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# PHARMACEUTICAL APPLICATIONS OF MARINE-DERIVED LIPIDS

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**Abstract**
Hyperlipidaemia (HLP) refers to an abnormally elevated blood lipid condition arising from dysmetabolism in lipids. In recent years, the frequency of HLP due to adverse dietary conditions has been growing with each passing year. Apart from this, pharmacological lipid-lowering drugs also in common practice have achieved greater improvement in circulating lipid levels with some side effects. Nonetheless, a range of physiological effects, including blood pressure, hypoglycemia, antioxidant, and antithrombotic properties, have been reported for the water's bioactive compounds. As a result, the hypolipidemic impact of marine bioactive substances with intricate and twisted structures has also gained attention. The therapeutic potential of marine-derived polysaccharides, unsaturated fatty acids, and bioactive peptides in HLP is the main focus of this investigation. Additionally, it provides a concise overview of the main ways in which these substances demonstrate their hypolipidemic effects in vivo.
**Keywords:** marine bioactive substances, hyperlipidaemia, lipid metabolism

## 1. INTRODUCTION

The two main risk factors for CVD are high blood pressure and dyslipidemia. A metabolic illness known as hyperlipidemia affects the body and is brought on by genetic or environmental factors that cause plasma concentrations of low-density lipoproteins, triglycerides, and cholesterol to rise while high-density lipoproteins fall. Currently, medication therapy and nutritional therapy are used to treat HLP [1]. However, it has been discovered that some patients experience adverse effects from the lipid-lowering statin medications. Therefore, the recommended method for preventing HLP is dietary therapy. Biotechnology and marine exploration technologies have advanced dramatically, and the seas, which make up around 71% of the Earth's surface, are rich in biological resources [11]. As a result, the development of marine active chemicals has advanced significantly, and the value of agricultural and animal output has increased in some countries with bigger marine resources[2]. Many marine species and a variety of biologically active compounds are created when environmental conditions, such as the ocean's specific temperature, pressure, and light, change. Proteins, pigments, polyunsaturated fatty acids, vitamins, and minerals are among the components that have been widely used as functional food ingredients [3].

The anticancer, lipid-lowering, and anti-inflammatory properties of certain edible marine species have also been discovered through research on the extraction, purification, activity, and molecular mechanisms of action of polysaccharides, fish oils, proteins, and active peptides obtained from the ocean[10]. Since 2016, there has been an increase in the quantity of articles on hypolipidemic active ingredients that come from marine sources[9]. This article discussed the several kinds of marine-derived hypolipidemic active compounds that have been identified, as well as how to assess their hypolipidemic activity and mode of action[4]. illustrates the number of publications on marine hypolipidemic compounds during that period and provides a schematic picture of the effects of recent research on marine active chemicals on human health [16]. The most generally recommended clinical drugs for the therapy of HLP at the moment are betablockers, ezetimibe, niacin, statins, and inhibitors[15]. These drugs have some unfavourable side effects even though they can lower blood lipid levels in HLP patients. Rhabdomyolysis, myalgia, and increased creatine kinase (CK) are the three most serious statin adverse effects[12]. Although niacin can increase HDL cholesterol (HDL-C) and decrease serum TC, it can also cause hepatotoxicity, flushing, nausea, and gastrointestinal distress.

## 2. REVIEW OF LITERATURE

While endogenous cholesterol is mostly produced by the body, mostly in the liver, exogenous cholesterol is mainly obtained through the small intestine and is obtained from food. The site of action of the most widely used lipid-lowering drugs is also included. Many biological processes, such as protein expression, antioxidant defence, signal transduction cascade activation, and mitochondrial integrity preservation, have been connected to a variety of bioactive compounds derived from marine sources. Extreme marine biotechnology is expanding quickly, and people are regularly discovering new bioactive compounds with therapeutic qualities. A variety of biological activities have been observed in seaweed polysaccharides, deep-sea fish skin and skeleton protein peptides, and polyunsaturated fatty acids with rich deep-sea fish oil. These include the anti-hyperlipemic effects of polysaccharides and protein peptides, as well as their cardiovascular-protective and antioxidant properties [5].
Many marine-derived bioactive substances have been connected to a variety of biological processes, such as protein synthesis, antioxidant defence, activation of signal transduction cascades, and preservation of mitochondrial integrity. Polyunsaturated fatty acids of rich deep-sea fish oil, polysaccharides from seaweed, and protein peptides from deep-sea fish skin and bones have been demonstrated to have a range of biological activities, such as cardiovascular protection, antioxidant activity, and therapeutic effects on hyperlipemia of polysaccharides and protein peptides[6]. With this, it is also an emerging trend that involves the combination of drugs. Combination with statins and ezetimibe is one example as it further reduces LDL-C levels and should be prescribed when achievement of LDL-C goals with the use of maximally tolerated statin monotherapies regimens is not possible. Through their combination, further ASCVD risk reduction would be attained with minimal concern over increased safety without diminishing effectiveness as a good form of treatment [13].
Marine organisms that inhabit a saline buffer environment with low temperatures, limited light sources, high salinities, low dissolved oxygen, and distinct water pressure are the primary source of the two types of polysaccharides—land-based and sea-based. These specific environmental characteristics result in different synthesis paths between materials produced from the land and the sea. Because of the favourable climate, marine polysaccharides have a distinct structure and biological mechanism.According to their sources, marine polysaccharides can be classified as either marine microbes, marine animals, or algae (known as brown, red, or green algae depending on pigment deposition). Algal polysaccharides make up the majority of macroalgae and phytoplankton species.

