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REVIEW



Fish for Health: Improved Nutritional Quality of Cultured Fish for Human Consumption

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ABSTRACT

In a global fight against over-nutrition, obesity and associated ailments, identification and consumption of healthier food than processed red meat products and fast-foods is crucial. Fish and seafood products appear as the healthier alternative animal products and the present paper highlight their nutritional merits and health attributes in a world where malnutrition but also under-nutrition is still negatively affecting the health and well-being of many people. The paper also provides the major studies conducted to enhance the nutritional profile of farmed fish through dietary fortification, and highlights the need to increase consumer awareness and understanding concerning the health benefits of fish and seafood products as an essential component of a healthy diet.

KEYWORDS

Malnutrition; Undernutrition; Aquatic foods; Aquaculture; Nutrient supply; Dietary fortification

1. The growing epidemic of obesity

Over the past 50 years, there has been a marked increase in the incidence of malnutrition, and in particular over-nutrition and associated ailments within developed and developing countries, including obesity, coronary heart disease, diabetes, and hypertension due primarily to the increased consumption of lower cost fast-foods (and to a lesser extent red meats and dairy produce), coupled with a more sedentary and less active lifestyle (Forouhi et al. 2018; Inyang and Stella 2015; Murray 2001; OECD, 2017; Prentice 2006; Roth et al. 2018; WHO, 2018a, 2018b; Zhong et al. 2020).

For the purposes of this paper fast-foods refers to food items that can be prepared and served quickly, and may include processed red meat products (hot-dogs, hamburgers, sausages, bacon, ham, spam, etc.), processed/refined carbohydrates (biscuits, cookies, donuts, pan cakes, muffins, crackers, bread, pizza, pasta), fried foods (french fries, hash browns, fried chicken, chicken nuggets), sugary drinks, and candy/ice cream (De Vogli et al. 2014);

It is generally believed that the increased proportion of total caloric intake derived from fast food has been due to a variety of factors, including (but not limited to) lower cost/affordability, bigger portion sizes, increased convenience, taste, and accessibility

(Finkelstein et al. 2014; Powell and Chaloupka 2009; Khan et al. 2012; Murray 2001; Xu et al. 2014);

According to the World Health Organization (WHO), the current global status of over-nutrition and obesity, and related ailments, can be listed as follows:

- Worldwide, obesity has tripled since 1975; 13% of the world's adult population were obese in 2016, including 650 million adults, 340 million children and adolescents aged between 5 and 19, and 40 million children under 5 being overweight or obese in 2016 (WHO, 2020);
- Worldwide, cardiovascular diseases account for over 17.8 million deaths annually (increasing by 21.1% between 2007 and 2017, with Ischemic heart disease, stroke, and hypertensive heart disease accounting for 8.93, 6.17 and 0.92 million deaths respectively in 2017; Roth et al. 2018), followed by cancers (9.0 million deaths), and diabetes (1.6 million deaths, with diabetes being a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation; OECD, 2017; WHO, 2018b, 2018c);

Apart from the obvious human cost of over-nutrition and obesity to humanity in terms of lives lost,

