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Eco Toxicological Effects of Endocrine Disruptive Compounds (EDCs) in Aquatics (Especially in Fish): A Review

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Abstract: ***This report provides an assessment of recent investigations into endocrine disruption in fresh and saltwater species of fish. Most work to date has concentrated on reproductive endocrine disruption. Laboratory studies have shown a variety of synthetic and natural chemicals including certain industrial intermediates, PAHs, PCBs, pesticides, dioxins, trace elements and plant sterols can interfere with the endocrine system in fish. The potency of most of these chemicals, however, is typically hundreds to thousands of times less than that of endogenous hormones. Evidence of environmental endocrine disruption ranges from the presence of female egg proteins in males and reduced levels of endogenous hormones in both males and females, to gonadal histopathologies and intersex (presence of ovotestes) fish. Overt endocrine disruption in fish does not appear to be a ubiquitous environmental phenomenon, but rather more likely to occur near sewage treatment plants, pulp and paper mills, and in areas of high organic chemical contamination. However, more widespread endocrine disruption can occur in rivers with smaller flows and correspondingly large or numerous wastewater inputs. In the present study, we focused on natural or synthetic chemical compound in water that effect on endocrine gland in aquatic animal, specially the fish.***

Keywords: Endocrine Disruptive Compounds (EDCs), Fish, endocrine system

1. Introduction

Recently, concern has arisen that certain environmental contaminants as well as some naturally occurring compounds have the potential to impact the endocrine. Research on the identification and effects of endocrine-active compounds has become an important area of life organism and environmental health research (Flik etal., 2006). In this presentation, compounds that either mimic or antagonize the action of naturally occurring hormones are termed endocrine disrupters or endocrine disrupting compounds (EDCs). The term endocrine disruptor is often used as synonym for xenohormone (Anway et al., 2005; Kim, 1999). Endocrine disrupting compounds encompass a variety of chemical classes, including drugs, pesticides, compounds used in the plastics industry and in consumer products, industrial by-products and pollutants, and even some naturally produced botanical chemicals. Some are pervasive and widely dispersed in the environment and may bio-accumulate (Babin, 2007). The term endocrine disruptor was coined at the Wingspread Conference Centre in Wisconsin, in 1991. A number of definitions currently exist. Endocrine disruptors are chemicals at certain doses, can interfere with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for development, behavior, fertility, and maintenance of homeostasis (normal cell metabolism). These disruptions can cause cancerous tumors, birth defects, and other developmental disorders. Any system in the body controlled by hormones can be derailed by hormone disruptors (Kavlock et al. 1996). Specifically, endocrine disruptors may be associated with the development of embryo ;deformations of the body (including limbs); breast cancer, prostate cancer, thyroid and other cancers; sexual development problems such as feminizing of males or masculinizing effects on females, etc (Hamadeh et al., 2002; Waters and Fostel, 2004) (Fig. 1).

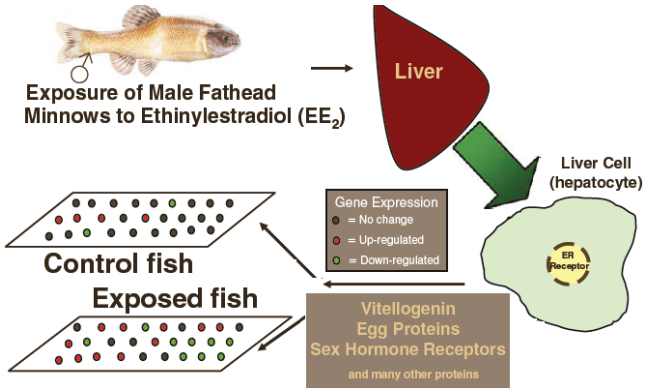

Figure 1: Effect of EDCs on gene expression

2. Endocrine System

Endocrine systems are found in most varieties of animals. The endocrine system consists of glands that secrete hormones, and receptors that detect and react to the hormones (Klinge et al., 2004). Fish consists of various glands located throughout the body, Figure 2 and Table 1.

