



Potential Harmful Effects of Heavy Metals as a Toxic and Carcinogenic Agent in Marine Food-An Overview

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THE survival of organisms is threatened with a variety of pollutants and chemical compounds and population growth. Natural phenomena and human activities, especially industrial activities increase contamination of water, soil and air. Population growth leads to increased exploitation of the sea and oceans, thus the consumption of seafood increases. In addition, the main food of the people in some areas is fish. Consumption of fish has numerous benefits to healthy for humans, but the existence of some heavy metals including lead, cadmium, and etc. may cause toxicity to marine organisms. The degree of heavy metal toxicity depends on their chemical form of metals. Some forms of metals are rapidly excreted and do not have the opportunity to be absorbed and stored in body tissues, accordingly they are not very toxic, while some forms of metals are highly toxic and lethal. These forms are slowly excreted from metals and have the ability to be absorbed and accumulated in fish muscles and other organs. Heavy metals cause harmful effects such as carcinogenesis, malformations, damage to the nervous system, damage to the reproductive system and infertility in men, liver failure and cardiovascular disease and so on. Therefore, in this review focused on concentration of heavy metals in fish muscle is essential to ensure the safety of this type of food.

Keywords: Heavy metals, Marine, Fish, Safety, Toxic, Carcinogenic, Toxicity.

Introduction

Recently, marine product consumption has increased due to increasing public awareness of their health effects and nutritional value [1]. Fish and seafood are now recognized as important sources of protein for human health [2]. In addition, fish and seafood are rich in omega-3 fatty acids, minerals, vitamins and are healthy and essential foods in human nutrition [2, 3]. Marine pollution can have negative effects on marine

life. In other words, the presence of hazardous chemical pollutants such as heavy metals in marine environments has damaged biodiversity, ecosystems and caused concern around the world [1, 4].

Exposure of marine organisms to heavy metals is problematic even at low amount of heavy metals in seawater, because these metals accumulate in the body of aquatic organisms and are transported to the human and other animal

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in food chains. Although some of the materials are essential for the body of living organisms but most heavy metals are harmful [5]. For example, lead consumption causes kidney or liver failure, Cancer and high blood pressure. Cadmium causes high blood pressure, neurological disorders, skeletal weakness, cardiovascular damage and carcinogenic effects [6]. Arsenic can endanger for human health. Abdominal pain, diarrhea, vomiting, and muscle weakness are symptoms of arsenic poisoning. The chronic intoxication leading to skin defects and cancer [6, 7]. Mercury poisoning causes damage to the nervous system, kidney damage, interference with the reproductive system and suppression of the immune system, and exacerbation of lupus [8-10].

Metal accumulation in fish depends on the geographical area, nutritional level, eating habits, age, size, exposure time, and regulations in that geographical area [11]. The main sources of pollutants entering the environment are human resources, which include discharge of public wastewater, agricultural drainage, discharge of industrial effluents, fuel combustion, mining, and leaks of chemicals, fuel and oil from ships passing through the sea [12]. Many studies have been performed on the bioaccumulation of heavy metals in marine fish [2-4, 6, 13-15]. In view of the above objectives, the present paper is designed to explain food safety concerns related to the accumulation of marine heavy metals.

Toxicity of Heavy Metals

Heavy metals or xenobiotics in excessive amounts are a potentially toxic agent. Heavy metals enter our bodies through foodstuffs, water, and air, and exert their toxicity by then bonding or combining with compounds such as sulfur, oxygen or nitrogen [16].

Their functional system is the inactivation of enzyme systems or important protein structures that eventually lead to cell dysfunction and death [16, 17]. The central nervous system, gastrointestinal tract (GI), cardiovascular system, hematopoiesis, kidneys, and peripheral nervous system are some of the organs involved. Toxicity of heavy metals due to their nature have different toxicity intensities, level of exposure, chemical and equilibrium conditions, mode of exposure, and age can all contribute to toxicity [18]. It is important to note that, unlike base metals, heavy metals in any amphibian can't play a biological role.

Heavy metals may be found in the body, but the important point is that they do not have a specific biological function [19-21]. Heavy and toxic metals enter the body in various ways and accumulate in the kidneys and liver, and this is due to the fact that the excretion of heavy metals is slower than its absorption. The process of accumulation of heavy metals is a completely biological process that occurs with the absorption of heavy metals in the meat of fish, beef and other animals and their accumulation in humans is due to the consumption of contaminated food. [22, 23]. This further demonstrates the need to control the levels of these toxic metals in food and food safety for human health. Heavy metals are a type of xenobiotic compound that has no beneficial role in human physiology and may even be toxic in some cases, such as lead and mercury, even in small amounts from exposure. Heavy metals rankings by ATSDR, the first, second, third and sixth hazards in this list are heavy metals: lead, mercury, arsenic and cadmium, respectively [18, 22-25].

