Mini Review

Bioactive peptides from fish by-products with anticarcinogenic potential

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Abstract

As a major cause of death, cancer has affected the world population, both directly and indirectly. There are however, growing numbers of cancer cases some of which could be prevented or even treated using natural compounds. Bioactive peptides from terrestrial and marine environment have been claimed to potentially reduce the risk of chronic diseases or maintain health. Fish processing industry produces more than 50% by-products which can be converted into valuable fish protein hydrolysate (FPH) by chemical or biochemical hydrolysis. This paper discusses the potency of fish by-products as sources of bioactive peptides with anticarcinogenic potential. Moreover, a short review about the antioxidant and anticancer activities of novel bioactive peptides isolated from fish by-products is presented.

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Introduction

According to the 2014 Food and Agriculture Organization (FAO) Fisheries and Aquaculture Department’s report, world per capita fish consumption increased significantly from an average of 9.9 kg in the 1960’s to 19.2 kg in 2012. Fish (including finfish, molluscs and crustaceans) currently represents about 16.6% of animal protein supply and 6.5% of all protein for human consumption with the value of exported products reaching US$136 billion (FAO Fisheries and Aquaculture Department, 2014). An increasing demand for fish products means greater volumes of fish processing by-products are generated. Fish waste or fish by-products are identified as leftovers that are not saleable in general but can be recycled after treatment or processing (Kim and Mendis, 2006). This includes viscera, heads, cut-offs, bone, skin, fins, roes and frames.

Fish by-products present a huge problem for environment and seafood industry. The amount of fish discarded by seafood industries vary within 50-75% of the total weight of the catch, depending on species, size, season and fishing ground (Rustad et al., 2011). In 2005, Food and Agriculture Organization reported significant decrease of fishery discards due to increased utilization of unwanted by-products (Kelleher, 2005). The utilization of fish by-products is an important production opportunity for the fishing and seafood processing industry, as it can potentially generate additional income as well as reduce disposal costs for these materials (Arvanitoyannis and Kassaveti, 2008). The most common approach in utilizing fish-by products is by converting unused fish parts into fish protein hydrolysate (FPH). Research on hydrolysis of fish protein has been developed from early 1960’s with the main objective to provide cheap nutritious fish protein for developing countries or to accelerate animal feed production (Kristinsson and Rasco, 2000). Fish protein hydrolysates possess desirable functional properties and a high nutritional value. They contribute to water-holding, texture, gelling, foaming and emulsification properties in different food systems (Rustad et al., 2011).

Fish protein hydrolysate can be produced by hydrolysing fish muscle or body parts using chemicals (acid or alkaline), or biochemical (microbial enzymes, digestive enzymes) added at appropriate levels in controlled systems (Ovissipour et al., 2012). The quality or properties of peptides liberated by FPH is highly dependent on the type of proteases or chemicals, temperature, pH and time implemented during hydrolysis (See et al., 2011; Nazeer and Anila Kulanndai, 2012). Protein hydrolysate usually consists
of small fragments of bioactive peptides that contain 2-20 amino acids though some have been reported to be more than 20 residues (Ryan et al., 2011). Bioactive peptides are inactive within the sequence of the parent proteins and may be released by hydrolysis or digestion (Sarmadi and Ismail, 2010). After digestion and being absorbed in the intestines, bioactive peptides enter the blood stream and reach the target sites (e.g. liver, colon) to exert the bioactivities (Erdmann et al., 2008). Several studies showed that bioactive peptides derived from fish by products may exert more than one physiological effect in human body (Je et al., 2009; Naqash and Nazeer, 2011).

Rodrigues et al. (2009) suggested that bioactive peptides with lack of toxicity to healthy cells would be a promising candidate for anticancer treatment. Peptide-based drug therapies are also known for their strong specificity, tumor penetrating ability due to their small size (Barras and Widmann, 2011). Anticancer peptides (ACPs) act against cancer cells through several mechanisms including: (1) cytoplasmic membrane disruption via micellization; (2) induction of apoptosis, and (3) interaction of peptides with cell surface gangliosides (Huang et al., 2011). Numerous researches showed that these ACPs are obtainable from various food proteins, particularly milk (Gill and Cross, 2000) and marine species (Zheng et al., 2011; Suarez-Jimenez et al., 2012). Interestingly, recent reports have also demonstrated that fish by-products can be used as valuable sources of ACPs (Picot et al., 2006; Alemán, Pérez-Santín, Bordenave-Juchereau et al., 2011). This review, therefore, will illustrate the recent advances of utilization of fish by-products as sources of novel bioactive peptides with anticarcinogenic potential.

