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Pharmacological potential of fish extracts

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ABSTRACT

In the recent years there has been an increased research interest to develop cardio protective and other pharmacological therapies from natural sources like animals and plants from marine origin. Fish proteins extracts and their and their hydrolysates are the best protein compounds in terms of nutrition and other health promoting benefits. The fish extracts are studied to larger extents and said has been proved that they contain promising health benefit molecules. Chemicals produced by or found in marine organisms have been shown to have a wide variety of applications as pharmaceuticals for humans and other animals. Several studies have stated that the compounds of fish muscle have antioxdative properties which include ascorbic acid, uric acid, glutathione, polyamines, histidine containing dipeptides and free amino acids Uses have included antibacterial, and antiviral and anti-tumor agents. Particular attention has been paid to a variety of toxins formed by marine organisms. Nutraceuticals constitute a variety of substances used in the food supplement and natural health markets. This review paper highlights the important functions and pharmacological potentials of fish proteins and their extracts.

Keywords: Proteins, Nutraceuticals, health promoting, antibacterial, food supplement.

INTRODUCTION

Proteins are important in food production both for their nutritional properties and also for their functional properties. Functional properties can be defined as the overall physicochemical behavior of performance of proteins in food systems during processing, storage, and consumption. The functional properties of fish proteins may be improved by the use of specific enzymes and by choosing a defined set of hydrolysis conditions, such as time, pH, and temperature, to partially hydrolyze the proteins to the desired extent (16). Fish proteins contain antioxidative activity and some functional properties (32), (33), (39), (60-62). Fish proteins

exhibits antioxidant properties as reported by several authors Sathivel et al (2003), Klompong et al (2007) and constitute a source of health beneficial molecules such as secretagogues, calciotropic hormones and growth factors (48). In addition hypotensive activity, immuno-stimulant activity and antiproliferative activity has been found as well. (47). Peptides that are inactive within proteins have showed physiological effects in the body and when released shows function as regulatory compounds with hormone like activity (17),(64). Osteoporosis, Osteoarthritis, cardiovascular disease (hypertension and stroke), diabetes, obesity and cancer are some of the wide-reaching diseases which may also occur due to the lack of dietary calcium.

The production of protein hydrolysates has been also used as a tool for the lipid recovery from by-products (8), (15), (38). Because some proteins possess a range of dynamic functional properties, fish proteins exhibits a wide spectrum of physicochemical behavior such as emulsifying activity, foamability and moisture sorption (36). Thus the modified proteins can be used as additives in food beverage and cosmetic systems (41). Bioactive peptides isolated from various fish protein hydrolysates have shown a numerous bioactivities such as antihypertensive, antithrombotic, immunomodulatory and antioxidative activities. Kim et al (2000) have reported that some peptides derived from fish showed antihypertensive activity inhibiting the action of angiotensin I converting enzyme (ACE) even stronger than that of many other natural peptides. These peptides exhibited in vivo activities by lowering blood pressure in spontaneously hypertensive rats (13), (22). Enzymatically hydrolyzed fish muscle peptides also have shown anticoagulant and antiplatelet properties tested in vitro and these results have suggested the capability of fish peptides to inhibit coagulation factors in the intrinsic pathway of coagulation (51).

Cardio protective functions of fish protein extracts

Isolation of potent anticancer compounds from fish tissue is also a strong argument to consider that by products could constitute a source of anticancer or chemo preventive molecules. Picot et al (2006) demonstrated that some fish proteins obtained by controlled enzymatic hydrolysis of muscle proteins, exert a significant antiproliferative activity on human cancer lines in vitro. The anthracycline antibiotic doxorubicin (DOX) is one of the most effective antitumor agents against human malignancies such as leukemia, lymphoma and many solid tumors. The treatment of cancer patients with DOX may be complicated by deleterious side effects like the direct damage to the heart which may lead to the development of acute and chronic congestive heart failure (CHF), malignant arrhythimas and death (10). The antioxidants are now much focused in order to know whether these antioxidants can prevent myocardial damage. A well known example for such a clinical application in the field of cardiovascular medicine are the fish derived long chain N-3 poly unsaturated fatty acids (14),(37). There is also evidence that aqueous fish derived substances such as taurine, have cardioprotective effects (14). Cardioprotection has been in the research focus for many years. Different pharmacological and non pharmacological strategies have been proposed to decrease myocardial damage e.g. during ischemia reperfusion injury and cardio toxicity (10). Several studies have shown beneficial cardiovascular effects of fish and its derivatives. They are very well known as polyunsaturated fatty acids. These fatty acids may enter the cellular membrane and alter membrane function resulting in antiarrhythmic effects (14). Evidences prove that dietary supplementation with fish oil preserves normal vasonation of atherosclerotic coronary arteries and reduce damage to the myocardium after ischemia and reperfusion in animal models **(**42), (49).