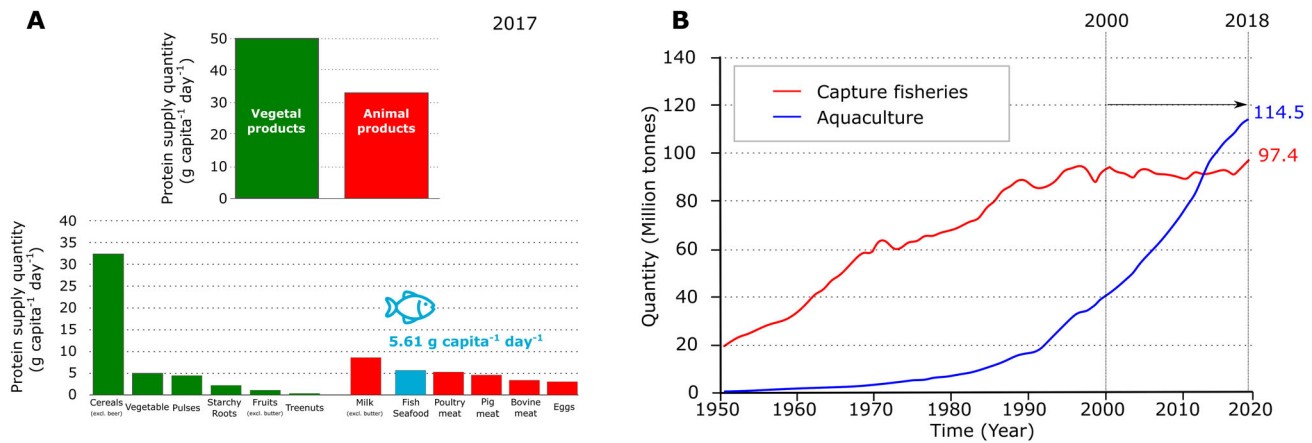


Figure 1. Daily per capita protein intake by animal and vegetal products (global and the top 6 for each category; A; FAO, 2020a) and the trends of global landings from capture fisheries and aquaculture (1950–2018; B; FAO, 2020).

the economic cost to society of dealing with these ailments is considerable (Cawley and Meyerhoefer 2012; Finkelstein et al. 2014; Xu et al. 2014). For example, the estimated cost of treating obesity in the U.S. between 2005 and 2010 reportedly increased by 48.7% from \$212.4 billion to \$315.8 billion, with the share of total health care spending of non-institutionalized adults devoted to treating obesity-related illness rising from 20.6% in 2005, to 27.5% in 2010, and to 28.2% in 2013 (Biener et al. 2017). According to these authors, the increase in expenditure costs has been due to a combination of factors, including increased costs, increased population growth, and an increase in the prevalence of obesity in the U.S. (Biener et al. 2017; Finkelstein et al. 2014). Moreover, dental caries (mainly due to the high dietary intake of free sugars) has been the most common noncommunicable disease worldwide and an expensive disease to treat, reportedly consuming 5–10% of the healthcare budgets in industrialized countries (WHO, 2017).

Notwithstanding the epidemic of overnutrition and obesity, at the same time there has also been a global concern for undernutrition and associated nutrient deficiencies (particularly within developing countries), including wasting (low weight-for-height; 49 million children under the age of 5 years), stunting (low height-for-age; 155 million children under the age of 5 years) and underweight (low weight-for age; 462 million adults), with over 45% of deaths among children under the age of 5 being linked to undernutrition (WHO, 2018a). In view of this double burden of both overnutrition and undernutrition, the United Nations (UN) Decade of Action on Nutrition (2016–2025) aims to address all forms of malnutrition, and in particular for policy action across 6 key areas:

- Creating sustainable, resilient food systems for healthy diets;
- Providing social protection and nutrition-related education for all;
- Aligning health systems to nutrition needs, and providing universal coverage of essential nutrition interventions
- Ensuring that trade and investment policies improve nutrition;
- Building safe and supportive environments for nutrition at all ages; and
- Strengthening and promoting nutrition governance and accountability, everywhere (FAO, 2017; WHO, 2018a).

2. Fish and seafood – a healthier alternative

Fish and seafood (includes all captured and farmed finfish, crustaceans, mollusks, and aquatic plants) offer a much healthier food source than terrestrial meat products (includes processed meats, red meat, poultry) in the global fight against malnutrition and obesity (Bogard et al. 2015; FAO 2018; Mohan Dey et al. 2005; Sargent and Tacon 1999; Solhelm 2010; Thilsted et al. 2014; Verbeke et al. 2005; VKM, 2014; Zhong et al. 2020); on a global basis fish and seafood products constituting the third major source of dietary protein consumed by humans after cereals and milk in 2017 and representing 17.1% of total animal protein supply (fish and seafood consumption being greater than the consumption of poultry meat, pig meat, bovine meat, or hens eggs; Figure 1A; FAO, 2020a). Compared with terrestrial meat products, aquatic animal foods (whether captured or cultured) having a higher protein content on an edible weight