Table 1 and **Figure 2:** The main endocrine glands in fish (Bond, 1979)

Gland/Hormone	Target Organ	Effect(s)
Pituitary		
Prolactin	various	osmoregulation, reproduction, growth, lipid metabolism, metabolism
Growth hormone	various	stimulation of growth
Thyroid stimulating hormone	thyroid	stimulation of thryroxine
Gonadotrophic hormone	gonads	stimulation of gonads
Isotocin, mesotocin	blood vessels	constricts gill blood vessels, systemic vasodilation
Thyroid		
Thyroxin	many	adaptation to environmental changes such as temperature or osmotic stresses
Calcitonin	gills and kidney	regulation of calcium metabolism
Corpuscles of Stannius		
Hypocalcin	gills	calcium homeostasis
Pancreas		
Insulin	all cells	increases glucose permeability
Glucagon	all cells	glycogen and lipic metabolism
Chromaffin tissue		
Adrenaline	circulation	gill vasodilation, system vasoconstriction
Noradrenaline	circulation	increase heart and glucose metabolism
Intrarrenal		
Corticosteroids	gills, kidney	stress response, osmoregulation
Gonads		
Androgens and estrogens	many, including brain	reproductive status and behavior; also of other fish (as pheromones)

Hormones travel throughout the body and act as chemical messengers. Hormones interface with cells that contain matching receptors in or on their surfaces. The hormone binds with the receptor, much like a key would fit into a lock. The endocrine system regulates adjustments through slower internal processes, using hormones as messengers. The endocrine system secretes hormones in response to environmental stimuli and to orchestrate developmental and reproductive changes. The adjustments brought on by the endocrine system are biochemical, changing the cell's internal and external chemistry to bring about a long term change in the body. These systems work together to maintain the proper functioning of the body through its entire life cycle. Sex steroids such as estrogens and androgens, as well as thyroid hormones, are subject to feedback regulation, which tends to limit the sensitivity of these glands (Flik et al., 2006). Although most of what is currently known about the effects of EDCs involves reproduction and reproductive behavior, other areas of the endocrine system, such as the thyroid, may also be targets for EDCs (Guillette et al., 2001; Katuli et al., 2014). Hormones work at very small doses (part per billion ranges). Endocrine disruption can thereby also occur from low-dose exposure to exogenous hormones or hormonally active chemicals that can interfere with receptors for other hormonally mediated processes (Bond, 1979).

Furthermore, since endogenous hormones are already present in the body in biologically active concentrations, additional exposure to relatively small amounts of exogenous hormonally active substances can disrupt the proper functioning of the body's endocrine system. Thus, an endocrine disruptor can elicit adverse effects at much lower doses than toxicity, acting through a different mechanism (Sumpter and Jobling, 1995; Panter et al., 2013).

Mode of Action (Anderson et al., 1996)

Endocrine disrupting compounds are believed to exert their influence by:

1) Mimicking the effects of endogenous hormones, such as the estrogens and androgens;

2) Antagonizing the effects of endogenous hormones;

3) Altering the pattern of synthesis and metabolism of normal hormones; and 4) modifying hormone receptor levels.

4) EDCs may also interfere with the binding proteins that act to transport endogenous hormones to their destination.

3. Types and Sources of EDCs

Various types of industrial and natural compounds have been identified as EDS that present in Table 2-4.

Table 2: Industrial compounds

Chemical/Class	Use/Source
Industrial Chemicals/Byproducts	
4-Nonylphenol	Surfactant intermediate/breakdown product
Bisphenol-A	Monomer of polycarbonate
4-tert-pentylphenol	Industrial intermediate
Phenanthrene	Fossil fuel combustion product
Dioxins	Industrial and waste incineration byproducts
Butyl benzyl phthalate	Plasticizer
Butyl benzyl -A	Plasticizer
Di-n-butyl phthalate	Plasticizer

Table 3: Pesticides

Chemical/Class	Use/Source
Pesticides	
Atrazine	Herbicide
Diazinon	Herbicide
Carbofuran	Insecticide
Toxaphene	Insecticide
Endosulfan	Insecticide
Lindane	Insecticide
DDT	Insecticide
DDE	Insecticide

Table 4: Metals and Natural steroids

Chemical/Class	Use/Source
Metals	
Mercury	Industry
Cadmium	Industry
Lead	Industry
Natural Products	
b-Sitosterol	Pulp and paper industry by-product
Genistein	Plant sterol
Daidzein	Plant sterol
Enterodiol	Plant sterol

4. Effect of various EDCs

Polybrominated diphenyl ethers (PBDEs) are a class of compounds found in flame retardants used in plastic cases of televisions and computers, electronics, carpets, lighting, bedding, clothing, car components, foam cushions and other textiles. After World War II, manufacturers saw the potential plastics could have in many industries, and plastics were incorporated into new consumer product designs (Hooper and McDonald, 2010).

Alkylphenols and alkylphenol polyethoxylates, (APEs), have received much of the recent attention because of their estrogenic effects in laboratory studies, and their presence in the aquatic environment. APEs are used as surfactants in many applications from soaps and detergents to pesticide formulation. APEs enter the aquatic environment via discharges from STPs, textile, and pulp and paper mills. Effects associated with APEs typically include elevated levels of the egg protein vitellogenin in males, reduction in gonadal development, and even intersex fish (Jobling et al. 1998).