Cancer and bioactive peptides from marine origin

Cancer is a leading cause of death worldwide. An estimated 14.1 million people were diagnosed with cancer across the world in 2012, with more than 8.2 million people dying from the disease (Ferlay et al., 2015). In Australia, over 43,000 people have died from cancer in 2012. It is also predicted that 1 in 3 Australians will be diagnosed with cancer by the age of 85 (Cancer Council Australia, 2015). Disturbingly, the number of cases of cancer diagnosed in Australia is projected to rise for both males and females and is expected to reach about 150,000 in 2020—an increase of almost 40% from 2007 (Australian Institute of Health and Welfare, 2012). Cancer is also notorious for its high cost of treatment. Recently, the Cancer Council Australia (2015) reported that $4.5 billion in direct health system were dedicated to covering cancer treatment costs.

The cause of cancers and how to prevent, treat or cure them has continually become the major topic in biomedical research and publications. Cancer can be defined as a group of diseases characterized by uncontrolled division and spread of abnormal cells (American Cancer Society, 2015). Whilst cell division is a normal physiological process that occurs in tissues, disruption of balance between cell proliferation and apoptosis may cause certain mutations in DNA and lead to cancer (Gerl and Vaux, 2005). Carcinogenesis or cancer development may occur in three stages, i.e. initiation, promotion and progression (Weston and Harris, 2003). It can be triggered by external factors (tobacco inhalation, chemicals, food contamination, and radiation) and internal factors (hormones, immune system damage, inflammation and physical conditions) (Anand et al., 2008). While several cancers are associated with infectious organisms and parasites (Oliveira et al., 2007), it is also increasingly evident that genetic background can affect individual’s susceptibility to carcinogens (Spitz and Bondy, 2006).

Cancer is mostly treated by surgery, or in some cases combined with chemotherapy and radiotherapy (American Cancer Society, 2015). However, such therapies often are associated with deleterious effects caused by drug-induced damage to healthy cells and tissue (Hubenak et al., 2014). Thus discovery of new safe cancer drugs becomes an important goal of research in biomedical sciences, with increasing number of new anticancer compound to be sourced from the marine environment (Jimeno et al., 2004; Simmons et al., 2005; Zheng et al., 2011). In 2010, an economic analysis estimated the value of anticancer drugs of marine origin at US $563 billion to 5.69 trillion, with 55 to 214 new compounds sourced mostly from Phyla Chordata, Mollusca, Porifera, Bryozoa, Proteobacteria and Cyanobacteria (Erwin et al., 2010).

As anticancer drugs, marine anticancer peptides (MACPs) induce cancer cell death through different mechanisms (Figure 1). Apoptosis, a programmed cell death, is the most preferable way of cancer cell death during treatment (Zheng et al., 2011). Apoptotic process can be triggered by p38 mitogen-activated protein kinases (MAPK) by inhibiting pro-survival gene Bcl-2 and induce pro-apoptotic gene Bax (Yip and Reed, 2008) or by activating Jun N-terminal kinase (JNK) and MAPK that lead to the release of cytochrome c (Cyt C) from mitochondria (Shieh et al., 2010). MACPs disrupt the tubulin-microtubulin equilibrium by inhibiting cell mitosis by binding to the protein tubulin and preventing polymerization into the microtubules (Islam and
Ishkander, 2004). Eventually, essential cellular functions, such as chromosome segregation and cell tumour maintenance will be affected (Hadfield et al., 2002). Angiogenesis or the formation of new blood vessels plays important role in the growth of tumours. Inhibition of vascular endothelial growth factor (VEGF) and hypoxia inducible factor 2 alpha (HIF2α) pathway by peptides directly inhibited tumor cell growth (Weidemann and Johnson, 2008).

