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Bioactive Compounds in Fish and Their Health Benefits

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Authors' contributions

This work was carried out in collaboration between all authors. Authors DNK and ATG designed the study. Author DNK wrote the first draft of the manuscript. Authors DNK and IOA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Fish have received considerable attention in the last several decades due to the presence of a unique blend of bioactive compounds like omega-3 polyunsaturated fatty acids, protein hydrolysates, polypeptides, peptides, amino acids, vitamins and minerals. The danger of developing chronic ailments such as cardiovascular diseases, type 2 diabetes and cancer; all-leading to mortality are observed to be lowered by increased intake of fish and fish products. The unique bioactive compounds in fish are pointers to the health benefits of fish ingestion. In this paper, bioactive compounds in fish and the health benefits associated with their consumption are reviewed.

Keywords: Fish; bioactive compounds; diseases; health benefits.

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1. INTRODUCTION

Fundamentally, nutrients in food nurture and support our bodies to remain fit. But it has also been proven that certain foods, in addition, provide health values such as inhibition or treatment of various kinds of ailments.

Currently, scientists are engrossed in the health advantages derived from foods, and there is, abundant substantiations of the promotion of human health by the foods and their constituents [1].

According to Gormley [2], “White fish (cod, hake, plaice) contains approximately 20% protein, 80% water, 0.5-3% oil with small amounts of vitamins, minerals, carbohydrate and other substances. Oily fish (mackerel, herring, salmon) also contain about 20% protein, but their water (62-70%) and oil contents (10-18%). The protein in oily and white fish breaks down on digestion into polypeptides, peptides and amino acids”. Most of which have bioactive properties, so are referred to as bioactive compounds.

Bioactive compounds are extra nutritional elements in foods which are naturally present in relatively little quantities. These substances are beneficial to human health [3]. These health benefits are achieved through multifactorial physiological mechanisms, including antioxidant activity, mediation of hormones, enhancement of the immune system and facilitation of substance transit through the digestive tract, butyric acid production in the colon, and absorption and/or dilution of substances in the gut [4].

The rise in ailments like cancer, diabetes, hypertension, obesity etc., associated with foods; have prompted people to prefer foods and food products that also provide functional and health benefits. Peptides obtained from fish have been proven to demonstrate antihypertensive, antioxidant properties *in vivo* and other bioactivities anti-proliferative and antimicrobial activities *in vitro*. These bioactives harbour huge potential [5]. The objective of this review therefore, is to discuss bioactive compounds in fish and their health benefits.

2. FISH

Based on the definition of Mifflin [6], fish refer to “the numerous cold-blooded vertebrate animals that live in water. Fish have gills for obtaining oxygen, a lateral line for sensing pressure changes in the water, and a vertical tail. Most fish are covered with scales and have limbs in the form of fins. Fish were once classified together as a single group, but are now known to compose numerous evolutionarily distinct classes, including the bony fish, cartilaginous fish, jawless fish, lobe-finned fish, and placoderms”. Also, Jónsdóttir [7] reported that “Fish represents a valuable source of nutrients; minerals, vitamins, essential fatty acids, and proteins in the diet of many countries. Fish contains about 80% (w/w) water, 8–25% proteins, 0.5%–30% fat, and 0.6%–1.5% mineral compounds. Fish contains abundant amounts of water-soluble vitamins, and fish oil (particularly from the liver) is rich in vitamins A and D". Research and utilising of seafood biotechnologies to produce innovative, functional food and medicinal products from fish sources is on a great rise due to the awareness of the correlation between fish ingestion and sound health. The particularly low incidence of heart disease in fish-eating populations has been attributed to high ingestion levels of omega-3 polyunsaturated fatty acids (PUFAs) which is constituted of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in fish oil [8].

In consonance with the above claims, intake of fish oil have been proven to reduce stiffening of arterial walls, decreasing the incidence of coronary heart diseases among people that eat many quantities of fish and their products. So the advantage of fish oil consumption is attributed to Omega-3 polyunsaturated fatty acids (PUFAs) level, specifically; because of the presence of the eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) which can lower blood pressure and viscosity [9]. According to a statement by Aluko [1], “Evidence suggests that the polyunsaturated fatty acids (PUFAs) are the most important bioactive lipids. However, apart from the oil, it should be noted that other nutrients in fish such as proteins, minerals (copper, calcium, selenium, zinc, and magnesium), and vitamins also have beneficial effects on human health [1].

