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REVIEW ARTICLE

The effects of endocrine disruptors on fish

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ABSTRACT

Nowadays, there are a lot of researches about the effects of endocrine disruptors on human and wildlife organisms. Endocrine disruptors are exogenous substances or substance mixtures that cause undesired effects in the organism or in future generations by altering the endocrine system of the exposed organism. Fish are exposed to endocrine disruptors in several ways including water, sediment, and diet. The toxic effects of endocrine disruptors on fish vary according to the exposure period, duration of exposure, chemical properties of the substances, and whether the exposed substance is single or mixed with other substances. Within the scope of this review, the classification of endocrine disruptors, their usage areas, their way of mixing into the aquatic ecosystem, and their toxic effects on fish will be explained.

Keywords: Endocrine disruptors, aquatic ecosystem, fish

1. INTRODUCTION

Endocrine disruptors (EDCs) can be produced either in nature or in industrial and have a wide range of usage areas including pesticides, personal care products, food contact materials, textiles, clothing, medical tubing, electronic and building materials. Rachel Carson mentioned about undesired effects of the manufactured chemicals on the birds population, in other words wild life, in her book, Silent Spring. Since then, it is understood that even though EDCs have been used and preferred various areas and made easier life for people, they tend to persistent in the environment and bioaccumulate in the organisms tissues. Therefore, their effects on human and wildlife have been very interesting research areas. Wild life and human populations are exposed to EDCs via food, water, air, through the skin, by transfer from mother to fetus (through placenta) or infant (through breast-feeding). Even though their first target mechanisms are endocrine systems of organisms, they also affect the other systems of the organisms such as neurological system [1]. In this review, the classification of EDCs, EDC contamination of aquatic ecosystems, exposure factors that can change the effects of EDCs on fish and the effects of EDCs on fish will be examined.

2. ENDOCRINE DISTRUPTORS

The endocrine system is a complex system that contained the thyroid, testis, ovary, pancreas, adrenal glands, and brain in mammals. However, the endocrine system organs in vertebrates vary according to the groups in which the organism is classified [2] (Fig 1).

Fish have pituitary, urohypophysis, thyroid, thymus, islets of Langerhans, chromaffin tissue, interrenal tissue, intestinal tissue in the gonads, ultimobranchial body, intestines, kidney, pineal gland, and Stannius bodies [2]. Like the other vertebrates, the pituitary secretes hormones which are responsible for the melanin pigment distribution in the cells, thyroid, and sex hormones secretion. The permeability of the gills is controlled by these hormones [3]. Thyroid gland hormones control all body systems including brain development, heart rate, blood flow, steroid hormone production, metamorphosis, migration of eyes, development of the dorsal ray. Thyroid hormones are

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secreted at high levels in freshwater migration and low levels in saltwater migration. The most common thyroid hormones in fish are triodotrione (T3) and thyroxine (T4) [3]-[4]. The androgen hormones secreted from the gonads are responsible for sexual development, reproduction, nest building, and swimming speed. The estrogen hormones decrease the belligerent behavior, and are responsible for fertilization and sexual activity. Prolactin hormone is involved in osmoregulation [4]. The regulation of calcium metabolism is controlled by the ultimobranchial body. The carbohydrate metabolism is controlled by the islets of Langerhans [3]. The melatonin hormone secreted by the pineal glands is involved in gonad development and adaptation to light / dark environments and seasonal adaptation [4].

Endocrine disruptors (EDCs) are exogenous substances or substance mixtures that cause undesired effects on the endocrine system of the organism [5]. These substances, acting on the receptors, bind to the receptor by mimicking the natural hormone, activate the receptor and produce a response (agonistic effect) or prevent the natural hormone from being activated by binding to the receptor (antagonistic effect) [6]-[7].