Anticancer peptides from fish by-products

Most marine-derived anticancer peptides have been isolated from molluscs, tunicates, ascidians and sponges (Suarez-Jimenez et al., 2012), while a number of anticancer studies involving fish by-products has been limited (Table 1). Cancer growth inhibitory activity was observed from peptides extracted from sepia ink oligopeptides. The peptide, identified as N Gln-Pro-Lys with a molecular mass of 343.4 Da, inhibited the proliferation of human prostate cancer (DU-145) cells (Ding et al., 2011). The antiproliferation activity was probably due to the presence of proline and lysine in the peptide sequence. Roomi et al., (2015) reported that nutrient mixture (NM) contained proline and lysine proved to be highly toxic for DU-145 cells. Furthermore, two antiproliferative peptides contained proline (Leu-Pro-His-Val-Leu-Thr-Pro-Glu-Ala-Gly-Ala-Thr and Pro-Thr-Ala-Glu-Gly-Gly-Val-Tyr-Met-Val-Thr), isolated from tuna dark muscle, also showed potential inhibitory activity on the growth of breast cancer (MCF-7 cells) (Hsu et al., 2011). Certain amino acids, however, behaved differently toward various cancer cell lines. Gu et al., (2015) reported that Cys promoted the proliferation of gastric cancer (GC) cells as well as breast cancer (BC). Asp and Arg stimulated the growth of BC while Glu induced the apoptosis of GC cells. Interestingly, Ala treatment showed opposite effects on the proliferation and of GC cells and BC cells, suggesting that Ala may be the key functional amino acid in different cancer metabolisms.

Peptides derived from snow crab by-products showed anticancer activity on colon, breast, prostate and lung cancer cell lines (Doyen et al., 2011). A promising anticancer peptide was also obtained from shrimp shells and was shown to significantly inhibit the growth of both colon and liver cancer cells (Kannan et al., 2011). Recently, small molecular size peptides (< 3 kDa) isolated from Flathead by-products was reported to inhibit the growth of HT-29 colon cancer cells up to 91.04% (Nurdiani et al., 2017). The profiles of most anticancer peptides isolated from fish by-products, however, were not yet identified or characterised so that the mechanism of anticancer activity of these peptides are largely unknown. In addition, despite the fact that peptides derived from fish by-products showed promising cancer cell growth inhibitor activity (Picot et al., 2006), the cytotoxicity effect of these peptides on normal cells were rarely discussed. Thus, further cell based and in vivo studies are required to ensure the efficacy and safety of anticancer peptides derived from fish by-products.

Radicals scavenging peptides from fish by-products

Cancer as well as many human diseases, including ischemia, diabetes, arthritis, can be triggered by excessive production of free radicals or reactive oxygen species (ROS) (Najafian and Babji, 2012). Several experimental studies suggested that ROS can act as both initiators and promoters of tumors by damaging cellular macromolecules such as DNA, proteins, and lipids, and by acting as cell-signaling molecules, in the form of nitric oxide (Benedetti et al., 2015). Furthermore, critical illness can drastically increase the production of ROS or reactive nitrogen species (RNS) (Abiles et al., 2006). Fortunately, high level of an antioxidant (>66% of recommended dietary intake) could reduce the risk for worsening oxidative stress by 94%, regardless of change in severity of illness (Abiles et al., 2006).

Antioxidants occur naturally in food and peptides with antioxidant activities have been identified from a number of aquatic species (Bernardini et al., 2011). In regards to fish by-products, several peptides with high antioxidant and/or free radicals scavenging activities are well-documented (Table 2). Generally, peptides with high free radical scavenging activity contain amino acids with sulfur-containing side chains (Cys and Met), aromatic side chains (Trp, Tyr, His and Phe) or hydrophobic amino acids (Val,
Leu and Ala) (Batista, 2013, Ngo et al., 2014). Je et al., (2005), for example, identified a sequence of high antioxidant peptide (Leu-Pro-His-Ser-Gly-Tyr) from Alaska pollack (Theragra chalcogramma) frame protein hydrolysate. Peptides contained Leu, Pro and Gly were also reported to act as a good electron donor and could react with free radicals to convert them to more stable products and terminate the radical chain reaction (Jaiganesh et al., 2011; Chi et al., 2015).