2.1 Bioactive Compounds

The term "bioactive" is composed of two words: bio- and -active. From the expatiation by Guaadaoui [10], “Bio- from the Greek (βío-) "bios" [bio-, -bio], refers to life. And -active from the Latin "activus", means, dynamic, full of energy, with energy, or involves an activity.” This activity involves all the occurrences which show

a form of life [11]. In other words, the term "bioactive" means "biologically active [12]. Hence; a bioactive compound can simply be referred to as a substance that has a biological activity [10]. In medical dictionaries, a bioactive substance is said to be a material that causes or stimulates a response in the living tissue [6]. This implies a compound (or a substance) have biological activity if it has a direct influence on a living thing. The source of bioactive compounds are either natural or synthetic (partially or totally). They generally contain chemicals that occur in little concentrations in plants and some foods such as fruits, vegetables, nuts, oils (fish) and whole grains and prompt action in the body that are of Health benefits. Thus, Guaadaoui [10] concludes that a bioactive compound is: "a compound which has the capability and the ability to interact with one or more component(s) of the living tissue by presenting a wide range of probable effects".

2.1.1 Food bioactive compounds

Food bioactive compounds are constituents of some foods which are capable of altering physiological activities in the body resulting in a beneficial health effect. Hence, for a compound to be defined as a "food bioactive compound", it must demonstrate a positive health benefit.

The definition above differentiates these vital food constituents' from many others that are bioactive, but with antagonistic effects and considered toxic. This also indicates the types of experiences that should be designed in ascertaining the bioactivity of food compounds [13]. Thus, food bioactive compounds are food constituents or dietary supplements, beside those required for the body's basic nutritional needs, and are credited for positive changes in human health status [14].

To elaborate further on the concept of bioactive compounds, the thoughts of other researchers are shared as followed;

According to Aluko [1], the word "nutraceutical," a blend of "nutrition" and "pharmaceutical" was coined by Dr. Stephen De Felice, a Physician in 1989. Who also, defined "nutraceutical" as "any food or parts of a food that provides medical or health benefits, including the prevention and treatment of diseases".

From this initial definition, the term "functional foods" has also been added to connect intake of some food/food products with disease prevention, treatment or improvement of health.

These health-promoting substances in foods are grouped into two broad categories:

1. Functional foods: Ross [15], declared food as "functional" if—"it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either and an improved state of health and well-being and/or reduction in risk of disease". Examples include; fish, tomato etc.

2. Nutraceuticals: Nutraceuticals are health-promoting substances/compounds isolated from food sources, used to produce medicines and generally sold as pills. Examples include isoflavones (compounds isolated from soybean seeds and converted into pills for use by women instead of synthetic drugs during hormone replacement therapy), fish oil capsules, herb extracts, antihypertensive pills (containing fish derived peptides) etc., [1].

2.2 Food Bioactive Compounds in Fish

Affirmation is that fish are sources of different abundant bioactive compounds [16]. This is in line with a report by Harnedy and FitzGerald [17] who stated that Proteins (amino acids/ Peptides /hydrolysates) and fatty acids, vitamins and minerals are among the bioactive compounds in fish.

2.2.1 Proteins

In the report by Hamed et al. [18] Proteins are said to be "complex polymers made up of a combination of 20 different amino acids coded by the gene (DNA) code along with some other amino acids". Proteins have many significant contributions in biology and food systems functioning as hormones, transport proteins and antibodies. Also, are needed nutritionally. Fish proteins are readily digested and absorbed by the body [18]. Bioactive peptides (hydrolysates) obtained by hydrolysis of protein have been receiving intensive investigation. These peptides have been isolated from fish species [19] and absorbed by intestinal enterocytes to reach the bloodstream, exerting beneficial biological activity on body functions and conditions. Peptides have opened new promising opportunities for the development of a wide

range of biotechnological products with enhanced bioactive properties. They have been reported to show a wide range of biological activity, including antimicrobial, anti-oxidative and antihypertensive activities [13]. Fish protein hydrolysates (FPH) hydrolysed from fish species such as tuna, mackerel etc., have exhibited antioxidant activity [20]. Two of these essential amino acids found in large quantities in fish proteins are lysine and methionine [18].

According to Joseph et al. [21], for over two decades, angiotensin I converting enzyme (ACE) inhibitory peptides from fish sources was first associated with sardine meat. Since, then, ACE inhibitory peptides have been discovered in various fish species, like shellfish, tuna, bonito, salmon and sardine. In consonance, there are many reports of crude fish protein hydrolysates containing ACE inhibitory peptides obtained from the hydrolysis of purified catfish protein. Most of the ACE inhibitory peptides released were found in the soluble protein fraction [21]. Among the water-soluble components, fish muscles abound with amino acids, mostly glutamic acid, proline, taurine, glycine, alanine and arginine. Fish is a good source of taurine a conditionally essential amino acid that has been shown to be involved in certain aspects of mammalian development. The molecule contains a sulfonic acid group, rather than the carboxylic acid moiety, that is not incorporated into proteins and is one of the most plentiful free amino acids in many tissues, including skeletal and cardiac muscle and the brain. Taurine is present in cod, mackerel, farmed and wild salmon, albacore tuna, ray, shark, whiting and several other species. There is a potential use of taurine to reduce blood pressure, improve cardiac performance and reduce blood cholesterol levels [22]. In confirmation, researchers in Europe have proved that taurine has an advantage in cardiovascular health and fish is a good source of it. The work of Gormley [2] has shown a consistent dissimilarity in the taurine content of four species in the recorded order as "plaice (126), cod (93), mackerel (69) and farmed salmon (53 mg/100 g)" This implies white fish have more taurine than oily Fish".