## 3. MATERIALS AND METHODS

Some sea species' viscera are also utilized as sources of bioactive polysaccharides; for example, sulphated polysaccharides from abalone viscera have hypolipidemic and anticoagulant properties, while squid viscera polysaccharides have immunological properties. Although sea plants and animals can also create polysaccharides, sea microbes are more widely used because of their high rate of reproduction and abundance of readily purified polysaccharides. Microorganisms are widely distributed on the bottom and exhibit a high degree of environmental adaptability. Furthermore, the majority of intracellular polysaccharides come from the cell walls of bacteria, actinomycetes, and marine fungus [7]. Microorganisms emit secondary compounds called extracellular polysaccharides, such as the antioxidant-active ones produced by the deep-sea fungus Aspergillus versicolor N2bc. Improvements in purification and identification methods have gradually led to a better understanding of the composition of polysaccharides. It has been shown that the structure of the polysaccharide chain, the quantity of hydroxyl groups, the kind of glycosidic bond, and the content of monosaccharides all significantly affect their bioactivity. Natural polysaccharides with a high glycoalkaloid acid content are generally more bioactive. A marine-sourced chitosan-oligosaccharide intervention dramatically raised HDL-C and decreased plasma TC in hypercholesterolemic hamsters while also boosting the relative number of Bacteroidetes in the gut.
Sargassum pallidum polysaccharides also increased the quantities of hepatic lipids while drastically reducing the buildup of liver fat and the expression of genes associated in fat creation. Sea cucumbers have demonstrated impressive activity in the study of active chemicals. AJP has a mean molecular weight of and is mostly composed of amino glucose, galactosamine, glucuronic acid, mannose, glucose, galactose, and fucose. Experiments showed that hyperlipidemic Wistar rats given AJP had significantly greater serum levels of HDL-C but significantly lower levels of TC, TG, and LDL-C. Thus, abalone visceral polysaccharides have been shown to raise HDL-C levels in the plasma of rats on a high-fat diet while lowering TC, TG, and LDL-C levels. Furthermore, there was a

noticeable increase in SOD activity and a decrease in MDA concentration. The majority of marine-derived polysaccharides are obtained from seaweed and other seaweed plants, and they have the same lipid-lowering properties as sulphated polysaccharides. However, the capacity of marine microbial polysaccharides to decrease lipids is very poorly understood[8]. In addition, the architectures of polysaccharides are linked to their hypolipidemic action. Thus, chromatographic and spectroscopic techniques for structural characterisation of polysaccharides can be used to screen for active molecules and examine the molecular mechanisms underlying their hypolipidemic effects[14].

Furthermore, because of their potential health benefits for humans, dietary fatty acids derived from deep-sea fish, such as salmon, cod, sardines, and Antarctic krill species, have attracted a lot of interest. Because of their nutritional and physiological benefits, deep-sea fish oils are abundant in unsaturated fatty acids, such as those in the Omega family of fatty acids, of which EPA and DHA are the greatest representatives[17]. Through the regulation of bile acid metabolism, dietary consumption of deep-sea fish oil supplemented with omega polyunsaturated fatty acids improves liver lipid metabolism. Additionally, DHA functions as a natural endogenous ligand for PPARs, causing them to initiate mitochondrial fatty acid β-oxidation. Current clinical guidelines propose treating severe hypertriglyceridemia with a DHA and EPA regimen.

## 4. RESULT AND DISCUSSION

DHA stops endoplasmic reticulum (ER) stress in mitochondria via turning on AMPK. Hepatic TG, MDA, serum tumor necrosis factor-α (TNFα), and nuclear transcription factor κB (NFκB) levels in the grass carp's diet were all markedly reduced by DHA supplementation. This action inhibited hepatocyte inflammation, lipid accumulation, and ER stress brought on by palmitic acid (PA) in vitro. used a zebrafish model caused by a high-cholesterol diet to evaluate the anti-cardiovascular benefits of fish oil rich in DHA and EPA against atherosclerosis.