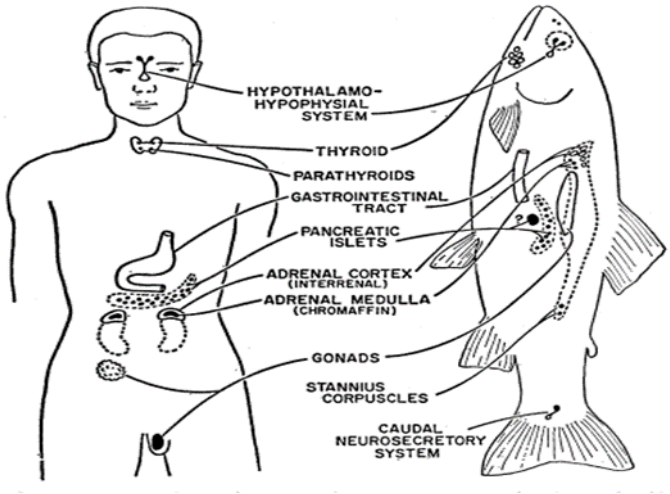

Fig 1. The endocrine system organs in human and fish [2]

Scientific Global Identification/Assessment of Endocrine Disruptors held by International Chemical Safety Program (IPCS), World Health Organization (WHO), United Nations Environment Program (UNEP), and the International Labor Organization (UNEP) made a definition of EDCs. According to this definition, EDCs are "exogenous substance/substance mixtures which affect the synthesis/production, release, transport, attachment, activity, and excretion of natural hormones responsible for homeostasis, reproduction, development and behavior" [5]. Another description of EDCs by the European Union is "secondary changes in the endocrine system affected by exogenous substances create an adverse effect in a healthy organism or its later generations" [8].

Human and wildlife organisms are exposed to many exogenous substances which have negative effects on their biological systems. Most of these substances have detected various environmental matrix including water, sediment, soil, lipid tissues of animals [6]-[9]-[10]. Laboratory experiments showed that the exogenous substances effect on the endocrine system, behavior, reproduction, growth, survival rate of the organisms [6].

2.1. The classification of EDCs

EDCs contain many chemical substances and can be classified into three ways that are natural, synthetic, and environmental [11]. Natural EDCs are phytoestrogens and mycoestrogens. Phytoestrogens are produced by plants such as isoflavone. Mycoestrogens are estrogen-like structures found in mushrooms. The effect of these compounds can be antiestrogenic or generally estrogenic [4]. Due to having natural hormones structure, they can easily collapse and they don't accumulate in the tissues of the organism [11]-[12]. Synthetic EDCs contain construction pills, hormonal treatment ingredients, and some animal additive substances [12]. Environmental EDCs include chemicals that are used in industrial activities. This group includes plastics and plasticizers (such as bisphenol A and phthalates), pesticides, industrial chemicals, organohalogen chemicals (including polychlorinated biphenyls, polybrominateddiphenyl ethers), organic tin compounds, polyaromatic hydrocarbons, drugs and metals [4].

2.2. Contamination of aquatic ecosystems with EDCs

EDCs have an important place in environmental toxicology studies due to adverse effects on humans and wildlife. These substances are contaminated into aquatic ecosystems in various ways such as domestic, municipal wastes, industrial wastes, forest fires, and mine wastes. They accumulate in the water, sediment, and aquatic organisms and therefore,they tend to biaccumalation and biomagnification in the tissues of

organisms via aquatic food web [1]-[13]. Fish, one of these aquatic organisms, are exposed to EDCs through water (skin and respiration) and diet (consumption of aquatic organisms affected by EDC) [14].

2.3. Factors that can change the effect of EDCs on the organism

Age of the exposure: It is thought that exposure to a developing organism and an adult individual to EDCs may produce different results [15]. It has been observed that exposure in the early stages of development causes more permanent damage [8].
The time after exposure: The effects may not be observed immediately after exposure to EDCs. These effects may occur the following years [8].

Mixture effects: In the environment, EDCs are not usually found alone. They are mixed with other EDCs. For this reason, organisms are under the influence of not just one substance but many substances at the same time. Thus, these substances can create an antagonistic or synergistic effect with each other [16].
Unusual dose-response relationship: EDCs act on organisms even at very low concentrations. It is important to know the critical window which occured in the developmental period of organisms [16].

