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THE ROLE OF MARINE COMPOUNDS IN CARDIOVASCULAR DISEASE TREATMENT

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Abstract
One of the most dangerous illnesses in the world is cardiovascular disease (CVD). Among the many adverse effects of the current treatment agent are bradycardia, arrhythmia, hypotension, and changes in various ion levels. In recent years, bioactive compounds derived from natural products—such as plants, microbes, and marine organisms—have gained prominence. Novel bioactive metabolites with a variety of pharmacological properties can be found in marine species. Sea-derived products including have shown amazing benefits against a variety of CVDs. The cardio-protective properties of marine-derived compounds against atherosclerosis, myocardial infarction, ischemic heart disease, and hypertension are currently given increased weight in reviews. In addition to therapies, the present state of sea-derived constituent usage, future prospects, and limitations have all been examined appropriately.
Keywords: marine drugs, CVDs, atherosclerosis, hypertension, myocardial infarction

1. INTRODUCTION

Among the most important human health issues worldwide are cardiovascular diseases (CVDs). It includes heart, vascular, cerebrovascular, and pulmonary circulation disorders that have greater incidence and recurrence rates [1]. The number of deaths from CVD is predicted to increase to 24 million by 2030, from 12.1 million in 1991 to 18.6 million in 2019. An estimated 135 million people are impacted by CVDs, which also cost USD 1.1 trillion. In 2019, CVDs accounted for approximately one-third of all deaths worldwide, killing 9.6 million men and 8.9 million women. 6.1 million of those murdered were in the 30- to 70-year-old age range. The country that caused the most deaths from CVD was China, which was followed by Indonesia, the US, India, and the Russian Federation. Globally, the percentage of men and women with CVDs is similar, despite the fact that women are more likely to die from these illnesses [2]. Numerous factors, such as diabetes, high blood pressure, hyperlipidemia, obesity, and smoking, might contribute to CVDs. However, the pathophysiology of CVDs is caused by mitochondrial dysfunction, which regulates the production of ROS.

Bradycardia, arrhythmia, hypotension, hypersensitivity, time-dependent effects, changes in potassium and sodium levels, and surgical complications are among the serious side effects that they are linked to. Low toxicity, lack of immunosuppression in CVD patients, and lack of multidrug resistance are characteristics of marine medications [10]. Because of their many biological activities, natural origin, and acceptable safety profile, marine natural materials are more feasible to use for CVDs. Marine natural goods are consequently more recent arrivals to the market to lessen the adverse effects of synthetic medications for CVDs and related conditions. Pharmaceuticals made from marine sources are better than other substances because they are less dangerous, have a greater range of chemicals, are more reasonably priced, and have shown therapeutic benefits [3]. The potential of marine natural products (MNPs) in medicine research is widely recognized, particularly in terms of enhancing current medications.

Most of the 28500 MNPs discovered up until 2016 showed anticancer and cytotoxic qualities. Numerous creatures with diverse physiologies and capacities for environmental adaptation can be found in the ocean as a natural home[2]. There are currently 32 animal phyla in the marine environment, 15 of which are exclusive to the marine environment out of the total of over 33 animal phyla. The oceans support more than 80 percent of all plant and animal life on Earth. In addition to marine bacteria, bioactive chemicals are present in sponges, tunicates, fish, soft corals, nudibranchs, sea hares, opisthobranchs, mollusks, echinoderms, bryozoans, prawns, shells, and sea slugs. There are many different types of new bioactive chemical structures with great therapeutic promise in marine environments. These molecules are complex by nature, and the physical and chemical conditions of the water promote their formation.

REVIEW OF LITERATURE

Since ocean invertebrates have become so vital in practice medicine, they have been researched extensively to unlock their applications. Therapeutic or medicinal activity and the processing and supply of materials were all recorded in previous texts. Some invertebrates found in the marine environment have been employed in drink, liquid forms, powdered foods, soup, and in the form of fresh or dried meat. Chinese medicine has also provided inputs into the research on sea drugs [9]. Local diaries, bibliographies, ancient prescriptions, dietetic prescriptions, and folk recipes have all aided us to acquire a thorough comprehension of marine drugs and other living things. Chinese marine Materia medica contains the aforementioned records as well as those that follow. The bioactive compounds are effective in cancer treatments that target cancer cells because they are specific to a certain target[4].