Free amino acids usually interact with free radicals but, the most efficient are the ones that can easily give away hydrogen atoms which include the amino acids having nucleophilic sulfur-containing side chains - cysteine and methionine or aromatic side chains (Tryptophan, Tyrosine, and Phenylalanine). This implies the specific compounds responsible for bioactivity of fish hydrolysates (peptides/amino acids) are: Cysteine, Methionine, Lysine, Taurine, Tryptophan, Tyrosine, and Phenylalanine. Also, Glutamic acid, Proline, Glycine, Alanine and Arginine. Thus, fish and fish extracts possess anti-hypertensive peptides (ACE inhibitors), which can lower blood pressure and hinder plaque of cholesterol deposits on the inner surfaces of the arteries obstructing blood flow [2].

2.2.2 Lipids and fatty acids

The chemical makeup of fish oil differs from oils of other sources and is mainly composed of two types of fatty acids, which are docosah-exaenoicacid (DHA) and eicosapentaenoic acid (EPA).

These are polyunsaturated fatty acids classified as omega-3 fatty acids and predominantly found in fish species with a higher unsaturated fat content. The polyunsaturated fatty acids in fish oil, contrary to saturated fats are readily digested for energy production and have been reported to have various bioactivities. Scientific researchers believe that EPA and DHA are two principal defensive compounds of fish oil that prevent chronic disease. Research results show that ingestion of fish raises the amounts of EPA and DHA in blood; invariably lowering the progression of coronary heart diseases through different mechanisms. Lowering the progression of coronary heart disease has become the assertion of the fact that these fatty acids in fish oil are involved in the prevention of diseases in human beings.

It has been found that fish oil also exerts their protective effect against heart diseases by decreasing serum triglyceride levels, improving heart function, lowering blood pressure, and decreasing inflammation [23]. Fish contains PUFAs and substantial amounts of monounsaturated fatty acids, which are considered beneficial as long as they are not oxidised [24]. Hence, the specific bioactive compounds in fish oil are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). This is further confirmed by Gormley [2], who has reported that in cardiovascular health, fish ingestion has the ability to counteract inflammation. This is connected with the decreasing danger of cardiovascular diseases through omega-3 polyunsaturated fatty acids (PUFAs), composed mainly of eicosapentaenoic acid and docosahexaenoic acid. They lower the

level of platelet assemblage in the blood, thereby thinning the blood and decreasing the tendency of formation of blood clots. It has been documented by Zheng [25] that "the recommended minimum daily intake of EPA/DHA varies from 250 mg to 1250 mg".

Similarly, other researchers have asserted this position that; the lipid fraction of seafood consists mostly of PUFAs, established as essential for human health [25]. Humans are incapable of synthesising PUFAs having longer than 18 carbon atoms; thus, they get them from food.

Synthesis of long chained PUFAs occurs in the algae eaten by fish; this has made fish the prime sources of long chained PUFAs for humans [26]. The long-chain omega-3 fatty acids are beneficial in the protection against Cardiovascular disease (CVD) [27] and are particularly present in the brown flesh of oily fish which contains most of the oil.

Main commercial sources of omega-3 PUFAs are the fatty fishes such as sardine, herring, salmon and mackerel [28]. This is in line with a report by Drevon [29] that, the significant amounts of long-chain omega-3 fatty acids are obtained from fatty fish (herring, mackerel, salmon, trout, eel, anchovies, sardines, etc.), in addition to fish oil, cod liver oil, tuna fish oil and krill oil. The fattier the fish is, the more EPA and DHA it will contain. The ratio of these two fatty acids will, however, differ between the species of fish. The omega-3 fatty acids in fatty fish or cod liver are not synthesised in the fish itself, but in microscopic organisms called phytoplankton before the marine fatty acids are transferred through the food chain to the respective fishes, seals and whales. The biological effects of the omega-3 fatty acids are much stronger than those of α-linolenic acid on parameters that are important for prevention of diseases[29].

2.2.3 Sterols

The sterol compounds are also a constituent of lipids from marine sources. They have been observed to decrease low-density lipoprotein (LDL) cholesterol amount*s in vivo* [30]. Another bioactivity related to sterols is an anti-inflammatory effect. Also, phytosterols are important precursors of some vitamins. For instance, Ibañez et al. [19] said: "ergosterol is a precursor of vitamin D2 and cortisone".

