of different amounts of polysaccharides, lipids, and proteins.

5. CONCLUSION

Modern biotechnologies are searching for novel sources of bioactive molecules with potential uses in a variety of commercial sectors, including the pharmaceutical and nutraceutical industries, as a result of the growing need for new medications with natural origins. The range of high-added-value chemicals that have been identified from marine species has sparked a lot of interest in immunomodulation as a health application in recent years. Over the past few decades, several biologically active compounds have been extracted or purified from various marine sources for use in innovative therapeutic applications using a range of techniques and processes. These compounds have been shown to exhibit a wide range of effects, including antiviral, anticancer, antiallergic, anti-inflammatory, immunomodulatory, and antibacterial qualities.These substances typically possess the capacity to stimulate immune response cells, including natural killer (large granular lymphocytes), dendritic cells, B and T lymphocytes, and macrophages. There are a few studies on the direct immunostimulant action on fishes and one on mesenchymal stem cells. Different coral species have distinct mucus glycoprotein chemical compositions.

Recently, the polysaccharide PPA—which is thought to have immunomodulatory activity—was isolated for the first time from coral americana.

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