basis than most terrestrial meats, a lower caloric density and generally being much leaner than red and processed meats, having the highest content of long-chain omega-3 polyunsaturated fatty acids than any other animal foodstuff, and generally having a higher mineral and vitamin content than most terrestrial meats and processed meat products (including vitamins - Vitamin A, Vitamin D, Vitamin E, Vitamin B₁₂, Folic acid, Choline, Coenzyme Q₁₀, and minerals - Calcium, Magnesium, Iron, Copper, Zinc, Iodine, Selenium, and trivalent Chromium: Reames 2012; Tacon and Metian 2013; USDA, 2018). Moreover, considerable scientific data exists concerning the direct health benefits of consuming fish and fishery products (including farmed aquatic plants or seaweeds), including (but not limited to) reduced risk of death from coronary heart disease and stroke (FAO/WHO, 2011; Forouhi et al. 2018; He 2009; Hellberg et al. 2012; Verbeke et al. 2005; Wallin et al. 2012), reduced risk of diabetes (Wallin et al. 2012), increased duration of gestation and improved visual and cognitive development (Hellberg et al. 2012), improved neurodevelopment in infants and children when fish is consumed before and during pregnancy (FAO/WHO, 2011), and reduced risk of thyroid cancer in women through seaweed consumption (Michikawa et al. 2012). Table 1 shows the reported functions and health benefit of the key nutrients found in aquatic food products.

Despite the above positive nutritional and health attributes, it must also be stated however that like any other food product, there are potential health risks to fish and seafood consumption depending upon their origin and processing. For example, although the greatest risk to human health is believed to be from the consumption of raw and/or unprocessed fish and seafood contaminated with pathogens (including parasites, nematodes, cestodes, trematodes, bacteria, and/or biotoxins depending upon the species), these risks can be eliminated through proper cooking, handling and storage (FAO/WHO/World Health Organization (WHO), 2003; Hellberg et al. 2012). Notwithstanding the above, there may be a risk from the presence of environmental contaminants (depending upon the aquatic species and origin), including (but not limited to) heavy metals (methyl mercury), persistent organic pollutants (POPs - PCBs, dioxins), veterinary drug residues, and micro-plastics (Berntssen et al. 2010; Domingo et al. 2007; FAO/WHO, 2011; Hellberg et al., 2012; Tacon and Metian 2008; Verbeke et al. 2005; VKM, 2014). Notwithstanding the above risks, it is generally believed that the higher nutritional value

and potential health benefits derived from increased fish consumption far out-way the potential negative risks to human health (FAO/WHO, 2003, 2011; VKM, 2014). In addition, fish and seafood products have, like any other food products found on the market, been through food safety measures and verification (from national regulations to International food standards) although ensuring food safety and security in a highly globalized world presents increasingly difficult (Fukuda 2015).

3. All fish are not all created equal

It follows from the above discussion that not all fish are created equal, and that their nutritional composition, contaminant burden (if any), and consequently their potential health value, will vary depending upon the fish species, its position in the aquatic food chain and feeding habit, its longevity and size before being consumed, its geographical origin and source (if harvested from a river, lake, estuary, or open sea; recreational fishery, wild caught or farmed), and the nutrient profile and composition of the feed fed if farmed (Cladis et al. 2014; Kwasek et al. 2020; Maule et al. 2007; Mohan Dey et al. 2005; Tacon and Metian 2013; USDA, 2018; VKM, 2014). For example, Bogard et al. (2017) reported the lower overall nutritional quality (in terms of the nutrients iron and calcium) of lower trophic-level farmed freshwater fish compared with wild-caught marine fish in Bangladesh. Similarly, higher levels of the heart healthy long-chain omega-3 polyunsaturated fatty acids (eicosapentaenoic acid - EPA and docosahexaenoic acid - DHA) have also been reported in wild-caught marine small pelagic fish species (mackerel, herring, anchovy) and higher trophic-level marine/brackishwater farmed fish species, compared with lower trophic-level farmed freshwater fish species (Cladis et al. 2014; Tacon and Metian 2013; USDA, 2018).