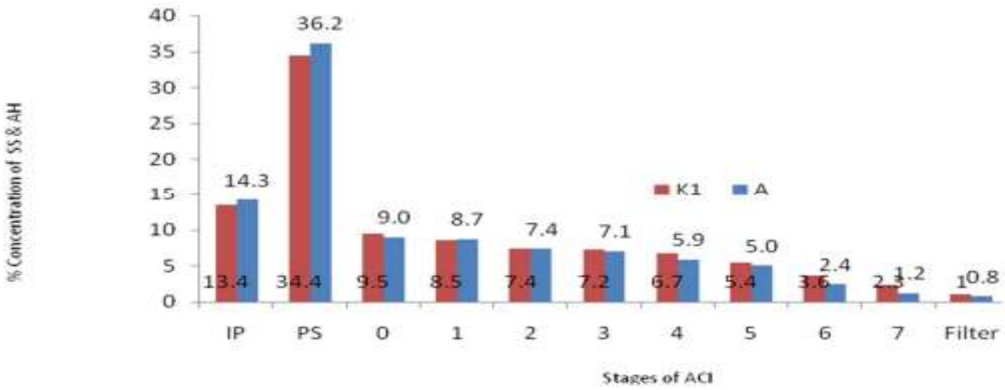


**Figure 1: ACI for % deposition profiles**

They discovered that the cholesterol levels of the zebrafish fed fish oil were 40% lower than those of the zebrafish on a regular diet. Additionally, the livers of the fish oil-fed group displayed a significant down-regulation ($p < 0.05$) of the fatty acid synthase (FAS) gene in comparison to the control group that was fed a conventional diet.

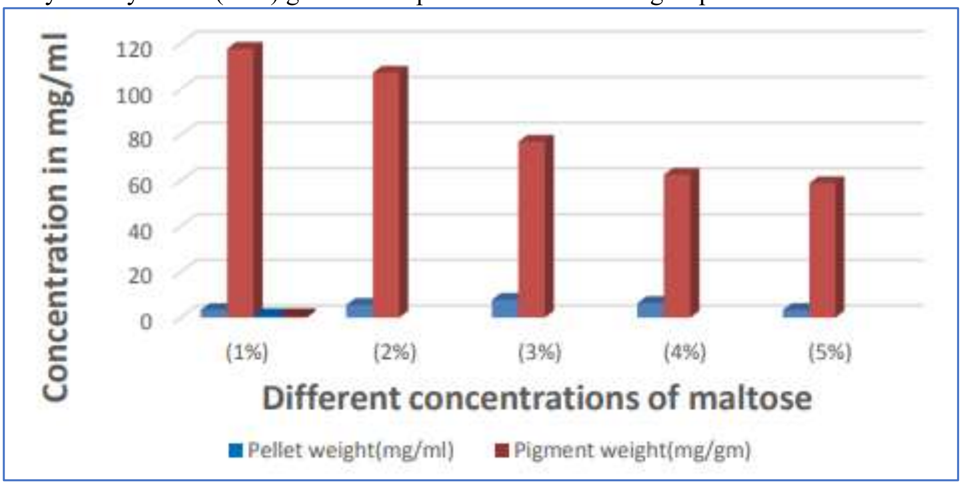


**Figure 2: Effect of different concentrations of maltose**

In order to prevent DHA degradation, a DHA liposome formulation in the form of an injectable nanomedicine was produced because oral delivery of DHA may have unstable bioavailability. This study discovered that DHA liposomes reduced the formation of foam cells, had potent anti-inflammatory and antioxidant qualities, and were readily phagocytosed by activated macrophages, all of which further slowed the progression of atherosclerosis[9-10].

