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Mercury Toxicity in Hormonal Effects to Fresh Water Fish *Cirrhinus Mrigala*

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Abstract: ***Mercury interfere with a number of processes, regulated by the thyroid hormones T_3 and T_4 including blood vessel dilation, neurotransmission and immune function.Mercury chloride exposure toxic to the kidney, stomach, and intestines and lead increased blood pressure. Mercury chloride is the chemical compound of mercury and chlorine with the formula $HgCl_2$. Mercuric salts generally target the gastrointestinal tract extensive precipitation of enterocytes protein occurs, with abdominal pain, vomiting and bleed diarrhea with potential necrosis of the gut mucosa. This may produce death either from peritonitis or from septic hypovolemic shock. Surviving patients commonly develop renal tubular necrosis with anuria. Brain dysfunction also occurs due to exposure of mercury. Plasma triiodothyronine (T_3) of fish Cirrhinusmrigala exposed to sub lethal concentrations of mercury was presented in Table 2. The plasma triiodothyronine (T_3) levels was decreased as the exposure period extended showing a percent decrease of-46.66, -53.84, -10.00, -64.28, -66.66 at the end of 7^{th}, 14^{th}, 21^{th}, 28^{th}, and 35^{th} day, respectively. Table 3 gives data on change in the plasma thyroxin (T_4) level of fish Cirrhinusmrigala exposed to sub lethal concentration of mercury. T_4 level was also decreased throughout the treatment period showing a percent decrease of -72.29, -73.10, -76.02, -79.86, -79.02 at the end of 7^{th}, 14^{th}, 21^{st}, 28^{th}, and 35^{th}, days respectively.***

Keywords: Mercury Toxicity, Hormonal Effects, *Cirrhinus, Mrigala*

1. Introduction

Pollution is the introduction of contaminants into the natural environment that causes adverse affect. Pollution can take the form of chemical substances. Water pollution by industrial effluents containing organics and heavy metals pose a serious hazard to the aquatic biota and public health (Velma *et al.,* 2009). Mercury chloride or mercuric chloride is the chemical compound of mercury and chlorine with the formula $HgCl_2$. Mercury is released in the environment as a result of both natural and human activities, and persists over time, though the form in which it exists changes over (USEPA, 1999). Once mercury enters water, either through air deposition or soil runoff, microorganisms such as bacteria transform inorganic mercury in the environment to methyl mercury, which can be bioaccumulated in fish. Among different hormonal studies thyroid hormone are very important for the growth factor. Mercury is a naturally-occurring metal used in man-made products and processes, and is emitted into air from industrial sources (USEPA 1997). Human exposure to mercury occurs by breathing. Three major types of mercury, 1) elemental mercury, found in thermometers, fluorescent bulbs, dental amalgam fillings, and other sources 2) organic mercury, predominantly methyl mercury, found in food such as fish, and ethyl mercury found in some vaccine preservatives and some antiseptics and 3) non-elemental forms of inorganic mercury, found primarily in batteries, some disinfectants, and some health remedies and creams (Bernhoft, 2011). Inorganic mercury is the mercury compound that includes mercury chloride, Mercury chloride is a white powder that is soluble in water (Aposhian *et al.,* 1983). Mercury chloride exposure is toxic to the kidney, stomach, and intestines and lead increased blood pressure (USEPA 1997).

Fish concentrate mercury in their bodies, often in the form of methyl mercury, a highly toxic organic compound of mercury. Fish products have been shown to contain varying amounts of metals, particularly mercury and fat soluble pollutants from water pollution. Mercury is known to bioaccumulate in human, so bioaccumulation in water food carries over into human populations where it can result in mercury poisoning. It is dangerous to both natural ecosystems and human since it is a metal known to be highly toxic, especially due to its ability to damage the central nervous system (Park *et al.,* 2008). Exposure of mercury to fish *Cirrhinus mrigala* affects the internal organs like gill, liver, kidney and especially it affects the hormone, the thyroid hormone. Thyroid hormone (THS) are known to play a crucial role in many metabolic processes and are essential for normal growth, differentiation and development of vertebrates (Morgado, *et al.,* 2007). In fish, TSH are implicated in reproduction and appear to be important in the regulation of development. High concentrations are present in fish eggs and increased levels are reported during metamorphosis on larval transition. Disruption of thyroid axis may seriously compromise normal development, differentiation, growth and reproduction in many fishes. Thyroid hormones have a small hydrophobic thyroxin nucleus that mediates their action by binding to specific nuclear receptors, which act directly on target genes bringing about a cellular response (Yen and Chin, 1994). Triiodothyronine (T_3) is the most active hormone and binds with high affinity to nuclear receptor (TLS) while L-Thyroxin (T_4) with low affinity has few direct actions (Hadley, 1996). Almost all TSH circulating in the plasma are bound to transporter proteins (Larsson *et al.*, 1985) and only free enter cells to elicit a response (Ishihara *et al.,* 2003).The balance of free to bound TSH in the plasma depends on plasma proteins although the importance of this interaction in both is entirely understood (Morgado *et al.,* 2007).Thyroid hormone are of particular interest as they regulate many metabolic processes and are paramount in early development, growth and reproduction (Eales and Brown 1993,). Natural variation in thyroid status of fish has been demonstrated in response to development state and age (Suchiang, *et al*., 2011).