2.2.4 More bioactive compounds of health benefits associated with fish consumption

a. Vitamins: The body needs vitamins for several chemical and physiological functions [16]. Fish oils are rich sources of vitamins A, D, and E. Vitamin A is concentrated mostly in fish liver oils. Halibut and cod liver oils are rich sources of vitamins A, and D. Sardine fish contains up to 4500 IU of vitamin A and up to 500 IU of vitamin D per 100 g of meat, with an average of 125 µg/g of oil. The vitamin A found in small fish species is particularly bio-available. A 3.5 oz portion provides 90% of the daily need of vitamin D. Herring, mackerel, salmon, and lake trout contain varying amounts of vitamin D in their tissues. Patients who consumed more amount of vitamin D and calcium contained in daily servings of dairy products and fish were 40% less likely to come down with polyps than people who consumed small quantity or no vitamin D. Fatty fish are one of the very few dietary sources of vitamin D [1]. Vitamin D deficiency results in osteomalacia (softening of adults' bones) in adults, which is the same as rickets in children [16]. This points to vitamins A, D and E in fish oils as bioactive components also.

b. Minerals: Essential minerals and trace elements abound in fish due to their ability to obtain inorganic atoms from sea or river water. These essential minerals are found in the higher level in seafoods compared to terrestrial foods. Hence, fish is one amongst most vital vegetable sources of Calcium (Ca). Therefore; fish intake could be useful for the management of Ca deficiency risk, in adolescents, pregnant women, and elderly persons [31]. Ca is necessary for bone formation and further maintaining strong bones during pregnancy and lactation. Ca demand rises at these stages, so it is key for the suitable growth and maintenance of calcified dental tissues also. Insufficient Ca dietary intake as required can lead to many diseases [32]. So, fishbone material derived from the processing of large fish is a useful calcium source [22]. Similarly, Gormley [2] support the fact that fish bones are a good source of calcium. Note that beside fish oil; proteins, minerals (calcium, copper, selenium, zinc, and magnesium), and vitamin B1 in fish are considered to have advantageous effects on health also [1]. Thus, calcium, copper, selenium, zinc, and magnesium in fish can be considered as bioactive compounds.

2.3 The Role of Fish Bioactive Compounds in Specific Disease Conditions

2.3.1 Cardiovascular diseases

It is observed in diabetic and overweight patients that there is a direct correlation between increasing levels of triglycerides and increased levels of blood clotting factors in the body. Naturally, this kind of relationship heightens the danger of blood clot formation and extremely damage, the usual operations of the cardiovascular system. However, the amount of triglycerides in the blood can be lowered by the intake of fish oil, which lowers the danger in the circulatory system connected with blood clotting.

Results from Epidemiological research reveal a decrease in the occurrence of coronary heart disease with increased frequent dietary consumption of fish. This is in line with a report by Aluko [1] which states that, "in men suffering from cardiac infarction, a 29% reduction in all-cause mortality within a 2-year period was observed when two fish meals (300 g) per week were introduced into their diet. This association was stronger in diabetic women where there was a 60% lowered risk of Coronary heart disease (CHD) in the group that had the highest fish intake when compared with groups with little or no fish in the diet. Even in patients that had already developed CHD, dietary intake of as little as 150 g of fish led to lower-risk of serious health complications". Thus, the cardiovascular health benefits derived from intake of fish can be said to be mostly due to the presence of the bioactive compound "omega-3 PUFAs" in fish. Since enrichment of sick person's diet with omega-3 PUFAs revealed a remarkable decrease in cardiovascular deaths and nonfatal cardiovascular incidences. According to Jump [33] “blood levels of omega-3 fatty acids are inversely proportional to the risk of adverse cardiovascular events such as stroke and sudden Death”. This is proved by the reduction of the amount of triglyceride and cholesterol in blood serum via ingestion of fish oil. High blood pressure is observed with ingestion of saturated fatty acids, but increased fish intake showed increased levels of EPA and DHA in the blood, which lowers blood pressure [34].

Fish intake showed a beneficial influence on cardiovascular disease (CDV) and Coronary heart disease (CHD) as proven by several researches carried out to validate the relationship between fish intake and reducing CDV and CHD. This is confirmed by the evidence that people like the Alaskans and Japanese who eat mostly marine foods develop fewer heart illnesses [16].