Causes exposure to toxic metals through pathways such as dust and inhalation of dust or vapor. Some metals, such as mercury, can be vaporized and inhaled in the production of fluorescent lamps. Also, some metals are inadvertently consumed through food and drink, which are the main purpose of this article. Depending on the type of heavy metal, dietary methods and age of people absorbing them through the gastrointestinal tract are different [16]. Heavy metal toxicity has been proven and there are several health risks associated with it. The toxic effects of these metals are harmful to the human body and its proper functioning. For example, sometimes metal acts as a similar element in the body while it may even interfere with metabolism. Sometimes the body has the ability to excrete a small number of metals such as aluminum, while some metals such as heavy metals in the body and the food chain come together and are chronic in nature [19, 24, 26, 27]. Toxicology and Disease Registry Agency show that lead, cadmium, mercury and arsenic, including toxic substances are very dangerous [24].

Toxicity Heavy Metals in Marine and Their Effects on Human Health

Marine heavy metal pollution is increasingly considered an environmental problem [28]. The marine environment can most likely be a place for storing heavy metals because heavy metals

are dumped into the sea in different ways [29]. Common trace metals in mercury (Hg), nickel (Ni), lead (Pb), arsenic (As), cadmium (Cd), chromium (Cr), copper (Cu), and zinc (Zn). Marine with different levels of biotoxicity. As, Cd, Hg and Pb are unnecessary elements with severe toxicity at low concentrations [30]. Organisms and microorganisms usually lack effective metabolic mechanisms to detoxify these metals and can sometimes be converted to more toxic compounds (eg, methylmercury (MeHg) and transported through food networks [29]. The following are some of the studies performed separately for metals.

Lead

Lead is found naturally in nature, like rocks, atmosphere and soil. Through the combustion of gasoline, tetraethyl lead is formed and enters the environment [31]. When lead is placed in the

marine environment, it easily enters bloodstream and accumulates in the several of tissues. The organic compounds of lead are more toxic than mineral compounds and are more easily absorbed by the gastrointestinal tract. Most toxic lead groups are methyl or ethyl [32, 33]. In accordance with regulations of South African Ministry of Health, the maximum lead level in fresh and processed fish is 0.5 mg/kg and the maximum lead limit by the European Commission has been approved 0.3 mg/kg [34, 35]. Therefore, excessive exposure to lead can lead to neurological problems, kidney failure, cardiovascular disease, high blood pressure weakness of muscle and joints, nausea, insomnia, anorexia, and various cancers and in some cases death [36-38]. In adults, 10% of lead is absorbed by the gastrointestinal tract, while in children it is 40-50%. Factors such as fasting, calcium deficiency, and iron and vitamin D deficiency increase lead absorption [6, 39].

TABLE 1 . Clinical Aspects of heavy metal Toxicities.

Metal	Primary Sources	Manufacturing Industries	Target Organs	Clinical Effects	Max. acceptable (conc. WHO)
Arsenic (As)	Dusts, Medicinal Uses of contaminated Water	Phosphate and Fertilizer, Metal Hardening , Paints And Textile	Pulmonary Nervous System, Skin	Respiratory Cancer, Peripheral Neuropathy, Dermatomes, Skin, Cancer	0.01 mg/l
Cadmium (Cd)	Industrial Dust and Fumes and contaminated Water and Foodstuff	Phosphate Fertilizer, Electronics, Pigments and Paints	Renal, Skeletal Pulmonary	Proteinuria, Glucosuria, Osteomalacia, Aminoaciduria, Emphysemia	0.003 mg/l
Lead (Pb)	Industrial Dust and Fumes and Polluted Food	Paints, Battery	Nervous System, Hematopoietic System, Renal	Encephalopathy, Peripheral Neuropathy, Central Nervous Disorders, Anemia	0.01 mg/l
Mercury (Hg)	Dust and Fumes and Polluted Water And Food	Chlor-Alkali, Scientific Instruments, Chemicals	Nervous System, Renal	Proteinuria	0.001 mg/l

Cadmium

Cadmium is the seventh toxic heavy metal on the list announced by ATSDR [40]. This element is highly toxic and has severe effects on biological systems [41]. Cadmium is formed through natural processes such as volcanic activities and wind hits rocks containing lead and human activities such as smelting, burning fossil fuels, burning waste and using special fertilizers for agriculture. In World War I, cadmium was used instead of tin, and then it was used in paints. Cadmium is mostly found in non-organic form in the 2+ oxidation state and is mainly present as $[\text{CdCl}_2^0]$ and $[\text{CdCl}^+]$ complexes in seawater [42]. The food safety authority of European Union has adopted a provisional tolerable weekly intake (PTWI) of $7 \mu\text{g} \cdot \text{kg}^{-1}$ body weight (BW) [35]. The Food and Agriculture Organization (FAO) provides for fish level of 0.05 mg/g and for bivalves and cephalopods is 1 mg/kg [43].

Ministry of Health of South Africa has been adopted 1.0 mg/kg for Cd in fish and processed fish [34]. Cadmium enters the body through inhalation or ingestion and causes acute and chronic effects. More than 500,000 workers in the United States are exposed to the toxic metal cadmium each year [44, 45]. If too much cadmium enters the body in excess, it can cause high blood pressure, nervous system interference, carcinogenicity, cell enzyme system interference, oxidative stress, and skeletal defects [40, 46].