Among metal, mercury has been regarded as a highly toxic to fish and other aquatic organisms. Mercury which has direct toxic effects and indirect effects mediated by the stress hormones, confinement is a stresses that has only indirect, hormone-mediated effects on the gill (Camargo *et al.,* 2002). Several authors reported the extreme toxicity of mercury to fishes (EPA, 1997). However only a few authors reported toxicity of mercury on primary stress responses of fishes especially the hormones like triiodothyronine (T_3) and thyroxin (T_4). Fish early life stages are thought to be more sensitive to environmental chemicals than adult fish (Coimbra and Reis-Henriques, 2007). Thyroid hormones importance in fish early developmental growth and reproductive is well known, as their presence in the oocytes resulting from material transference. Thyroid hormones actions are mediated by the binding of T_3 which formed after T_4 denomination to nuclear receptors. In fish, the origin of T_3 and T_4 both hormones can be endogenous and or/ exogenous. Thyroid hormones were found to be present in eggs and their importance even at early life stages. The main secretion product of the thyroid gland is Triiodothyronine (T_3).The activation to T_3 is carried out almost entirely in peripheral tissues by denomination of the outer ring (ORD) of T_4 Deiodination of the inner ring (IRD) result in the production of the inactive metabolite 3, 3', 5, '-T_3 (Rt_3) (Vasser, *et al*., 1996). IRD also inactivates T_3 by converting it to 3, 3'-diiodothyronine. Denomination controls plasma and tissue thyroid hormone levels and thyroid hormone biological activity. The enzymes responsible for thyroid hormone denomination are called Iodothyronine (Vander Guyton *et al.,* 2001).

Alterations of plasma thyroid of fish were observed by many authors like nitrite in *oreochromis mossambicous* (Subash peter *et al.*, 2007), copper (Anderson 1996), Cadmium (Hoole, 1997), Cadmium in *Peralichty dentatus* (Anderson, 1986, Hoole, 1997). *Cyprinus carpio* to environmental acidic (Nagae *et al*., 2001). Environmental salinity in *Teleosts* (Shepherd *et al.*, 1997). Nitrite in sea bream and teleost *Sparus saeba.* (Deane *et al*., 2007). *Hoplias malabaricus* exposed to methyl mercury showed decreased hormonal status (OliveraReiberio *et al.*, 2006).Exposure of mercury chloride showed an increase in plasma T_4 and T_3 in *Juvenile rainbow trout*, (Bleau *et al*., 1996). Hormones have been measurable in blood and circulating levels and are exposed to xenobiotic. Chemicals in species hormones usually act on several target tissues, and osmoregulatory hormone may regulate ion or water change across gills, kidney, intestine and skin in a fish and its secretion may be subjected to complex feedback (Folmar *et al*., 1993) reported that aquatic toxicologist, measurement of circulating levels hormones can provide additional information on the sub lethal effects of many chemicals. The author stated that significant changes in circulating hormone levels may be observed. The Main function of thyroid gland is to synthesis the Iodothyronine, 5, 3', 5' tetraiodothyronine, (T_4) Thyroxine and 3, 5, 3' Triiodothyronine (T_3). These are peptides containing iodine. The two most important hormones are T_3 and T_4 and these hormones are essential for life and have effects on body metabolizing growth and development. Thyroid plays an important role in ion regulation, energy metabolism, growth and reproduction (Vander Geyten *et al.*, 2001). Environmental pollutants cause an impairment of fish internal function and a characteristic elevation of plasma thyroid hormones may not be able to compensate overall fitness for the survival (Buckman *et al.*, 2007). Fish also sensitive to nutritional state due to stress of thyroid hormones. In fish, hormones are critical towards maintaining proper physiological function and amongst the hormones found in fish the thyroid hormones, thyroxine (T4) and triiodothyronine (T3) are known to play an important role in fish growth (Higgs *et al*., 1982) and early development (Lam, 1980).