Beside amino acid composition, the antioxidant nature of FPH is highly dependent on peptide size and disruption of tertiary structure of parent protein by hydrolysis (Elias et al., 2008). The type of substrate, type of protease, and conditions implemented during hydrolysis influence the degree of hydrolysis of FPH as well as molecular weight of peptides produced (Sun, Shen and Luo et al., 2011). As proteases have specific cleavage positions on polypeptide chains, fish protein hydrolysate may contain different mixtures of high, medium or low molecular weight peptides with various bioactivities (Nasri et al., 2013). Several authors reported that high antioxidant activity was inversely related to molecular weight (Je et al., 2007; Yang et al., 2009; Hsu, 2010; Sabeena Farvin et al., 2014) as low molecular weight peptides interacted more effectively with radicals, thus interfering with the oxidation process (Wang et al., 2012). This was contracted by Alemán, Giménez, Pérez-Santin et al., (2011) who reported a direct relationship – higher molecular weight exerted a greater ABTS activity, which was attributed to a large number of free amino acids and small peptides without antioxidant capacity.

In order to further examine the protective effect of peptides against reactive oxygen species, several researchers performed cell-based studies. Mendis, Rajapakse, Byun et al. (2005), for instance, investigated antioxidant activities of jumbo squid skin gelatine by assessing two purified peptides (Phe–Asp–Ser–Gly–Pro–Ala–Gly–Val–Leu and Asn–Gly–Pro–Leu–Gln–Ala–Gly–Gln–Pro–Gly–Glu–Arg) on cultured human fibroblast cells to overcome tert-butyl hydroperoxide-mediated oxidative cell death. The study showed that both peptides exhibited a dose-dependent cell viability enhancement effect. Similarly, purified peptides from skate (Okamejei kenojei) exhibited an inhibitory activity against the elevation of intracellular ROS in the activated cells. The peptide sequence was found to be Met–Val–Gly–Ser–Ala–Pro–Gly–Val–Leu and Leu–Gly–Pro–Leu–Gly–His–Gln (Ngo et al., 2014). In order to prove the efficacy and safety of antioxidative peptides, further cell based as well as in vivo studies are required.
Table 2. Free radical scavenging activities of peptides isolated from fish by-products