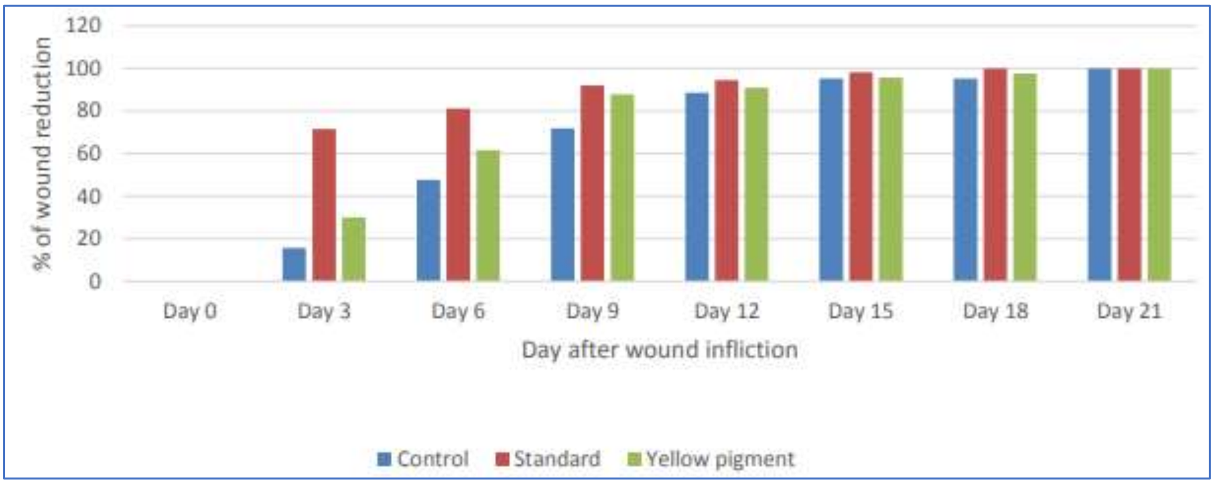


**Figure 3:Percentage reduction of wound size**

An essential and reliable source of material for the study and application of unsaturated fatty acids is the abundance of marine biological resources that are available globally. To date, deep-sea fish and shrimp polyunsaturated fatty acids have been used to create health foods and medications. Furthermore, fish oil water-in-emulsions, microencapsulation technologies, and other delivery systems have proven to be successful alternatives despite the fishy odor's limited use.

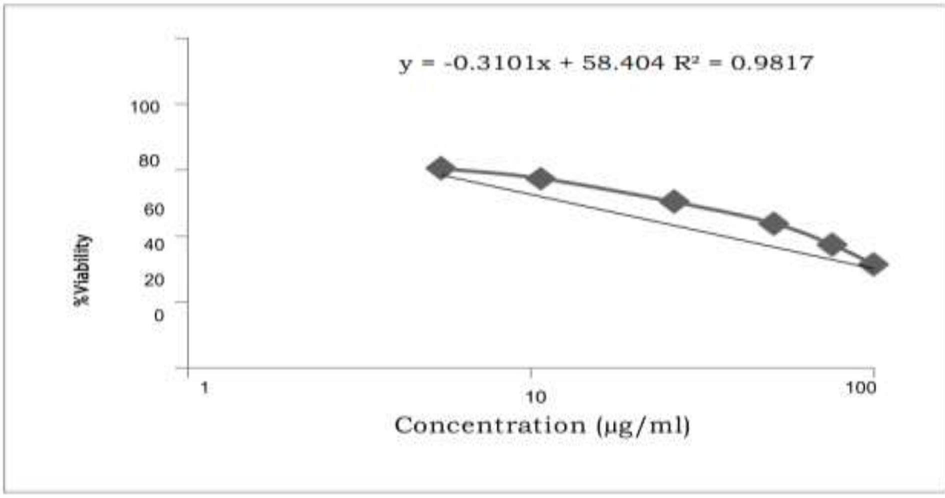


**Figure 4: Anticancer activity of pigment extract**

Marine bioactive peptides are the subject of extensive investigation due to their many bioactive qualities, safety, and absence of toxicities. They have anti-inflammatory, antioxidant, and anti-thrombotic qualities, among other things. The muscle or viscera, skin, shell, bone, and other remnants of marine organisms are traditional sources of marine bioactive peptides.

## 5. CONCLUSION

Marine bioactive compounds are special resources for the creation of products with lipid-lowering properties because of their complex structures and diverse origins. Even though China and other nations are currently conducting more study on sea-derived bioactive compounds that lower cholesterol, several problems still need to be sufficiently addressed in related studies, like the ones listed below. There is insufficient research on the precise molecular mechanism, structural characterisation, constitutive connection, and composition of active ingredients. In addition, there is less report on how active components affect metabolic processes of organisms. There are still issues with the process for getting rid of bioactive compounds, because marine-derived bioactive components are complex and diverse in composition. It is unclear how much of the reported bioactive chemicals are bioavailable, and there is few information on how they are transferred and absorbed within the body. Remember that test animals' metabolism of bile acids and cholesterol is different from ours. Humans have LDL-dependent lipoprotein metabolism, whereas rodents have HDL-dependent metabolism. Thus, findings from experiments conducted on mice and rats may not necessarily be translated to humans.

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