Moreover, it is also evident that the rivers and oceans where our wild-fish are being caught or fished are also suffering from an ever-increasing torrent of environmental pollutants from wastewater treatment plants, urban and agricultural runoff, and from the air (Escher et al. 2020; Johnson et al. 2020; Schmid et al. 2007; Weber and Goerke 2003; Xanthos and Walker 2017). The net result of this has been the progressive accumulation of many of environmental pollutants within the aquatic food chain, including most of the wild-caught species currently being used as human food (Barber et al. 2006; Davis et al. 2004; Klumpp et al. 2002; VKM, 2014).

Table 1. Reported function and health benefits of key nutrients commonly found in aquatic food products.

NUTRIENT	REPORTED FUNCTION & HEALTH BENEFITS
Vitamins	
Vitamin A ^{1,2,3}	Vitamin A is critical for vision as an essential component of rhodopsin, and the normal differentiation and functioning of the conjunctival membranes and cornea (preventing blindness in children); keeps tissues and skin healthy, and plays an important role in bone growth and is involved in immune function, vision, reproduction, and cellular communication; supports cell growth and differentiation, playing a critical role in the formation and maintenance of the heart, lungs, and kidneys; and may play a protective role against cancer, age-related macular degeneration, and measles.
Vitamin D ^{1,2,3}	Vitamin D aids calcium absorption in the gut and maintains normal levels of calcium and phosphorus in the blood, the mineralization of bone (bone health), and the formation of teeth and bones; Vitamin D sufficiency preventing rickets in children and osteomalacia in adults (together with calcium, vitamin D also helps protect older adults from osteoporosis); plays a role in the modulation of cell growth, neuromuscular and immune function, and reduction of inflammation; and may play a protective role in the prevention and treatment of diabetes, hypertension, glucose intolerance, and multiple sclerosis.
Vitamin E ^{1,3}	Vitamin E functions as an antioxidant, protecting cells and susceptible chemicals (Vitamin A) and lipids (rich in unsaturated fatty acids) from free radicals and consequent oxidative damage; plays a role in anti-inflammatory processes, inhibition of platelet aggregation, and immune function; and by limiting free-radical production may help prevent and/or delay the chronic diseases associated with free radicals such as cardiovascular disease, cancer, eye disorders, cognitive decline, and Alzheimers disease.
Vitamin B ₁₂ ^{1,3}	Vitamin B ₁₂ is required for proper red blood cell formation, neurological function, and DNA synthesis; assists in making new cells and breaking down some fatty acids and amino acids; aids in lowering homocysteine levels and the possible risk of heart disease; and low tissue Vitamin B ₁₂ levels have been positively associated with cognitive decline.
Choline ^{1,2}	Choline is needed to produce acetylcholine, an important neurotransmitter for memory, mood, muscle control, and other brain and nervous system functions; plays a key role in metabolizing and transporting fats; serves as a metabolic source of methyl groups, including the synthesis of the phospholipids phosphatidylcholine and sphingomyelin vital for cell membranes; plays important roles in modulating gene expression, cell membrane signaling, and early brain development; and may play a protective role in cardiovascular and peripheral artery disease, neurological disorders, and nonalcoholic fatty liver disease.
Coenzyme Q ₁₀ ³	Coenzyme Q ₁₀ functions as an endogenous antioxidant, and is used by cells in aerobic metabolism, and for the production of energy for cell growth and maintenance; and also plays a role as an cells immune enhancer (low blood levels of coenzyme Q ₁₀ have been detected in patients with some types of cancer).
Folic acid ^{1,3}	Folic acid is essential for new cell creation, for preventing brain and spine defects when taken early in pregnancy, and functions as a coenzyme in amino acid metabolism and for the synthesis of nucleic acids (RNA, DNA; a folate deficiency leading to megaloblastic anemia; and may play a protective role against reduce the risk of cardiovascular disease and stroke, colon cancer, autism spectrum disorder, dementia, cognitive function, Alzheimer's disease, depression, preterm birth, and congenital heart defects.
Minerals	
Calcium (Ca) ^{1, 3}	Calcium is essential for building and protecting bones and teeth, is required for muscle contraction and relaxation, nerve impulse transmission, blood clotting, hormonal secretion, enzyme activation, maintaining healthy blood pressure; and may have a protective role on bone health and osteoporosis, cardiovascular disease, hypertension, cancer of the colon, rectum, and prostate, kidney stones, and weight management.
Chromium (Cr) ^{3,4}	Trivalent Chromium is an essential component of the hormone insulin and is actively involved in carbohydrate, fat and protein metabolism, helps to maintain normal blood glucose levels, is needed to free energy from glucose; and may have a protective health effects on diabetes, reduced blood lipid levels, and weight loss.
Copper (Cu)	Copper plays an important role as a cofactor in iron metabolism and red blood cell formation, immune function, energy production, iron metabolism, neuropeptide activation, connective tissue synthesis, neurotransmitter synthesis, regulation of gene expression, brain development, pigmentation, and oxidative damage; and may play a protective role against cardiovascular disease, Alzheimer's disease, and dementia.
Iodine (I)	Iodine is an essential component of the thyroid hormones which regulate many important metabolic activities, including protein synthesis, the regulation of body temperature, nerve and muscle function, reproduction, and growth; and may have a beneficial effect on mammary dysplasia and fibrocystic breast disease, fetal and infant development, cognitive function during childhood, fibrocystic breast disease, and radiation-induced thyroid cancer.
Iron (Fe)	Iron is an essential component of hemoglobin and myoglobin and assists with the transport of oxygen in the body, supporting muscle metabolism and healthy connective tissue; required for the synthesis of amino acids, collagen, neurotransmitters and neurodevelopment, cellular functioning, hormone synthesis; and the prevention of iron deficiency anemia in pregnant women and infants.
Magnesium (Mg) ^{1,3}	Magnesium functions as a cofactor for numerous enzyme systems and metabolic processes, including protein synthesis, blood glucose control, blood pressure regulation, and energy production; contributes to the structural development of bone and is required for the synthesis of DNA, RNA, and the antioxidant glutathione; plays a role in the active transport of calcium and potassium ions across cell membranes, nerve impulse conduction, muscle contraction, and normal heart rhythm; and may have a protective role against hypertension and cardiovascular disease, diabetes, osteoporosis, and migraine headaches.