Much less is known whether aqueous components of fish like proteins, peptides and amino acids can protect the heart on a wet weigh basis. The aqueous phases generally contribute to 95-99% of the total edible parts of seafoods (10). They also proved that the aqueous fish derived compounds may play an important role in cardio protection. Taurine is generally found in high levels in seafood **(**45**).** It is involved in radical scavenging membrane regulation, osmoregulation and regulation of calcium homeostasis **(**40**).** In animal models and in human trials the settings of CHF, taurine was found to have beneficial effects on cardiac function and morphology (20), **(**58**).**

Angiotensin Converting Enzyme (ACE) Inhibitory Activity

Different biological properties have been attributed to peptides and they have been shown to have influence as antioxidants, antimicrobials, surfactant agents and angiotensin converting enzyme(ACE) inhibitory activity (44).Angiotensin-converting enzyme (ACE) inhibitory activity was frequently reported from a variety of fish species. Kawasaki et al(2000) found that sardine muscle hydrolysate, prepared by using an alkaline protease, showed potential α-glucosidase inhibitory activity and significant antihypertensive effect on mild hypertensive subjects via ACE inhibition (25). Astawan et al (1995) found that Indonesian dried-salted fish hydrolysate, prepared by pepsin action, showed high ACE-inhibitory activity.

Researchers have identified and reported specific peptides from animal and fish proteins responsible for ACE inhibition (5), (58), (59), (63).Besides ACE-inhibitory activity, other biological properties has also been reported. Rozenn et al (2000) extracted several fractions from cod muscle hydrolysate, which contained biologically active peptides such as growth factors, gastrin and cholecystokinin. Bernet et al (2000) reported that FPH (Gabolysat PC60) had diazepam-like effects on stress responsiveness of the rat's pituitary–adrenal system and sympathoadrenal activity. Fouchereau-Peron et al (1999) isolated an acidic fraction from a fish protein hydrolysate with calcitonin-gene-related-peptide-like biological activity. It is well documented that hydrolysed fish muscle inhibits ACE more effectively than non-hydrolysed samples. Among seafood, hydrolysed protein from tuna (34), channel catfish (59), and chum salmon (46) has been reported to show ACE inhibitory activity.

Antioxidative functions

Reactive oxygen species (ROS) include hydroxyl, superoxide, peroxide radicals and their active precursors, the singlet oxygen are invoved in a variety of pathologies leading to the damage of host cells. ROS can be removed by a cascade of innate antioxidant defense systems, including superoxide dismutase (sod), catalase and glutathione peroxidase hydrophilic scavengers (19). Excessive ROS levels induced by UV irradiatin may destroy the innate antioxidant defense systems resulting in DNA damage, protein carbnylation and lipid peroxidation as well as causing severe health problems such as cancer, neurological degeneration and aging (68).

Radicals including reactive oxygen and nitrogen species cause diseases; therefore, the removal of such radicals to reduce the risk of disease is recommended. 2,2-Diphenyl-1-picrylhydrazyl (DPPH) is a relatively stable radical and frequently used as a first approach fort evaluating radical scavenging activity. Jao and Ko (2002) and Wu et al (2003) reported the DPPH radical scavenging activity of peptides and free amino acids from hydrolysed tuna cooking juice and mackerel muscle hydrolysate. Peptides derived from fish proteins have shown the ability of