Hypertension, the most hazardous of all cardiovascular disorders, contributes significantly to chronic renal disease, ischemic heart disease, stroke, dementia, and other CVDs. Age-standardized prevalence estimates show that 32% of women and 34% of men aged 30 to 79 worldwide suffered from hypertension in 2019. Numerous marine natural products, such as bioactive chemicals, chito-oligosaccharide (COS) derivatives, and phlorotannins, have been produced by marine animals. These items are converted into nutraceutical drugs to treat hypertension and are used as leads for ACE inhibitors. In order to avoid some serious side effects, marine natural ACE inhibitors are recommended as substitutes for synthetic drugs. They also have a high potential for becoming innovative therapeutic drugs to treat hypertension. In a culture setting, high-level marine proteins that are used to treat hypertension are typically proteolyzed to produce biopeptides, also referred to as fish protein-derived ACE-inhibitory peptides. These two peptides have been shown to have ACE binding and inhibitory action by in vitro and in silico molecular docking investigations [5].

Alginate oligosaccharides (AOS), one of the most researched marine-derived substances, inhibit P-selectin to alter the hemodynamics of pulmonary hypertension in the rat model of monocrotaline (MCT), reduce vascular luminal area, and prevent perivascular inflammation. Omega-3 Q10, a polyunsaturated fatty acid (n3-PUFA) supplement, appears to lower diastolic blood pressure and associated hypertension symptoms in older persons more than soybean oil supplementation, according to another study. In addition, Sámano MJ et al.'s controlled trial research assessed how ACE medications and the filamentous, gram-negative cyanobacterium Spirulina (Arthrospira) maxima affected endothelial damage and oxidative stress in SAH patients.

2. MATERIALS AND METHODS

Furthermore, there are a few of the main causes of atherosclerosis. However, through controlling the formation of plague, thermo-inflation plays a vital part in the pathophysiology of atherosclerosis. A number of medications with marine origins have been researched to prevent thrombo-inflammation in cardiovascular diseases. It was discovered that the fungus Amphichorda feline (Beauveria feline) contains another cyclodepsipeptide marine chemical called Isaridin E, which inhibits platelet activation, aggregation. It has no effect on platelet aggregation caused by collagen or thrombin. In a mouse carotid $FeCl_3$ model, isaridin E demonstrated dose-dependent antithrombotic activity without prolonging the bleeding period. By reducing blood lysis time, raising H_2O_2 expression, and releasing H_2O_2 with PGI_2 production induction, F-fucoidan (FD), a polysaccharide produced from the brown algae Laminaria japonica, may benefit patients with CVD. It also has an antithrombotic impact. n-3 Ocean-derived sources of omega-3 polyunsaturated fatty acids contain PUFA, which has anti-thrombotic and anti-atherosclerotic properties and may ideally prevent heart failure by lowering the risk of ischemic heart disease

[12]. Coronary artery blockage produces MI, which results in a shortage of oxygen and nutrients as well as the permanent necrosis and death of cardiomyocytes. Among other CVDs worldwide. Marine-based metal nanoparticles are being used in a novel way to treat myocyte repair and thrombus dissolution in myocardial infarction. Gold nanoparticle (GNP) anti-myocardial infarction activity was a novel approach that involved the preparation of the two. At 5 g/kg, DHA was demonstrated to have a protective effect against MI in in vivo research using a rat model[6].
Insufficient coronary artery perfusion to the myocardium causes IHD. The pathogenesis of IHD is mostly caused by endothelial dysfunction. IHD is the leading cause of morbidity and mortality among all CVDs. According to research from 2016, it is the cause of 9 million deaths worldwide. Because of its affective action and superior results, marine medications are superior to synthetic ones while treating IHD. The sodium form of echinochrome A is comparable to histochrome, a marine medication that mimics a typical sea urchin pigment. When used with patient-derived human CPCs to treat heart disease, this incredibly safe and efficient cell-priming agent prevents cardiac progenitor cells (CPCs) from undergoing cellular apoptosis by upregulating Bcl-xL and B-cell lymphoma 2 (Bcl-2) proteins and downregulating Bax cleaved caspase-3 and phosphorylated histones. In vitro studies of echinochrome A (Ech A), a naturally occurring color produced from sea urchins, revealed that marine anti-thrombotics, such as sulfated polysaccharides, were important due to their distinct mechanisms of action and bleeding-free effects. They have new ways to function as antithrombotic agents because of the strong negative charge that sulfation imparts, which enables them to interact with proteins and molecules involved in crucial biological processes like coagulation. Furthermore, the polysaccharides Fucoidan from brown algae and Enteromorpha prolifera polysaccharides (EPPs) from green algae both show anti-oxidant, lipid-lowering, and antiangiogenic properties. Alginate (ALG), mostly obtained from brown seaweed, is a useful treatment for coronary artery disease because it can increase HDL-C and lower serum levels of TC, TG, and LDL-C [14]. Among the carotenoids, fucoxanthin from brown algae is one such chemical that inhibits oxidation and fat buildup. Fucoxanthin controls metabolic syndrome to prevent heart attacks. Once more, astaxanthin, another carotenoid, demonstrated a beneficial effect on heart attack by regulating several biological processes, including lowering inflammation, increasing oxidative stress, increasing antioxidants, and changing lipid and glucose levels by blocking the TLR4/NF-κB/ROS signalling pathway[7].