<table>
<thead>
<tr>
<th>Fish species</th>
<th>By products used</th>
<th>Enzyme used/ Treatment</th>
<th>Reported radical scavenging activities</th>
<th>Sequence of isolated peptide</th>
<th>Reported mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alaska pollack (Theragra chalcogramma)</td>
<td>Frame</td>
<td>Mackeral intestine, crude enzyme (MIC)</td>
<td>Hydroxyl</td>
<td>Leu-Pro-His-Ser-Gly-Tyr (872 Da)</td>
<td>Chelating and lipid radical-trapping ability of the imidazole ring of His. Tyr is a potent hydrogen donor. (Je et al., 2005)</td>
</tr>
<tr>
<td>Alaska pollack (Theragra chalcogramma)</td>
<td>Skin</td>
<td>Neumose, Flavoutrazine, Alcalase, Trypsin, Proteinase, and Papain</td>
<td>2,6-Diaryl-1-pycrylhydrazal radical (DPHH)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bigeye snapper (Plectarchus macrocephalus)</td>
<td>Skin gelatin</td>
<td>Pyloric caeca extract</td>
<td>DPPH, 2, 6-Azobis-(ethylbenzeneazoine-6-sulfonic acid) (ASTS)</td>
<td>-</td>
<td>Peptides acted as hydrogen donors. (Phanurant et al., 2010)</td>
</tr>
<tr>
<td>Bigeye tuna (Thunnus obesus)</td>
<td>Head</td>
<td>Alcalase</td>
<td>DPPH, hydroxyl, superoxide, and alky</td>
<td>H-Leu-Asn-Leu-Asp-Thr-Leu-Val-Thr-Arg</td>
<td>The peptides acted as potent electron donors. (Yang et al., 2011)</td>
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<tr>
<td>Bigeye tuna (Thunnus obesus)</td>
<td>Dark muscle</td>
<td>Alcalase, α-chymotrypsin, Neumose, Papain, Pepsin, and Trypsin</td>
<td>DPPH, hydroxyl, superoxide, and alky</td>
<td>-</td>
<td>Peptides acted as electron donors. scavenged the cellular radicals and enhanced the viability of term-10 haloperidol- induced cytotoxicity. (Je et al., 2008)</td>
</tr>
<tr>
<td>Black Pomfret, (Parapristolepis niger)</td>
<td>Viscera</td>
<td>Pepain, Trypsin, and α-chymotrypsin</td>
<td>DPPH</td>
<td>Ala-Met-Thr-Gly-Leu-Val-Arg (T81.9 Da)</td>
<td>Peptides acted as electron donors. (Jagannath et al., 2011)</td>
</tr>
<tr>
<td>Black scabbardfish (Aphanius carpio)</td>
<td>By products</td>
<td>Pepain, Trypsin, and α-chymotrypsin</td>
<td>DPPH</td>
<td>-</td>
<td>Active peptides transformed radicals to more stable products. (Balita et al., 2016)</td>
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<tr>
<td>Bluefin leatherjacket (Lutineolex septentrionalis)</td>
<td>Visceral waste</td>
<td>Alcalase, Trypsin, and α-chymotrypsin</td>
<td>DPPH</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Common tuna (Thunnus albacares)</td>
<td>Roe</td>
<td>Alcalase</td>
<td>DPPH</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cod (Gadus morhua)</td>
<td>Skin gelatin</td>
<td>Alcalase, α-chymotrypsin, Neumose, Papain, Pepsin, and Trypsin</td>
<td>DPPH</td>
<td>-</td>
<td>Peptides donated hydrogen to radicals, resulting in formation of more stable aldehyde and reduced oxidation of lipoproteins. (Stykel et al., 2009)</td>
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<tr>
<td>Common tuna (Thunnus albacares)</td>
<td>Backbones</td>
<td>Protease</td>
<td>DPPH</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Cod (Gadus morhua)</td>
<td>Backbones</td>
<td>Papain, Pepain, and Trypsin</td>
<td>DPPH, superoxide, and hydroxyl</td>
<td>Leu-Glu-Val-Lys-Pro (505.5 Da)</td>
<td>Peptides inhibit the radical-induced peroxidation chain reaction by increasing solubility of peptides in egg. (Hashem and Nair, 2013)</td>
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<tr>
<td>Cod (Gadus morhua)</td>
<td>Skin gelatin</td>
<td>Trypsin, α-chymotrypsin, Neumose, and Trypsin</td>
<td>DPPH, superoxide, and hydroxyl</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cod (Gadus morhua)</td>
<td>Frame</td>
<td>Papain, Trypsin, papain, α-chymotrypsin, Alcalase and Neumose</td>
<td>DPPH, hydroxyl radical, hydroxyl radical-induced DNA damage protective properties</td>
<td>Hs-Gly-Pro-Asp-Glu-Val-Leu-Arg</td>
<td>Peptides decreased dibutyryl peroxide-induced cytotoxicity on human embryonic lung fibroblasts and protected induced DNA damage, Liu and Ai reacted rapidly to the hydrophobic PUFAs. (Kim et al., 2007)</td>
</tr>
<tr>
<td>Horse mackerel (Magalorhaxis cirratus)</td>
<td>Viscera</td>
<td>In vivo gastrointestinal digestion</td>
<td>DPPH, hydroxyl radical, hydroxyl radical-induced DNA damage protective properties</td>
<td>Hs-Gly-Pro-Asp-Glu-Val-Leu-Arg</td>
<td>Antioxidant activities are due to hydrophobic amino acids present in peptide sequences. (Mandool, Rajoopath, &amp; Ken, 2005)</td>
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<tr>
<td>Pacific cod (Gadus macrocephalus)</td>
<td>Skin gelatin</td>
<td>Alcalase, Neumose, Papain, Trypsin, Pepain, and α-chymotrypsin</td>
<td>DPPH, hydroxyl radical, hydroxyl radical-induced DNA damage protective properties</td>
<td>Hs-Gly-Pro-Asp-Glu-Val-Leu-Arg</td>