2. Specimens Collection

Healthy specimens of *Cirrhinus mrigala* were obtained from Tamilnadu Fisheries Development Corporation Limited, Aliyar, Tamilnadu, India. Fish of the same age and size which hatched from the same lot of eggs were collected, the age of the fish being 2 to 3 month old. They were safely brought to the laboratory in well packed polythene bags containing aerated water and stocked in a large cement (36'x 18'x 19') tanks. Fish were acclimatization for about 20 days before the commencement of the experiment. During the acclimatization period, fish were fed *ad libitum* with rice bran and ground nut oilcake in the form of dough once in daily. Water was replaced every 24h after feeding in order to maintain a healthy environment for the fish. This ensures sufficient oxygen supply for the fish and the environmental is devoid of any accumulated metabolic waste. The feeding was withheld for 24h before the commencement of the experiment and to keep the specimens more or less in the same metabolic state. After acclimatization, fish with an average length about 7.0-8.0cm and average weight of 5.0-6.0g were selected. The fish were introduced into glass aquarium (26'×18'×18.5'cm) which was washed thoroughly and maintained in the laboratory. Fish belonging to both sexes were used. These fish served as the stock for experiment schedule. Tab water free from chlorine was used for the present study. The hydro-biological features such as temperatures, pH, salinity, dissolved oxygen, total alkalinity, and total hardness were estimated for each set of experiment as these factors have a significant influence on the biodegradability and toxicity of pollutants. Temperature was determined by using a thermometer and pH value by pen type ph meter (pH scan, Intec cybernetics Pvt. Ltd, Singapore).The salinity of water was determined by Mohr's method using potassium chromate as an indicator. Dissolved oxygen was estimated by Winkler's method using starch as an indicator. Total alkalinity was determined by using methyl orange as an indicator. Total hardness was measured by using ammonia buffer solution and Erichrome black T as an indicator. The above physico chemical analysis of water used in the present experiment was carried out as per APHA *et al.* (1998).

3. Materials and Methods

Hormone Analysis

Thyroxin (T_4) and Triiodothyronine (T_3) were estimated

using Enzymes linked immune absorbent assay (ELISA of hormones) using Kits.

4. Results

Plasma triiodothyronine (T_3) of fish *Cirrhinusmrigala* exposed to sub lethal concentrations of mercury was presented in Table 2.The plasma triiodothyronine (T_3) levelswas decreased as the exposure period extended showing a percent decrease of -46.66, -53.84, -10.00, -64.28, -66.66 at the end of 7th, 14th, 21th, 28th, and 35th days. Table 3 gives data on change in the plasma thyroxin (T_4) level of fish *Cirrhinusmrigala* exposed to sub lethal concentration of mercury. T_4 level was also decreased throughout the treatment period showing a percent decrease of.-72.29, -73.10, -76.02, -79.86, -79.02 at the end of 7th, 14th, 21st, 28th, and 35th, days respectively.

Table 2: Changes in the plasma triiodothyronine (T_3) level of fish*Cirrhinus mrigala* exposed to sublethal concentration of mercury for 35 days

S. No	*Exposure Period*	*Control*	*Experiment*	*Change %*	*Calculated t Value*
1	7	0.15 ± 0.02	0.08 ± 0.01	-46.66	0.238
2	14	0.13 ± 0.01	0.06 ± 0.02	-53.84	0.058
3	21	0.10 ± 0.02	0.09 ± 0.02	-10.00	1.533
4	28	0.14 ± 0.04	0.05 ± 0.01	-64.28	0.666
5	35	0.09 ± 0.03	0.03 ± 0.05	-66.66	0.384

Table 3: Changes in the plasma thyroxin (T_4) level of fish *Cirrhinus mrigala* exposed to sublethal concentration of mercury for 35 days.