These advantages connected with fish intake points to the low occurrence of ventricular fibrillation, usually observed during myocardial infarction. Dietary enhancement of hypercholesterolemic animals feed with fish oil lowers the risk of atherosclerosis and the stiffening of arterial walls. It has been documented by Aluko [1] that, "in a rat model of myocardial dysfunction, dietary fish oil increased the level of long-chain and n-3 polyunsaturated fatty acids (PUFA) in cardiac cells when compared to the control. Consumption of fish oil is also able to reduce the occurrence of platelet aggregation in the blood circulatory system. Some of the pathological changes associated with ischemia-reperfusion such as the decreased force of cardiac contraction, increase in coronary perfusion pressure, the appearance of ventricular arrhythmias, and release of creatine kinase and thromboxane B2 in the coronary effluent were all attenuated by fish oil supplementation. The beneficial effects of fish oil in reducing postoperative body temperature mortality have also been demonstrated in clinical studies”. Hence, fish oil consumption has a direct positive influence on the heart. As mentioned earlier, all these evidences prove that the omega-3 fatty acids (polyunsaturated fatty acids-PUFAs) are the most vital bioactive components in fish. This further is, explained by Aluko [1] that “the beneficial health effects of PUFAs seem to be dependent on their isomer configuration as the cis -isomer is the predominant bioactive form. Moreover, fatty acids in the cis -configuration have a rigid nonlinear structure, which enhances membrane fluidity when incorporated into cells. Increased membrane fluidity enhances cell to cell communication and helps maintain normal homeostasis or prevent the development of metabolic disorders”.

2.3.2 Cancer

Cancer refers to a disease condition where cells abnormally continue to grow and divide. These abnormal cells kill by assaulting and destabilising normal body tissues [2]. Therefore, encouraging apoptosis is a significant focus for anticancer cure [35]. Much research has been done to validate the link between cancer prevention and

fish intake [36-38]. The antiproliferative activity of Fish Protein Hydrolysates *in vitro* on 2 lines of breast cancer cells have been evaluated by Picot et al. Kim and Wijesekara [39,35]. Inhibition of the cancer spread has been noticed and an evaluation of the hydrolysates composition revealed that they are made of a complex mixture of free amino acids and peptides of different molecular weights ranging up to 7 kDa with smaller quantities of lipids and Sodium chloride. Antitumoral and antimetastasis characteristics of fish oil (omega-3 fatty acids) were tried on mice. According to Najafian and Babji [16], "The mice were fed a diet rich in omega-3 fatty acids and a few parameters such as tumour growth, body weight, and lung metastasis was followed. The control diets contained soybean oil. These diets were tested in combination with the conventional cytotoxic agent cisplatin. Fish oil suppressed tumour growth and reduced the metastatic load".

Despite scarce information on the beneficial impact of fish ingestion on cancer development and advancement, evidence shows that fish constituents may provide some protection against the development of tumours. Especially, that there is considerably scientific proofs that food products containing fish oil; rich in omega-3 Poly Unsaturated Fatty Acids such as DHA and EPA can safeguard against the development of tumours. EPA in the diet has proven to reduce rectal polyp numbers and size in persons suffering familial adenomatous polyposis (FAP). In these patients, the FAP was suppressed to an extent that is like the effect of celecoxib drug. Note that fermentable fiber inclusion in diets can remarkably increase the anticancer impart of fish oil due to the production of butyrate from fiber fermentation, which beneficially combines with fish oil PUFAs, particularly DHA in the destruction of cancer cells. The capability of the colon epithelial cells to go through differentiation appropriately is accelerated by fish oils and vitamin D, this reduces the danger of random genetic alteration that could result in new unwanted traits [2].

2.3.3 Diabetes

Fat-free fish protein diets used in animal studies have positively lowered insulin resistance indicating such diets would be effective in glucose management in humans [40]. As a confirmation, cod protein inclusion in a high-fat and sucrose diet provided protection against progression of obesity associated with insulin resistance and glucose tolerance as demonstrated based on insulin sensitivity experiments that, glucose quantity required to induce hyperglycemia was significantly higher for cod-fed rats than casein-fed rats [41]. So, cod protein improved insulin-dependent glucose uptake pointing to enhanced insulin sensitivity in compared to casein. The increased insulin sensitivity was linked to the lowered level of fat deposits and weight gain. The same pattern was observed with cod protein fed to human beings [1].