<td>Peptides acted as potent electron donors and inhibited the oxidative damage of DNA. (Ngo et al., 2010)</td>
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<tr>
<td>Sardine (Sardinops sagax)</td>
<td>Heads and/or Viscera</td>
<td>Crude enzyme from Mackerel muscle/Intestine, crude enzyme from viscera of sardine (S. aurita), hepatopancreas of cuttlefish and</td>
<td>DPPH</td>
<td>-</td>
<td>Peptides acted as potent electron donors. (Barkia et al., 2010)</td>
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<tr>
<td>Fish</td>
<td>Tissue</td>
<td>Enzyme Activities</td>
<td>Antioxidant Activity</td>
<td>Refs.</td>
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<tr>
<td>Sardinella aurita by-products</td>
<td>Heads</td>
<td>Aconitase, crude enzyme from Aspergillus clavatus ES1, alkaline proteases from B. licheniformis NH1, crude enzyme from viscera of sardine (Sardinia pilchardus)</td>
<td>DPPH and hydroxyl radicals scavenging activity</td>
<td>(Bougatief et al., 2010)</td>
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<td></td>
<td>Hods</td>
<td>Autolysis</td>
<td>DPPH</td>
<td>(Nazier, 2011)</td>
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<td>Seela (Sphyraena barracuda) and Ribbon Fish (Leptarsa catus savala) Shrimp</td>
<td>Backbone</td>
<td>Papain, Pepsin and Trypsin</td>
<td>-</td>
<td>(Nazeer, 2011)</td>
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<tr>
<td>Silver carp (Hypophthalmichthys molitrix)</td>
<td>Processing by-product</td>
<td>Alcalase, Flavourzyme, Neutrase, Papain, Pepsin, Trypsin, and Proctamex</td>
<td>-</td>
<td>(Seewysa et al., 2011)</td>
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<tr>
<td>Skate (Okamejikenojiri)</td>
<td>Skin gelatin</td>
<td>Alcalase, Flavourzyme, Neutrase, and Proctamex</td>
<td>Protective effects in human umbilical vein endothelial cells</td>
<td>(Ngo, 2014)</td>
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<tr>
<td>Skipjack (Katsuwona pelamis)</td>
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<td>Alcalase</td>
<td>DPPH, ABTS and superoxide anion</td>
<td>(Lentarinsawat et al., 2013)</td>
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<td>Tilapia</td>
<td>Skin</td>
<td>Gelatin</td>
<td>DPPH</td>
<td>(Yang, 2009)</td>
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<td></td>
<td>Frame</td>
<td>Protease E, Pepsin, Trypsin, Favourzyme, Neutrase, Gelatin, and Papain</td>
<td>DPPH, superoxide anion radical, hydrogen peroxides and hydroxyl radical</td>
<td>(Fan, 2012)</td>
<td></td>
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<tr>
<td>Tuna (Oreochromis niloticus)</td>
<td>Backbone</td>
<td>Alcalase, a-chymotrypsin, Neutrase, Papain, Pepsin, and Trypsin</td>
<td>DPPH, hydroxyl, superoxide</td>
<td>(Jo, 2007)</td>
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<tr>
<td>Tuna</td>
<td>Liver</td>
<td>Alcalase, Neutrase, Proctamex, and Flavourzyme</td>
<td>DPPH, hydroxyl, superoxide, hydroxyl-radical-induced DNA damage protective properties</td>
<td>(Ahn, 2010)</td>
<td></td>
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<tr>
<td>Tuna (Katsuwona pelamis)</td>
<td>Dark muscle</td>
<td>Orientase and Proctase XXIII</td>
<td>DPPH</td>
<td>(Hsu, 2010)</td>
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<tr>
<td>Tuna (Katsuwona pelamis)</td>
<td>Liver</td>
<td>Flavourzyme, Alcalase, Proctamex, and Neutrase</td>
<td>DPPH, hydroxyl, hydroxyl peroxide, oxidative DNA, damage protective activity</td>
<td>(Je, 2009)</td>
<td></td>
</tr>
<tr>
<td>Tuna Halibut and Jumbo flying squid</td>
<td>Skin and tunic</td>
<td>Alcalase Collagenase, Trypsin, Pepsin</td>
<td>-</td>
<td>(Alemán, Giménez, Montero, 2011)</td>
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<tr>
<td>Walleye Pollock (Theraclu giogramma)</td>
<td>Skin</td>
<td>Trypsin and Flavourzyme</td>
<td>DPPH, superoxide anion radical, hydroxyl radical and hydrogen peroxide</td>
<td>(Zhuang, 2009)</td>
<td></td>
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</tbody>
</table>
Conclusion

This review discussed the potential of fish by-products as natural sources of bioactive peptides with antioxidant and anticancer properties. Based on evidence of potential health benefits, bioactive peptides derived from fish by-products have promising applications as natural nutraceuticals. Until now, however, a limited number of cell-based as well as in vivo studies on antiproliferative and antioxidant activity of peptides from fish by-products have been performed to date. Further research on utilization of fish by-products for treatment and management of cancer is essential in order to improve our understanding about its mechanism and application.

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References


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