S. No	Exposure Period	Control	Experiment	Change %	Calculated 't' Value
1	7	1.480.40	0.410.21	-72.29	0.724
2	14	1.450.43	0.390.09	-73.10	0.674
3	21	1.460.30	0.350.06	-76.02	0.612
4	28	1.490.32	0.300.11	-79.86	0.806
5	35	1.43 0.21	0.30 0.10	-79.02	0.681

5. Discussion

The inhibition of hormone synthesis was proposed to occur via conversion of mercury to mercury chloride that in turn inhibits rate limiting enzymes. It is currently limited in understanding as to how mercury impairsT_4 levels, over the long term, as this study was performed over a7-day period but, it is possible that over a prolonged period of mercury exposure, T_4 levels would have fallen to an extent that would have ultimately affected serum T_3 levels. The fact that mercury chloride can be produced from mercury, opens the possibility that mercury may interfere with a number of processes, that are regulated by this hormone including blood vessel dilation, neurotransmission and immune function. Mercury chloride production from mercury is favoured by low P^H, hypoxia and by high mercury. Mercuric salts (typically $HgCl_2$) generally target the gastrointestinal tract and the kidneys. Extensive precipitation of enterocytes protein occurs, with abdominal pain, vomiting, and bleed diarrhea with potential necrosis of the gut mucosa. This may produce death either from peritonitis or from septic hypovolemic shock. Surviving patients commonly develop renal tubular necrosis with anuria. Brain dysfunction is less evident than with other forms of mercury.

Thyroid dysfunction seems associated with inhibition of the 5' deiodonases, with decreased free T_3 and increased reverse T_3. Evidence suggests disruption of numerous sub cellular elements in the central nervous system and other organs and in mitochondria adverse effects have also been described on heme synthese, cell membrane integrity in many locations (Berlin, *et al*., 2006), free radical generation (Oliver *et al.*, 2000), neurotransmitter disruption, and stimulation of neural excitoxins, resulting in damage to many parts of the brain and peripheral nervous system. Methyl mercury has been associated with reduction in Natural Killer cell activity, as well as an imbalance in Th2: Thl ratios favoring autoimmunity (Rosenstreich, 2007).Thyroid hormone receptors possess equivalent trans activation domains and have some structural functional similarity, suggesting that these nuclear receptors may enhance transcription of target genes by similar mechanisms as summarized above. The thyroid and corticosteroid systems interact at multiple levels to influence several physiological processes like development, growth or behaviour. Thus, the hypothalamo –pituitary – interrenal axis modulates the thyroid axis in fishes and other vertebrates. Many natural or synthetic chemicals are now routinely observed in water. Evidence revealed that these compounds might interfere with endogenous endocrine systems of wildlife and humans. Thus, it is now essential to monitor their presence in the environment. Aquatic organisms in fish models are widely used in ecotoxicology and for the development of transgenic techniques.

Hormones are produced in Lymphoid tissues. The regulation of hormone secretion by the hypothalamus and pituitary has been established as the hypothalamus-pituitary-Inter renal (HPI) axis in fish (Wendelaar Bonga, 1997). The endocrine system of tales fish produces a variety of hormones like growth hormone, steroid hormones, gastrointestinal hormone, pancreatic hormones, thyroid hormone, (T_3 and T_4). In this thyroid T_3 and T_4 hormone plays an important role. Fish eggs contain maternally derived thyroid hormone. In *Rainbow trout* (Yada *et al.,* 2002) interaction between the endocrine showed a gradual acclimation improved non specific immunity in hormones. Due to interaction the Brown trout *Salmontrutta* also showed activation of lysozyme and phagocytosine (Marc *et al.,* 1995). In *Oreochromismossambiocus* (Yada *et al.*, 2000) showed an increased due to water salinity on immune function. During acclimation of Brown trout, positive relation between enhancements of immune function and an elevation in hormone level has been observed, (Marc *et al.*, 1995). In addition to stimulation of body growth and metabolism hormone is known to facilitate adaptation to a hyper osmotic environment in several *Teleosts*, the secretion of endogenous hormone is stimulated in response to

environmental salinity. Increased secretion in hormone in fishes seems to enhance not only osmoregulation but also immune function. In flat fish *Limandalimanda* the hormone level is decreased due to acute hypoxic level (Pulsford *et al*., 1994). In *Cyprinuscarpio* there is a decrease in level due to intake of acidic water, result in respiratory bursts (Nagae *et al*., 2001). Where as in *Rainbowtrout* the hormone level increased (Yada *et al.,* 2001) due to salinity, the stress response on fish immunity to water acidification to the charges in environmental P^H. In fresh water *Juvenile* the elevations of circulating hormones such as thyroid hormones were observed the changes in the development of body colour, changes in purine nitrogen metabolism, black margin of fins, changes in body form (Dickhoff *et al.*, 1997). However, acidification also has direct effects on the physiology of fish; the most important physiological disruptions involve ion regulation and associated growth and hormones (Tam and payson, 1986). *Hoplias malabaricus* exposed to methyl mercury showed decreased hormonal status (OliveraRiberio*et al.*, 2006).Exposure of mercury chloride showed an increase in plasma T_4 and T_3 in *Juvenile rainbow trout*, suggesting that Hg activates the hypothalamus pituitary-thyroid (HPT) axis (Bleau *et al*., 1996).