2.3.4 Obesity

Obesity is defined by Galgani and Ravussin [42] as "a chronic metabolic disorder caused by an imbalance between energy intake and expenditure [42]". Obesity also has a negative social effect. Obese individuals are often ridiculed and suffer discrimination on account of their weight. Hence, obesity is an embarrassing physique [43]. The rising rate of obesity has become a global medical concern. Fortunately, fish oil has been scientifically proven to be capable of achieving weight loss. For instance, in an experiment, the body mass index of fish-eaters was compared with that of meat-eaters and the persons who ate fish had a lower body mass index [44]. This is in consonance with the findings of Najafian and Babji [16] that, "DHA and EPA prevent obesity by inhibiting key enzymes responsible for lipid syntheses, such as fatty acid synthase and stearoyl-CoA desaturase-1. These enzymes enhance lipid oxidation and thermogenesis, and they prevent free fatty acids from entering adipocytes for lipogenesis [16]". In Aluko's [1] work, salmon diet prohibited dietary fat-mediated rise in weight of epididymal white adipose tissue compared to casein. Reduction in weight indicated that salmon protein boosted energy expenditure compared to casein. Increasing deposits of epididymal white adipose tissue are a danger signal indicating initiation of obesity associated with insulin resistance which is connected with higher water retention. These observations, clearly demonstrate that fish protein intake does not only promote energy expenditure but also heighten insulin sensitivity, decreasing water retention in the body and invariably reducing body weight hence controlling obesity. Usually, amongst other benefits, protein diets have a satiating characteristic, validating weight loss observed with increasing fish intake. Since the satiating effect would naturally lower food and total caloric ingestion. And the proteins are merged into the lean muscles instead of fat

being deposited into the adipose tissue which leads to weight gain [1]. Similarly, Jun et al. [45] report that bioactive compounds present in functional foods propose a practical, advantageous approach to obesity. Many have the potential to aid in lowering cholesterol, increasing satiety, and increasing the rate at which fat is oxidised. Together, these are paramount in lowering overall adipose tissue in the body and restoring the body back to a healthy weight. Functional foods are an easy and efficient way for the general public to increase their health and fight off obesity in addition to their other lifestyle changes. Used in conjunction with proper diet and exercise, functional foods can prominently assist in weight loss and management.

2.3.5 Brain function

Depression lowering, first stage development, and cognitive tasks preservation in old age are the major areas where fish ingestion is of advantage to the human brain. These advantageous benefits are achieved via omega-3 fatty acids (PUFAs) present in fish oil and the numerous intrinsic antioxidant components that normally prevent oxidative damage of the PUFAs in the fish. Regular dietary fish intake is proven to lower indicators of depression in patients [1]. The positive link between fish intake and fetal development and early life is anchored on the enormous quantities of DHA that are infused into the brain and retina. Firm linear packing of DHA is not possible because of the structural frame of the cis-double bonds, so large quantities of this fatty acid results in enhanced fluidity of cell membranes of the brain and retina. Therefore, DHA-engendered fluid cellular structure is proposed to improve the optimal performance of the organs by increasing the competence of signalling mediators - a few like ions, eicosanoids, sugars move necessary in and out of the cells. Enhanced performance of the brain and retina was observed when pre-matured babies were fed with DHA-enriched diets while the ones without DHA came up lacking proper cognitive and retina functions. Also, mothers who had fish oil-enriched diets during pregnancy had babies who grew exhibiting superior mental and problem-solving abilities, including hand and eye movements. For the preservation of cognitive tasks during older ages, fish oil has been shown to mitigate intellectual deterioration [1] Omega-3 fatty acids of fish oil are said to be connected with brain development, and very vital for vision and reproductive system. This can be attributed to DHA since it is a constituent of brain nerve synapse in the retina, testes and sperms. Therefore, Omega-3 fatty acids of fish oil accomplish a very important function in the development and performance of the brain, reproductive system etc. [23].

2.3.6 Immune system

The danger of inflammation is greatly lowered when the body's immune cells accumulate EPA and DHA through regular dietary fish oil ingestion, the pro- inflammatory fatty acids like omega-6 PUFAs and arachidonic acid are substituted by EPA and DHA (anti-inflammatory fatty acids). This is consistent with the report by Aluko [1] that; "consumption of 150 g of salmon three times a week led to reductions in pro-inflammatory markers such as C-reactive protein, interleukin-6, and prostaglandins, which indicates improvements to the immune function". Women who eat large amounts of fatty fish during pregnancy usually suffer less food intolerance and give birth to children with lower risk of respiratory disorders. None intake of fish at childhood results in higher tendencies of asthma development. Ailments like asthma or allergy are likely to occur in adults who take insufficient dietary fish [1].

2.3.7 Digestive tract system

Similar to the immune system, the ingestion of fish oil has lots of advantages in the prevention of several digestive tract ailments like inflammatory bowel disorders. Increased fish oil intake leads to EPA and DHA getting increasingly accumulated and enters into cell membrane phospholipids substituting the n-6 PUFA (linoleic and arachidonic acids) resulting in positive functional effects in membrane receptors. Also, the rise in butyrate level in the bowel is usually achieved with increased intake of fish oil. This results in a healthier bowel [1].

2.4 Antioxidant Activity of Bioactive Compounds in Fishes

Antioxidant refers to compounds that even when present in low concentrations can prevent oxidation by free radicals in the body. Therefore, antioxidants function to protect our body against oxidative stress and the advancement of sicknesses [46]. Hence the capabilities of a substance classified as an antioxidant is exhibited by its positive demonstration to prevent or treat degenerative diseases such as

cardiovascular disorders, cancer, inflammatory disorders, diabetics etc. [16].

Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are naturally produced in the body during cellular metabolism. But ROS and RNS attack the cell membranes in the body which, if unreversed degenerates to several terminal diseases, so the body produces its own antioxidants (endogenous antioxidant) that counteracts the activities of the ROS and RNS. But in some instances (like ageing, immune deficiency etc.) can make the ROS and RNS overpower the body's produced antioxidants hence the need for external sources (exogenous antioxidants) from foods like fish, eggs, soya bean, milk etc. to assist the body fight [1].

Fish protein hydrolysates from fish species such as tuna, mackerel, yellowfin sole, and Alaska Pollock have been proven to exhibit antioxidant capabilities [21]. The hydrolysates or Peptides extracted from fish are gotten from the muscles, viscera, skin, bones and scales.

The antioxidant capabilities of the fish hydrolysates or Peptides are profitable for health as proven by the characteristics of antioxidants to protect the body against ROS and RNS molecules, which attack membrane lipids, protein and DNA, leading to degenerative sicknesses like dementia, cardiovascular disorders, diabetes, cancer, obesity etc. [5]. This is in line with the statement that demonstrated antioxidant properties of Fish hydrolysates/peptides as scavenging of ROS free radicals and prevention of ROS-induced oxidation of cell membranes. And peptide size and amino acid profile to determine the effectiveness of fish protein hydrolysates or peptides [35].

Recently, the use of natural antioxidants obtained from food sources is becoming popular due to efforts to dissociate from the potential dangers posed by synthetic antioxidants [5].

Few examples of fish that show evidence of antioxidant potentials are as follows:

Fish protein hydrolysates / peptides from mackerel were observed to demonstrate antioxidant activity *in vitro* [47]. This agrees with the result that; Peptides isolated by hydrolysis of mackerel fish muscles with Protease N prevented the autoxidation of linoleic acid [21].

Enzymatically isolated Tilapia fish protein hydrolysates also showed antioxidant potential [48].

More low molecular weight peptides/ hydrolysates from salmon fish muscle were observed to be generated with increasing rate of hydrolysis of salmon fish muscle, which in turn increased the free radical scavenging capability of the salmon fish muscle hydrolysate. This confirmed the antioxidant ability of salmon fish muscle [49].

The antioxidant ability of tuna fish protein hydrolysate was exhibited by its ability to prevent hydroxyl radical-induced DNA damage. As is known fact DNA damage is responsible for the initiation of several terminal illnesses like coronary heart disease, diabetes, cancer etc. [1].

Thus, regular fish intake would prevent or treat such sicknesses.

2.5 The Recommended Dietary Intake of Fish

Several epidemiological studies have shown correlations between fish consumption and the death rate from heart ailments. Results revealed that; individuals who at least eat some fish weekly had a lower CHD death rate than those who did not at all. Hence, concluded that; inverse relationship exists between fish ingestion and death from CHD [50]. Similarly; Fish consumption was linked with lowering the danger of severe heart diseases, stroke etc. [51]. Also, in [52]'s account, there is a connection between regular weekly fish consumption and lower CVD risk factors like arterial diseases, obesity, high blood pressure, etc. Thus, according to evidence-based guidelines the following recommendations for dietary intake of fish are made:

2.5.1 Healthy individuals (for maintaining a healthy life style): 2 times per week

The dietary intake of at least two fatty fish dishes per week is recommended by international and national associations to guarantee an adequate dietary supply of Omega-3 PUFAs [53]. Consumers are advised to frequently take fish (at least two weekly) to take advantage of the antioxidant (bioactive) substances in fish and ensure sustenance of good Health [1].

2.5.2 Chronic diseased persons: 2-4 times per week

Measurable imparts on risk factors are only noticed after intakes of about 1-2 g/day of omega-3 fatty acids, which is equivalent to eating fatty fish 2-4 times a week. If the fish intake is not possible, a daily dose of cod liver oil or fish oil will provide the necessary amount of omega-3 fatty acids.

If 1-2 g/day of EPA and DHA obtainable from fish is eaten in combination with adequate amounts of fruits and vegetables and just little of saturated fatty acids, many individuals will enjoy better, state of well-being [54].

2.5.3 Pregnant women: Daily per week

For pregnant women, there are some data demonstrating beneficial effects of 2.5 grams marine omega-3 fatty acids daily for the mother as well as for the child [55-56]. DHA is essential for this development, and expectant mothers have an increased need for DHA, which they can get from a combination of supplementation (e.g. Capsules) and eating oily fish [53]. From epidemiological studies, mothers who eat fish at least four times weekly had babies with better developmental scores than those who did not. Also, DHA is observed to be more in breast milk of lactating women whose fish intake was on a regular basis. The degree of sharpness of infants' sight is positively related to the quantity of DHA in breast milk. Hence increased fish consumption is key for the lactating mothers [1].