exerting potent antioxidative activities in different oxidative systems (23), (31), (50). Levels and compositions of free amino acids and peptides were reported to determine the antioxidant activities of protein hydrolysates (67). Kim et al. (1999) and Jung et al (2005) reported that peptides from fish hydrolysates are capable of accelerating calcium absorption. Peptides are also prone to digestion during gastrointestinal passage and absorption (11). Bernet et al (2000) reported that fish protein extracts had diazepam like effects on stress responsiveness of the pituitary adrenal system and sympathoadrenal activity. Kim et al (2001) isolated antioxidative peptides from gelation hydrolysate of Alaska Pollack skin. Ren et al (2010) reveled that the grass carp myofibrillar protein hydrolysate had a distinct inhibitory effect on lipid peroxidation and low density lipoproteins oxidation. Antioxidant peptides have been formed from porcine myofibrillar proteins by protease treatment as reported by (55). They concluded that fish proteins may have a role as a cardio protective nutrient. Fish skin extracts which represents as processing waste is found to be rich in collagen peptides which are highly bioactive. Ren Shuwen et al (2010) reported that tilapia fish skin have complexes which have antioxidant effects. They concluded that protein oligosaccharides complexes can be used for potential applications in pharmaceutical, cosmetic and food industries.

Distinctive functions of fish extracts

A dietary combination of fish oil and fish protein extracts for wistar rats resulted in lower levels of plasma cholesterol and higher levels of hepatic cholesterol compared with dietary fish oil or fish proteins (18). They also reported that fish protein hydrolysates reduces plasma total cholesterol, increases the proportion of HDL cholesterol and lowers acyl COA cholesterol acyltransferase activity in liver of zuker rats This shows that the fish protein hydrolysates can also implement its effect in cholesterol reducing properties this is mainly due to lowering of high-density lipoprotein cholesterol. The inclusion of fish protein hydrolysates in diet may afford more sufficient digestible protein which could be impacted better into the immune system of fish. Furthermore, fish proteins are likely to contain a large amount of bioactive sequences and constitute a potential reservoir for potent immune-modulators (7).The significant in vivo anti-anaemia activity of the fish protein hydrolysates in mice suggested that the proteins supplied raw material for hematogenic action. The nutrition supplement, e.g. amino acids and mineral Fe, of the fish protein for anaemic mice was helpful to improve the counts of RBC, HGB and WBC in blood of animals in trial (66). This study emphasizes that the fish protein contains significant in vivo anti-anaemia activity.

Moreover, the utilization of proteins or their hydrolysates for food and cosmetic applications not only presents additional advantages over other antioxidants, but also they confer nutritional and functional properties (6), (43). Fish protein hydrolysates such as skin gelatin hydrolysate from brown stripe red snapper (26) or meat protein hydrolysates from yellow travelly (32), (33), round scad (61), (62), mackerel (67) and loach (69) have been reported to exhibit antioxidant activity. Fish protein hydrolysates can be used in food systems, comparable to other pertinent protein hydrolysates (35).

CONCLUSION

It has been estimated that by 2020 heart diseases and stroke will become the leading cause of death and disability worldwide (WHO 2009). The optimal macro nutrient intake to prevent heart

diseases(OMNI HEART) trial demonstrated that partial substitution of carbohydrate with protein sources low in saturated fat content can lower blood pressure, improve lipid levels, facilitate short term weight loss and reduce the risk of CHD (2). The mechanisms by which protein could exert its beneficial effects include an increased intake of biologically active amino acids or peptides (2). These findings have led to the development of nutritionally enhanced food products designed to suit specific health concerns, particularly with relevance to the management of lifestyle related diseases (9). According to the World Health

Organization, 600 million people with high blood pressure are at risk of heart attacks and heart disease-related complications. Approximately 5million premature deaths occur worldwide every year. Among people with hypertension, 90% is not aware of its problems and consequences. High blood pressure is a major leading cause of strokes and kidney failure, blindness and even dementia. Cardiovascular diseases (CVD) are a major health problem and the leading cause of death worldwide, both for women and men (52). In Europe, CVD causes nearly half of all deaths (48%), and is the main causes of the disease burden (23% illness and death) (1). Millions of deaths occur from heart disease alone each year, and patients seldom notice symptoms until organs have already been damaged. The reports from various studies suggest that fish proteins and their extracts, hydrolysates have an enormous biological and pharmaceutical application which has to be focused in a much broader sense and apart from research activities necessary measures have to be taken for the implementation of these biological and pharmaceutical functions under clinical trials.

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