3. RESULT AND DISCUSSION

Valvular heart disease (VHD) is a collection of common cardiovascular disorders that accounts for 10–20% of all heart surgeries carried out in the United States. Heart valve issues include atresia (incorrect opening), stenosis (narrowing of the valve aperture), and regurgitation (flaps not closing) [13]. The seaweed microalgae Phaeodactylum tricornutum is the source of fucoxanthin, a marine carotenoid with anti-inflammatory and antioxidant properties. Chiang et al.'s study showed how dogs' cardiac valves and interstitial cells provide protection[15]. The findings showed that by modifying the Akt/ERK pathway, fucoxanthin treatment significantly decreased the amount of ROS produced by H2O2, DNA damage, cell survival, and the expression of protein-associated apoptosis and calcification[11]. The dog's E/e value and left atrium to aortic (LA/AO) size ratio, which indicate mitral valve inflow, leakage, and left ventricular diastolic dysfunction, were also improved by long-term (0.5–2 years) treatment.

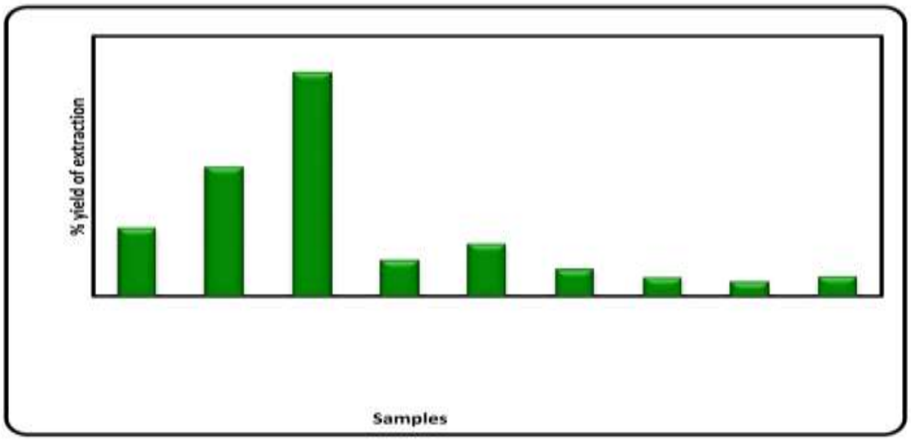

Figure 1: Percentage yield marine

The saltwater fish Gadus morhua is an excellent source of high-quality protein and the fat-soluble vitamins EPA and DHA. Because cod is a lean fish, its liver stores fat in the form of triacylglycerols. It has demonstrated cardioprotective properties against platelet aggregation and atherosclerosis. Triacylglycerols are lipids that are stored in the tissues of sardines (Sardina pilchardus), a common commercial fish in the Mediterranean [8].