Epigenetic and genotoxic effects: Due to epigenetic and genotoxic effects, EDCs can show their effects on the individual, on future generations, and subpopulations [17].

3. EDCs EFFECT ON FISH

3.1. Reproductive health and EDCs

Except for some special conditions, reproduction in fish is an event that takes place in the form of external fertilization. Fertilization takes place by the combination of the egg and sperm released by the female and male individuals in the water environment. Therefore, the chemical properties of the water environment are important for the healthy fertilization of the egg and sperm [18]. Therefore, many studies have been conducted to understand the effects of EDCs on reproductive health. Studies have reported that the amount of vitellogenin, which is an important hormone in reproduction, decreases after plasticizers (bisphenol A) exposure of goldfish [19], Japanese medaka [20], zebrafish [21], and fathead minnow [22]. However, it was reported that exposure to polychlorinated biphenyls (PCB 126 and PCB 153) caused the increase of the vitellogeninof Gilthead seabeam [23]. The production of egg and sperm also decreased after the exposure of the phthalates (di(2-ethylhexyl) phthalate and mono-(2-ethylhexyl)-phthalate)[24]-[25]. It was observed that pesticide (DDT, malathione and atrazine) exposure has effects on the female reproductive system such as narrowing of fish ovaries and a decrease in egg diameter [26]-[27]-[28]. Exposing to polybrominated biphenyls (PBDE 47 and PBDE 71) resulted in the decrease of cumulative egg production [29]-[30] and sperm counts [29]-[31]. It has been observed that the ratio of males and females in thezebrafish population changes as a result of exposure to EDCs [32].

3.2. Development effects and EDCs

The growth stages in fish progress as fertilization, the formation of the blastopore, egg sac and exit from egg sac, the flexibility of notochord, metamorphosis, juvenile and mature individuals. In these developmental stages, embryonic deformation and disorders in tail development occur in organisms exposed to EDCs [33]. Studies have been reported that exposure to bisphenol A caused pericardial edema, bleeding, congestion in embryos, and the development of the round tale of the larvasof Japanese medaka [34] and zebrafish[35]. Exposure to organic tin compounds (zinc pyrithioneand copper pyrithione) made disorders in tail development of Japanese medaka [36], notochord bending, cardiac and ovarian edema, and anomalies in swimming sacs of zebrafish [37] It was observed that polybrominated biphenyls (PBDE 47) caused pericardial edema, tail deformation, and notochord twisting in embryos and larvas of zebrafish[38]. It was reported that after male zebrafish exposed to dibutyl phthalate and mated with healthy female zebrafish, such malformations like edema, bent trunk were occurred in their embryos [39].

3.3. Growth effects and EDCs

There are many studies that have been obtained population growth rate and survival rate effects of EDCs on fish. Studies are noted that bisphenol A caused the decreasing of somatic growth rate, gonadosomatic index and survival rate [22]-[40]-[41]. Although exposure to pesticides (hexazinone and atrazine) decreased the somatic growth rate of red drum larvae [42] and Atlantic salmon[43], exposure to sodium perchlorate salts at very low concentration increased the growth of mosquitofish [44]. Besides, some EDCs like nonylphenol and arsenic don't affect the growth [45]-[46].

3.4. Histopathological changes and EDCs

EDCs alter the normal pathologies of the tissues and organs. It was observed that atrazine, one of the pesticides, caused autolysosome, emphysome, and vacuolization of mitochondria in kidney and spleen organs [47]. Exposure to sodium perchlorate salt made hypertrophy in thyroid gland tissue of stickleback [48]. In a study investigating arsenic exposure of tilapia, histopathological findings were detected as epithelial hyperplasma, edema, lamellar fusion, aneurysm, and necrosis in gill tissue; focal lymphotic and macrophage infiltration in liver tissue; a hollow appearance and elongation in liver cells (hepatocytes), vacuole degeneration, focal necrosis and nucleus hypertrophy [49]. It has been determined that cell height in thyroid gland epithelial cells and deterioration in colloidal matter occurred in polybrominateddiphenyl ether exposure of fathead minnow [50]. Hyperaemia, epithelial lifting, fusion of secondary lamellae, telangiectasia in gill tissues and