Bisphenol-A is the monomer of the plastic polycarbonate. Approximately 1.6 billion pounds are produced in the U.S. each year. Much of the polycarbonate eventually winds up in landfills. Bisphenol-A appears to be an estrogen mimic, with a demonstrated affinity for rat ER (Krishnan et al., 1993). The testes were processed for histologic analysis. At concentrations of 640 and 1,280 □ g/L, bisphenoł-A had a significant inhibitory effect on weight and length in males by Day 71. Egg production was inhibited and that hatchability was reduced Sohoni et al. (2001).

Polycyclic aromatic hydrocarbons, (PAHs) are found in fossil fuels such as oil and coal and are released into the environment through combustion, surface runoff, oil spills, recreational boating and shipping, municipal waste effluents and atmospheric deposition (Kime, 1998). In urban areas it is thought that the majority of PAHs are the result of atmospheric deposition from the combustion of fossil fuels (Kim, 1999). Kim (1999) noted that while PAHs may function as weak ER agonists, they are expected to bind preferentially to the Ah receptor, triggering the induction of Ahresponsive genes which can lead to an antiestrogenic effect (Kim, 1999).

4-tert-pentylphenol. This compound has also shown some estrogenic potential. Gimeno et al. (1998a) investigated the effects of 4-tert- entylphenol (TPP), an industrial intermediate, on the common carp Cyprinus carpio. Exposure of the male carp to TPP resulted in elevated vitellogenin levels and the inhibition of spermatogenesis. Exposure of fish to each concentration also resulted in reduced testicular growth, with a correspondingly lower testicular weight. In three out of five fish exposed to the higher TPP concentrations, disorganization of the seminiferous lobules, atrophy of the germinal epithelium, and some tissue necrosis was observed (Gimeno et al., 2008).

Dioxins. are not intentionally manufactured but are typically forme and released through industrial activities such as chlorine bleaching at pulp and paper mills, chlorination at waste and drinking water treatment plants, and from municipal solid waste and industrial incinerator emissions. Anderson et al. (1996a) have shown in vitro that both the dioxin TCDD (2,3,7,8 tetrachlorodibenzo-p-dioxin) and the furan 2,3,4,7,8-pentachlorodibenzofuran are estrogen antagonists. As with some of the PAHs, there appears to be a relationship between E2 antagonism and induction of the CYP1A1 protein (Anderson et al., 1996).

Pesticides- As is clear from Table 3, a large number of compounds in this family of pollutants have endocrine distribution compound property. Katuli et al (2014) showed that diazinon, which is a member of this family of pollutants can be on hormones such as cortisol and thyroid hormone is effective and thereby reducing the osmotic adjustment in exposed Caspian roach fingerling fish (Katuli et al., 2014).

Trace elements- occur naturally in the earth's crust but are concentrated and introduced into the environ ment through mining and manufacturing processes. Kime (1999) has pointed out that trace elements which induce the production of metallothioneins in the liver or gonads might disrupt gamete production by disturbing normal zinc homeostasis, essential for the development of both eggs and sperm. Cadmium, at aqueous concentrations of 50 ppm, has been shown to significantly decrease sperm motility (Kime et al., 1999). Mercury has been shown to have a major impact on sperm motility at a concentration of only 1ppb (Rurangwa et al., 1998), and to have a direct effect on the egg micropyle, preventing entry of sperm (Kime et al., 1999).

In addition to the involvement of the hormone binding to the position, EDC also cause changes in gene expression and secretion of hormones and various glands and therefore cause secretion of different hormones. Many other applications, such as enzymes, the production will be affected by this material. In fact, the effect of EDC on gene expression of these enzymes occur (Moggs et al. 2004).

5. Species

Most reported examples of what would now be considered cases of endocrine disruption of reproduction in wildlife have occurred in aquatic organisms, or species that feed on aquatic organisms. The reason is that water is the final destination of many of these compounds. Many of the investigations into EDCs in the aquatic environment have involved fish because of similari ties in the endocrine system to higher vertebrates (Sumpter, 2002). Mollusks and reptiles have it been shown that exposure to an endocrine disrupting chemical (or mixture of chemicals) can lead to population declines (Ashfield et al., 1988).