Arsenic

Arsenic is one of the most toxic heavy metals in the world. It is the twentieth most abundant metal and is widely found in a variety of environments [47]. The toxicity of arsenic depends on its chemical formula. In fact, inorganic arsenic is trivalent and pentavalent, which is extremely toxic. Inorganic arsenic is soluble and stable. Arsenic and salts or esters of arsenic acid known as arsenate are inorganic forms of arsenic that are toxic and lethal to humans and living organisms. Absorbs quickly in the GI tract and accumulate in muscles, while its organic form is rapidly excreted and does not accumulate in the body. Arsenic can be absorbed through swallowing, inhalation or through the penetration of mucous membranes or skin into the body [40]. Inorganic arsenic is found in large amounts in water sources, while organic arsenic is usually found in meat resources of marine animals and ruminants (meat and fish).

Therefore, the main source of arsenic entering the body can be the human diet. More than 90% of the arsenic measured in fish is in the form of arsenobetain (a non-toxic form) [48]. However, there are limits to the amount of arsenic in marine aquatic arsenic. However, strict monitoring is carried out in this regard and the permissible limit is 3 mg / kg per fish and fish processed by the Ministry of Health of South Africa [21]. And the amount of PTWI for humans is $15 \mu\text{g} / \text{kg}$ body weight for the mineral arsenic [49]. Arsenic is a protoplasmic toxin because it primarily affects the sulfhydryl cell group and disrupts the function of cellular respiration, cellular enzymes, and mitosis. In acute exposure, abdominal pain, diarrhea, vomiting, muscle weakness, and hot flashes is observed while in chronic exposure it causes skin defects and cancer [7, 50].

Mercury

Mercury is the most abundant metal in fish and seafood, in other words, the source of mercury in the human body is food sources. In recent years, mercury pollution has been 10 times higher than before the industry [51]. Source of mercury in the environment include forest fires and volcanic activity, Fossil fuels and melting of other metals including lead, copper and zinc are major sources of mercury production. Fossil fuels and smelting metals such as copper, zinc and lead are major sources of mercury production. Mercury is used in paints, electrical equipment, pesticides, dentistry and medicine [52]. The organic mercury is more toxic because they are more stable and easily accumulate in tissue of fish and the human body. Inorganic mercury, on the other hand, is not toxic because it is rapidly excreted and not absorbed by the fish. Inorganic Hg are including mercuric acetate ($\text{HgC}_4\text{H}_6\text{O}_4$), mercuric chloride (HgCl_2), mercuric sulfide (HgS) and mercurous chloride (Hg_2Cl_2). Other organic Hg forms include dimethylmercury (DMHg) and ethylmercury (EthHg). Dimethylmercury has carbon-metal bonds and is stable in aquatic environments. Therefore, it does not enter the food chain, unless partial demyelination of DMHg occurs, in which case it can enter the food chain as CH_3HgCl and CH_3HgOH [40]. Methylmercury in the brain kills cells in specific areas of the brain, such as the cerebellum, cortex, and other focal areas. Toxic effects are seen on other parts of the body, such as the pituitary gland, liver and

kidneys. Methyl mercury has a longer half-life than inorganic mercury. Excretion of mercury from the body is a slow process and occurs mainly through feces [53]. Mercury in fish is stored more in muscle tissue, so it is dangerous to human health because it is the most consumed part of fish. Methylmercury is a more stable form of organic mercury that is absorbed up to 95% by the intestines and then spread throughout the tissue [35]. The maximum permissible level of mercury in 1 mg/kg fish was reported by the European Commission and South African Health [35, 51]. Symptoms of mercury poisoning include blurred vision, hearing loss, headache, anesthesia, nausea, imbalance, fatigue, and tremors [54]. Low levels of methyl mercury cause cardiovascular disease [54]. Chronic exposure to methyl mercury, on the other hand, causes damage to the pituitary gland, liver damage, thyroid problems, damage to the testicles and prostate, and damage to the sweat and salivary glands [9, 55]. Children exposed to mercury have long-term speech and motor problems. Consumption of fish in human diet is very important and is rich in unsaturated fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) [56, 57]. Therefore, it is essential to use safe and secure fish free of heavy metals. The US Food and Drug Administration (FDA) recommends avoiding predatory fish such as sharks due to their high mercury content [6, 9, 10].

Conclusion

Accumulation of heavy metals in seafood such as fish is a new threat to human health. Consumption of foods containing heavy metals is the main way these metals enter the food. This review article includes a summary of heavy metal contamination in fish and their impact on the general health of society and humans. Given that consumption of seafood, especially fish in human nutrition plays an important role and more pollution from industrial sources, so government must take strict measures to control industrial waste and chemical pollutants and their entry into the control of the marine environment do it.

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Conflict of Interest

This is a review article, no conflict of interest.

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