hyperaemia, mononuclear cell infiltration vacuolization of hepatocytes, hydropic degeneration in liver tissues were observed in the imidacloprid pesticide exposure of Nile Tilapia[51]. Exposure to propoxur made hyperemia, branchitis in primary lamella, and telangiectasis, hyperplasia, fusion, epithelial lifting, and epithelial desquamation in secondary lamella of gill tissues; hemorrhage, destruction, prenephritis, and inflammation and desquamation in the tubules; edema in the kidney; passive hyperemia, albumin, and hydropic degeneration in the liver; and hyperemia, chromatolysis, and glial proliferation in the brain tissues of common carp [52].

3.5. Thyroid hormone and EDCs

Triodotrione (T3) and thyroxine (T4) hormones secreted from the thyroid gland in fishes are responsible for the brain, skeletal and organ development, migration of eyes and the formation of dorsal fin rays at the embryonic stage, physical, and morphological changes (smoltification), sexual maturation, and adjusting the metabolic rate [4]-[5]. For this reason, changes in plasma levels of T3 and T4 hormones in fish exposed to EDCs may cause many effects. It has been determined that fish exposed to arsenic have a decrease in T4 hormone levels and a decrease in migration movements from sea to freshwater [53]. It was observed bisphenol A and bisphenol S caused the increasing level of T3 hormone of juvenile brown trout [54].

3.6. Biochemical parameters and EDCs

EDCs change the biochemical parameters of fish including lipid, protein, and enzyme. In fish exposed to arsenic, apoptosis and necrosis events were observed in the cell division cycle. An increase in catalase enzyme activity was detected with a decrease in superoxide dismutase and glutathione peroxidase enzyme activity [55]-[56]. Common carp were exposed to esbiothrin(pesticide), total antioxidant status was decreased at first and then increased in time [57]. It was observed that malondialdehyde levels increased while glutathione-s-transferase levels decreased exposure to pesticides [51]. Bisphenol A exposure of bighead carp increased thiobarbituric acid reactive substance (TBARS), reduced glutathione (GSH) whereas catalase, superoxide dismutase, peroxidase, and total proteins were decreased [58]. It was observed to bisphenolA exposure disrupted lipid metabolism and decreased the oxidative stress response in the liver of common carp [59]. In another study with Bisphenol A, it was concluded that the ratio of protein and nucleic acid (RNA: DNA) decreased with the observation of histopathological changes in fish gonad tissues [40].

3.7. Genotoxic effects and EDCs

There are many studies that have been obtained genotoxic effects of EDCs on fish. Increases in micronucleus frequencies and DNA strand breakage levels were observed in fish exposed to pesticides (esbiothrin and fenitrothion) [57]-[60]. It was recorded that exposure to dialkyl phthalate,bisphenol A and tetrabromodiphenylether caused increasing micronucleus level and nuclear anomalies were recorded as blebbed, notched, and lobed nuclei [61]. In the long term exposure to bisphenol A, it was observed morphological abnormalities of erythrocytes (such as broken nucleus, lobed nucleus, micronucleus, and blabbed nucleus) of bighead carp [58]. Bisphenol A and bisphenol S caused increasing micronucleated cells of juvenile brown trout [54].

4. CONCLUSION

As a result of the contamination of EDCs in aquatic ecosystems, changes in antioxidant mechanisms, histopathological differences, disease formation and related deaths, physiological dysfunctions, teratogenic effects, changes in reproductive behaviors, and a decrease in the reproduction rate have been observed as a result of studies on fish from aquatic organisms. The presence of EDCs in very low amounts and in the mixture increases the effect on non-target organisms even more. Although there are many studies about these substances, their mechanism of action has not been fully understood yet. For these reasons, various national and international regulations regulated within the framework of the production, distribution, and use of EDCs should be followed, and the people who use these substances should be trained. In addition, the ways these substances enter aquatic ecosystems should be examined and these routes should be reduced as much as possible.

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