(Continued)

Table 1. Continued.

NUTRIENT	REPORTED FUNCTION & HEALTH BENEFITS
Selenium (Se) ^{1,3}	Selenium is an integral part of selenoproteins which play important roles in reproduction, thyroid hormone metabolism, DNA synthesis, and protection from oxidative damage and infection; and may play a protective role against cancer, cardiovascular disease, cognitive decline, and thyroid disease.
Zinc (Zn)	Zinc is important for cellular metabolism, and plays an important role in immune function, protein synthesis, wound healing, DNA synthesis, and cell division; supports normal growth and development during pregnancy, childhood, and adolescence; required for proper sense of taste and smell, and immune function; and may have a protective role against age-related macular degeneration.
Lipids	
Long chain omega-3 polyunsaturated fatty acids - EPA & DHA ^{1,3,4,5}	Long chain omega-3 polyunsaturated fatty acids are an integral part of phospholipids and an essential component of all cell membranes; serve as an energy source for the body, are used for the synthesis of eicosanoids that regulate blood clotting, contraction and relaxation of artery walls, and inflammation; and have been shown to reduce the risk of cardiovascular disease, cancer, Alzheimer's disease, dementia, cognitive function, age-related macular degeneration, dry eye disease, and rheumatoid arthritis.
Protein	
Protein ^{3/}	Proteins are essential components of all living cells, enzymes, hormones, are necessary to build, maintain, and repair muscle, and are important for neural function, digestive function, and are composed of essential and non-essential amino acids.
Taurine ^{6/}	Taurine is an amino acid involved in cell volume regulation, serving as a precursor of the bile salts, and is one of the most abundant amino acids in the brain, retina, muscle tissue, and body organs; and taurine deficiency associated with cardiomyopathy, renal dysfunction, developmental abnormalities, and severe damage to retinal neurons.