6. Effective Factors

Scope effect of EDCs due to the presence or absence of certain factors can be different. Some of these factors include:
1. Source
2. Concentration
3. The period of exposure
4. The effects of synergy with other existing EDS
5. The stage of life

6. and environmental factors (including oxygen, temperature, salinity and the presence of other stressors).
The effect of these factors relatively is known. This means that in high concentrations and longer period of time in most cases we can see more severe impact. There are cases that in lower concentrations most effects viewed and its reasons are not clear. For materials and components, including the components of the EDCs, standards have been determinate. Since EDCs in very low concentrations have negative effects on the endocrine system inside, concentrations that may be considered less than the standard rate, therefore change in the standard rate according to negative effects EDCs on the endocrine system is controversial (Guerrero-Bosagna et al. 2005). One of the most attractive above factors have been many studies is exposure time. According to the studies, most critical phase of marine organism life in expose to EDCs is during embryonic development. When, most of the evolution of different structures and different systems for life in outside world happened (Thomas and Doughty, 2004).

Exposure time
Numerous studies found that EDS can prevent proper sexual differentiation of the genotype status. Also it has been shown in other studies; these substances alter the functioning of thyroid hormone that can trigger the disorder of sexual differentiation. In support of these results other studies suggested exposure adults with some concentrations of EDCs have not many negative effects. However, in these studies it was found that the low concentration of the EDCs can have a broad impact on fetal organisms so that the life in these organisms after hatching or birth could be faced with a serious problem (Thomas and Doughty, 2004).

7. Entrance Methods

Entrance methods with respect to location and living conditions of different organisms are different. For example, in most terrestrial organisms, including humans, the major direction is through the food that contaminated with this material. In the case of fish there is a different situation. As mentioned above, the amount of entering material in the aquatic environment and subsequent exposure of aquatic organisms to these substances further. The main entrance for entry of EDCs to aquatic body is through the water. According to the flow of water, this material can easily be transferred in total body water and due to the influence of these substances in very low concentrations as EDCs, impose their negative role. The transfer of these materials through the fed can be as the next stage. Where the organisms in the food chain from the bottom of the food chain plant compounds, or benthos lower consumption and higher-rank creatures that are carnivorous creatures called chains are lower, consume plant compounds or benthos and creatures with higher position, which are called carnivorous creatures, are lower chain. And thereby bioaccumulation occurs in them. This is noteworthy that entry of the EDCs in water environment may be done through different ways the most important of them include: direct release of municipal and industrial wastewater into the environment, excessive use of pesticides and agricultural fertilizer and enter this material through groundwater drainage to larger aquatic environment. The note that there are is, influence of various factors on the rate of drainage (Sumpter, 2002).

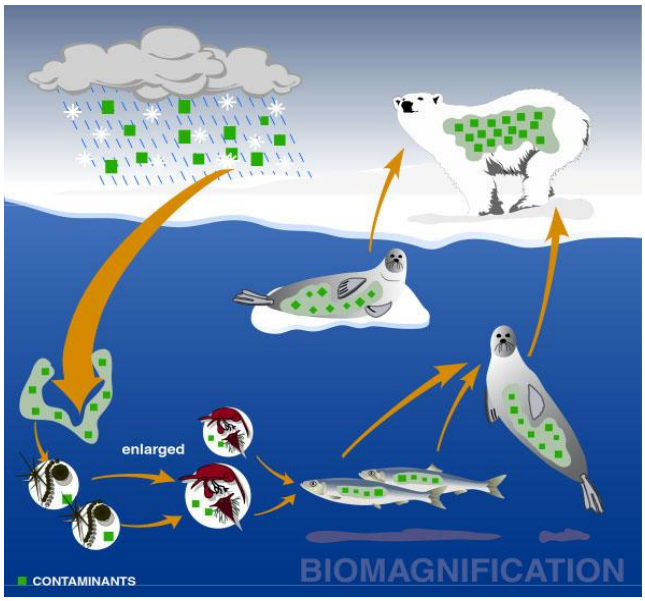

Figure 3: The cycle of EDCs and its bioaccumulation in the organism.

8. New Methods for Determining the Effects of EDCs

Determine the effects of chemicals on different systems of living organism and the amount of dangers of excessive use of these materials by using the software. Some of these methods include:

- Toxic mechanisms (or modes) of action- (MOA)
- Registration, evaluation, authorization and restriction of chemicals – REACH

Knowledge of this software's serves as a basis for effective extrapolation of biological effects across species, biological levels of organization, and chemical structures. This information can help identify potentially sensitive responses and even species prior to extensive testing, thereby optimizing time and resource use (Ankley et al., 2014). Using this method will ultimately lead to improved environmental management of new chemical substances to control environmental health.

9. Conclusion

Endocrine disrupting compounds or EDCs have the potential to interfere with a variety of life processes controlled or influenced by the endocrine system. A number of synthetic and natural chemicals have been shown to adversely affect the endocrine system in fish. To date, most of the research on endocrine disruption in fish has concentrated on reproductive effects. Other areas of the endocrine system in fish and higher vertebrates are also at risk and therefore, more research is needed.

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