2.5.4 Children: At least once a week

Fish muscle proteins are rich in essential amino acids so are recommended to be given to children or used to enrich their meals, especially where the meals are cereal-based [16].

Another vital benefit of fish for children is fish oils' involvement in the development of the brain and retina. These effects are specifically related to the DHA component of the oils. Premature infants may particularly suffer from lower levels of DHA and, if fed on formulas devoid of DHA, their DHA level would be adversely affected. From findings of this review; children also should eat fish muscle protein at least once a week [57].

2.5.4 Elderly people: At least once a week

Research results have revealed a 60% reduction in the danger of cognitive deterioration among elderly people in the US that took oil-rich fish at least once weekly [1].

Overall, everyone is advised to Consume fish at least once-twice a week (150 - 200 g/serving) [14].

2.6 Health Hazards of Fish Intake

Health Hazards of Fish consumption have to do with biological and chemical contaminants which are of great concern to consumers. Fish and shellfish are reported to harbour more than 10 different categories of bacteria. Though many not , however, generate metabolites during storage that give off-flavours or odours leading to non-acceptance of the fish. Fish harvested in coastal areas could have more pathogens as a result of human faces or industrial discharges in the water. Other pathogens may be introduced during handling and processing of the fish [2].

Increased consumption of fish is desirable from a beneficial dietary perspective like increased consumption of oily fish, but exposure to contaminants contained in the fish need to be minimised. There has to be a balance between the beneficial effects in reducing heart disease from high fish consumption against the negative effects of chemical contaminants such as dioxin and polychlorinated biphenyls (PCBs) exposure [58]. And also, pollution with various hazardous components as industrial waste, metals etc. [22].

There is a great tendency of unsaturated fatty acids to produce highly oxidised products as a result of long period usage of fish oil, Heightening oxidative stress connected with the fish oil intake which reduces the body's endogenous antioxidant [1]. In the agreement, polyunsaturated fatty acids have been reported to be vulnerable to lipid oxidation, which is a drawing back for their use in functional foods [18].

Furthermore, [1] reports more potential negative outcomes of omega-3 fatty acids as followed: -

a. Delayed blood clotting is observed with very high dietary intake (20 g/day) of omega-3 fatty acids [1]. This is in consonance with the findings

of Gormley [2] that, EPA and DHA lower the rate of platelet aggregation, thinning the blood, hence decreasing the rate of clot formation.

Recommended minimum daily consumption of EPA/DHA differs from 250 mg to 1250 mg. An average meal of salmon/mackerel will adequately provide these quantities.

b. Ingestion of oils or foods that are rich in or enriched with omega-3 fatty acids may cause abdominal discomforts and nausea (vomiting) in some individuals [1]. Although concern about pollutants in fish (food products of marine origin) has been expressed, there seem to be markedly more advantages than the harmful effects of consuming fish as a result of the presence of omega-3 fatty acids which has been proven to be quite beneficial to human health in appropriate amounts. This is in addition to the positive effects promoted by replacing unhealthy nutrients like hard fat with fish oil [59]. Thus, to mitigate these risks, it will be advisable to keep to the fish dietary recommendations as documented by the researchers above. Also, risks associated with fish consumption (bacteria, viruses, chemicals, faecal pollution, industrial waste, metals, etc.) can be minimised by good in-factory hygiene, proper cooking of fish before eating, sourcing of fish from clean-water locations, high personal hygiene in cleaning and handling fishes will go a long way to help. Also, use of other dietary antioxidant is encouraged as stressed by Aluko [1]. This is in line with the opinion of Hamed et al. [18], that polyunsaturated fatty acids should be used regularly in combination with other sources of antioxidants to prolong shelf-life of functional foods. Note that the slow rate of blood clotting does not occur with reasonable intake of omega-3 fatty acids quantities [1].

3. CONCLUSION AND RECOMMENDATIONS

3.1 Conclusion

The profound health benefits derived from fish bioactive compounds indicated the need for continued promotion of the health properties of fish by all as a route to increase fish consumption and improve the health of people. Fish possess high quality and easily digestible proteins due to their low amount of connective tissues which has been reported to improve the health status of people living with chronic diseases such as hypertension, diabetes, cancer and obesity.

3.2 Recommendations

Fishes should be consumed with whole grains, combining with proper amounts of fruits and vegetables, since they are prone to oxidation as a result of their high contents of polyunsaturated fatty acids. Fish consumption should be given more preference over white or red meat in order to take advantage of the rich repository of their valuable omega-3 and their good quality protein which is easily digested due to the low amount of connective tissues. Health potentials of fish should be maximised by using fish wastes such as the head, fins and internal organs which are also good sources of bioactive compounds for the formulation of nutraceuticals.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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