¹HHPS (2009).²Solhelm 2010.³NIH, 2020.⁴Anderson (1992).⁵HHPS (2011).⁶Ripps and Shen (2012).

4. Need for aquaculture and nutrient fortification

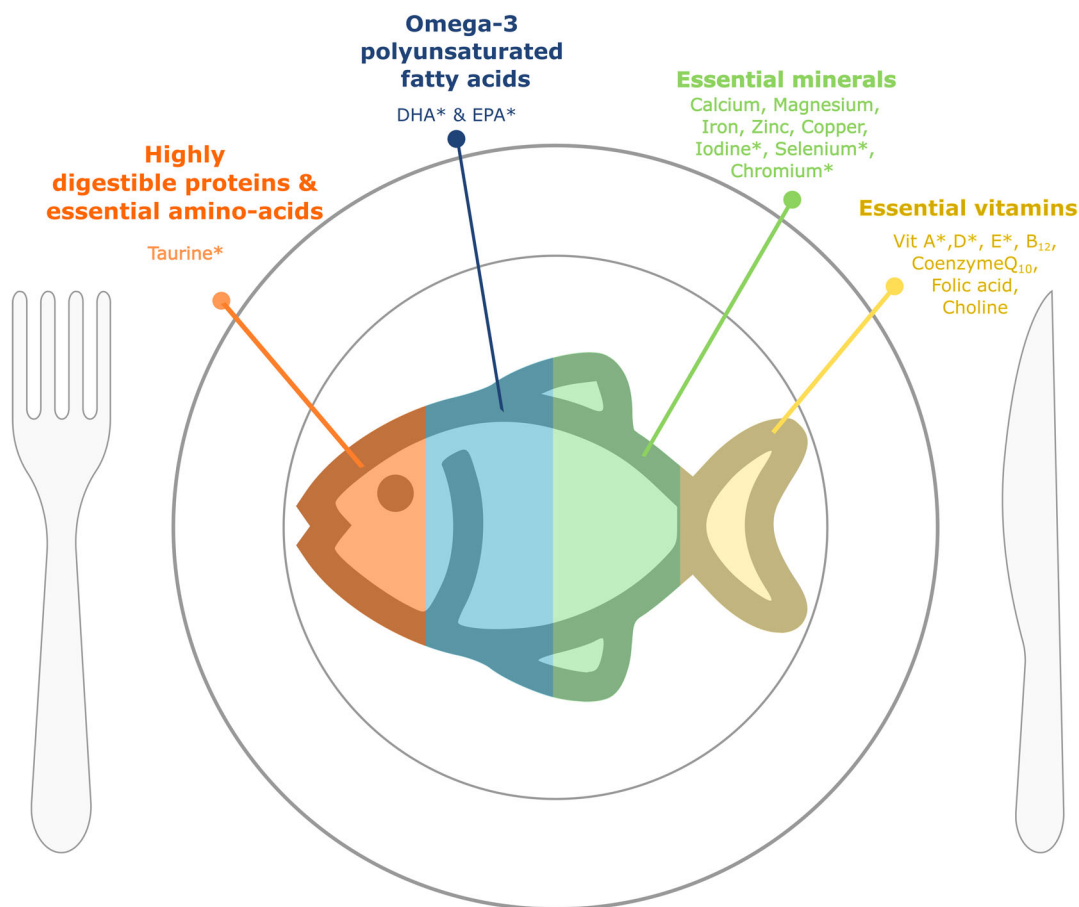
In view of the dilemma of rising and un-controllable environmental pollutant levels within wild-caught fish (depending on their geographical origin and position in the aquatic food chain; Nicklisch et al. 2017), and the general stagnation of capture fisheries worldwide (FAO 2020b; Figure 1B), it is clear that aquaculture is the only long-term solution and hope for the increased mass global production of safe and wholesome aquatic food products (Tacon 2020). Moreover, in marked contrast to wild-caught fish, with aquaculture it is also possible to improve the nutritional quality of the flesh of the cultured fish or shrimp species, and consequently enhance its potential health value, by dietary manipulation and/or nutrient fortification (Lie 2001, 2008; Rosenlund et al.; 2011).