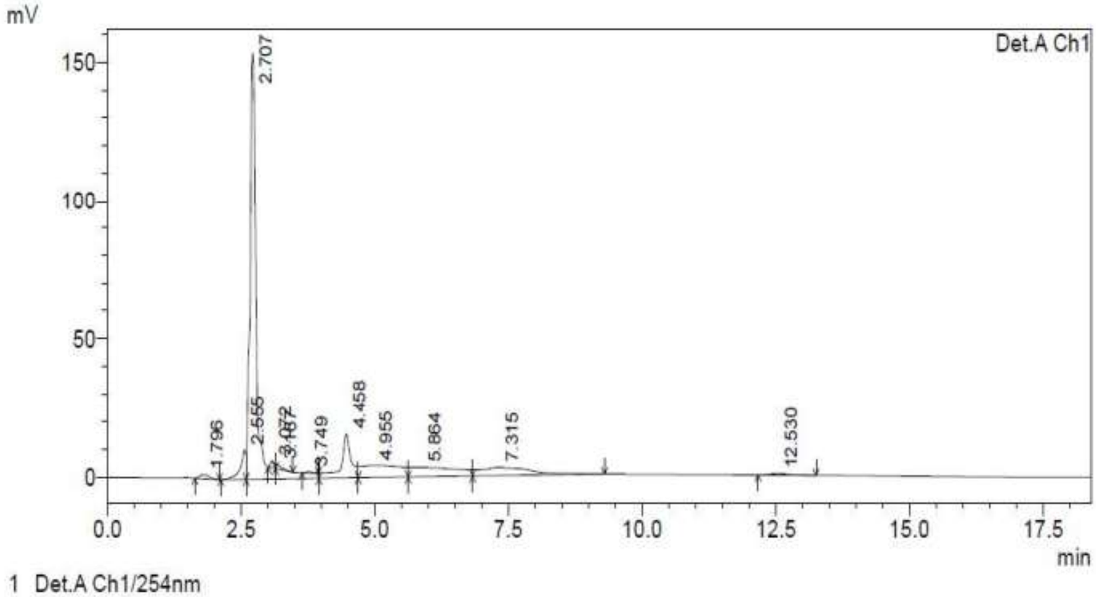

Figure 2: HPLC chromatogram of Fraction-1

It has been shown that dietary polar lipids derived from marine sources alter the phospholipid milieu in PAF cell membranes or directly or indirectly inhibit PAF from attaching to a particular PAF cell membrane receptor.

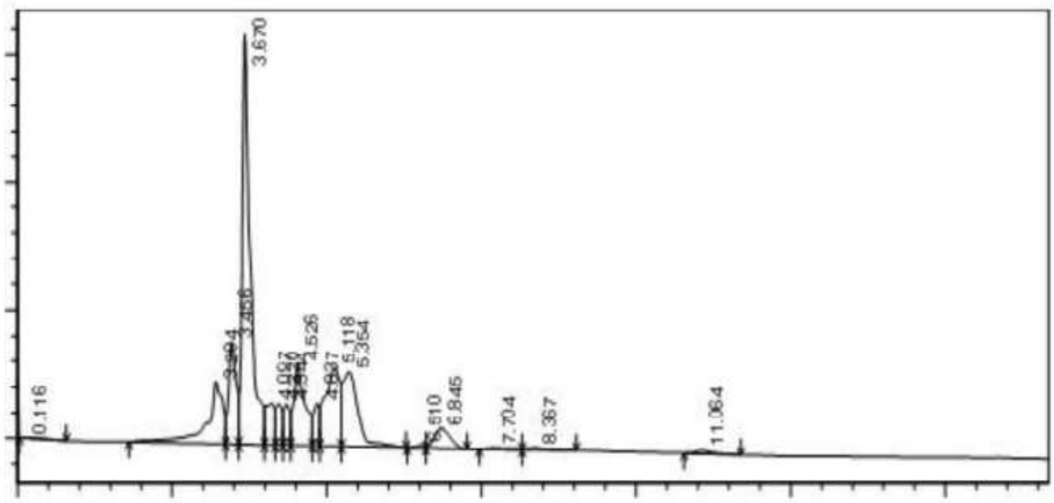

Figure 3: HPLC chromatogram of Fraction-2

These lipids provide a number of advantages, including the ability to block PAF formation and bring blood PAF concentrations down to homeostatic levels. By altering PAF metabolism and reducing PAF activity and concentration in the blood, polar lipids from gilthead sea bream (Sparus aurata) showed an anti-atherosclerotic impact.

4. CONCLUSION

In the pharmaceutical sector today, several synthetic medications are the most commonly utilized. For centuries, the pharmaceutical industry abandoned bioactive chemistry research in favor of generating synthetic compounds. However, since the early 2000s, research on natural chemicals has resumed, finding a place in studies related to biomedicine. One of the main factors driving this shift back to natural medicines is the greater biocompatibility of natural chemicals over produced pharmaceutical goods, even when taking into account the wide range of these molecules and their effects. Over the past ten years, research on marine compounds and their derivatives has increased in the fields of medicine and pharmacology. Without a doubt, one of the causes is the variety and number of secondary metabolites and accessible chemicals brought about by the waters' numerous unfavourable conditions and the almost infinite variety of organisms that call them home. Additionally, thousands of compounds of marine origin are added to the marine compound library each year. To find treatments for CVDs, these substances must be addressed. A nano-formulation process is also required to provide marine-based compounds that are the precise target of interest to eliminate unwanted effects. Unlike the original chemical, scientists can employ compounds derived from marine sources as direct leads to create new, more selective drugs. This implies that marine natural products can be used as a useful "library" of natural products to develop new treatments that enhance existing ones, boost the efficacy of prescription drugs, and have positive additive or synergistic effects on cardiovascular diseases.

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