Thus, there is considerable scientific evidence for the health benefits of omega-3 polyunsaturated fatty acids (PUFA), and in particular EPA and DHA, against coronary heart disease, stroke, and diabetes (Table 1; Calder 2004; Rosenlund et al. 2011; Ruxton et al. 2007; Sargent and Tacon 1999; Wallin et al. 2012). As a consequence of these known health benefits, considerable research effort has focused on the enrichment of fish fillets with heart-healthy PUFA through dietary manipulation prior to harvest, including Atlantic salmon (*Salmo salar*; Kousoulaki et al.

2016; Lie 2008; Nanton et al. 2012; Sprague et al. 2016; Rosenlund et al. 2011; Torstensen et al. 2004), Channel catfish (*Ictalurus punctatus*; Manning et al. 2006; Manning et al. 2007), Tilapia (*Oreochromis sp.*; Jiratanan 2007; Ng et al. 2013; Petenuci et al. 2018; Sarker et al. 2016; Stoneham et al. 2018; Watters et al. 2013) and shrimp (*Litopenaeus vannamei*; Nonwachai et al. 2010).

Other nutrients with potential health-benefits which have been shown to be enhanced within fish flesh through dietary fortification, include (but not limited to), 1) Iodine: Atlantic salmon *S. salar* (Julshamn et al. 2006; Schmid et al. 2003), Chars *Salvelinus sp.* (Schmid et al. 2003), Rainbow trout *Oncorhynchus mykiss* (Ribeiro et al., 2017), 2) Selenium: African catfish *Clarias gariepinus* (Luten et al. 2008; Schram et al. 2008), Atlantic salmon *S. salar* (Berntssen et al. 2018; Lorentzen et al. 1994; Sele et al. 2018), Rainbow trout *O. mykiss* (Ribeiro et al., 2017), 3) trivalent Chromium: Nile Tilapia *O. niloticus* (Li et al. 2018), 4) Vitamin E: Atlantic salmon *S. salar* (Harare et al. 1998; Sigurgisladdottir et al. 1994; Waagbø et al. 1993), Rainbow trout *O. mykiss* (Mihalca et al. 2011), and 5) Taurine: African catfish *Clarias gariepinus* (Luten et al. 2008) and Rainbow trout *O. mykiss* (Anderson 1992; Aksnes et al. 2006).

In addition to nutrient enrichment, the levels of environmental pollutants such as POPs and heavy metals, and possible adventitious dietary toxins (such as mycotoxins), can be reduced within fish fillets through



** Nutrient levels shown to be enhanced through dietary fortification*

Figure 2. Farmed fish: a superfood with multiple health attributes.

dietary formulation changes, by substituting contaminated fish oils and fish meals with alternative less contaminated or adulterated dietary lipid and protein sources (Bell et al. 2005; Berntssen et al. 2005; Berntssen et al. 2011; Goncalves et al. 2020; Haldorsen et al., 2017; Heshmati et al. 2019; Turchini et al. 2019).

5. Need for improved communication

In view of the above review, there is an urgent need to increase public awareness and understanding concerning the nutritional merits and health-benefits of increased consumption of fish and seafood products, including the inclusion of fish and aquatic foods as an essential component of a healthy diet and national dietary nutrient requirement guidelines (HHP, 2011; Mozaffarian and Ludwig 2010; NHMRC, 2013; Skerrett and Willett 2010; USDHHS/USDA, 2015; Figure 2).

Finally, although fish and seafood currently constitute the main source of animal protein consumed within most Asian countries (FAO, 2020a; Tacon and

Metian 2018), at the same time, there is also a rapid rise and adoption of western-style fast-foods within these countries, and consequent increased risk of obesity and related ailments (Henry et al., 2020; Pan et al. 2012; Wallin et al. 2012, 2016). It follows therefore, that education of the consumer is key, and that more healthy fast-food options be developed and promoted, including fast-food products derived from fortified farmed fish or shrimp.

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