Postulated hypothesis on the thyroidal involvement in osmotic and ionic balance in fish and the wide interest in these hormones in the following decades, its osmoregulatory role in fish remains to be defined. A conclusive effect of THS has not yet been demonstrated, however, on the one hand, THS were reported to maintain Na^+ and osmotic balance during an osmotic challenge in *Fundulusfheteroclitus*. T_4 probably plays a more important role in the development of hypo-osmoregulatory ability than in hyper-osmoregulation. In *hagfish* (Zapata *et al.*, 1996), cat fish *Ictaluruspunctuates* (Wilson *etal*., 1997), *Atlanticsalmonsalar*, channel cat fish and buffer fish *Spheroidscephalous* (Charlemagne *etal*., 1998), *Rainbow trout* (Hansen *etal*., 1991) and *Japaneseflounder* paralichthy olivaceus (Park*etal*., 2001) showed a decreased in T_3 and T_4 hormone due interaction between Endocrine and immune system, *Cyprimuscarpio* to acidic water resulted a decreased in hormones T_3 and T_4 (Negae *et al.*, 2001). Decreased when hormones exposed to metals, such as copper, aluminum and cadmium (Hoole, 1997). Chemical pollutants have been reported to affect thyroidal hormone status in many fish species (Vander van *et al.,* 2006), but the effect of mercury on this group of hormones in fish has yet to be reported. It is found that serum T_4 decreased upon exposure of *Sea bream* to mercury where as levels of serum T_3 remained altered. This was different to vibriosis where a parallel decrease of both T_3 and T_4 during disease progression was observed (Deane *et al*., 2001) and taken together these results indicate the chemical and pathogenic stressors have different effects of thyroid hormone status in *Sea bream*. In animals, enzymatic conversion of T_4 to T_3 occurs via the action of 5' monodeiodinase as a serum T_3 remain unchanged, and then it is possible that mercury exposure may not have modulated this enzymatic conversion process, but further studies would be needed to verify this. However, it was observed that as mercury exposure concentration increased from 25 to 50mg/1 then the % decline in serum T_4 increased, suggestive of a concentration dependent effect, and a plausible explanation for the reduced serum T_4 could be via inhibition of T_4 synthesis.

Mercury seems to be of the metals causing serious immunosuppressant in fish. There is a decrease of thyroid hormone (TH) in gold fish *CarassiusauratusandTrout* (Thuvander, *et al.*, 1989) due to endocrine disruption. In *Tinca*, gold fish (cooper *et al.*, 1989,), *Oreochromisniloticus* (Kurrogi and lida, *et al*., 1999), Salvelinus alpines (Hogland *et al*., 2000), *KillifishFondles* heteroclites (Miller and Tripp, *et al*., 1982). *Seabreamsparesaureate* (Ortuno *et al*., 2001) showed a decreased in T_3 and T_4 hormones. Besides the lethal of low amounts of copper in environmental heater a sub lethal level results in increased hormones levels in fish (Anderson, 1996). Aluminum exposure showed an increased in hormone in trout (Brown and Sadler, *et al*., 1989). Cadmium is also known to increased the hormones level in *Trout* (Olsson *et al*., 1995). During fasting in immature carp *Cyprinuscarpio* the hormone level increased. Heavy metals like Mercury, copper and cadmium showed an increased in hormone levels in *Trout* (Marc *et al*., 1995).When Atlantic salmon (Salmon salary) induced to acid and Limed river waters the T_4 hormone is increased and T_3 Triiodothyronine is gradually decreased (Brown *et al*., 1993).In kernel Extract the hormone level is increased (Subash peter, *et al*., 1993).In the present study the significant decrease in plasma T3 and T4 level of fish *Cirrhinus mrigala* during acute and sublethal treatment might have resulted from disruption of numerous sub cellular elements in the central nervous system. Damage to many parts of the brain and peripheral nervous system due to disruption of cell membrane integrity in many locations, free radical generation, neurotransmitter, and stimulation of neural excitoxins, resulting due to exposure of mercury and an imbalance in Thyroid gland activity. Plasma levels of other pituitary hormones (i.e.,) TSH triiodothyronine (T_3), thyroxin (T_4), Organodotropins, Growth hormone (GH), and Adenocorticotropic hormone (ACTH)) were differentially modified. Among these hormones T_3, T_4 reported that mercury differentially affects the secretary patterns of hormone and demonstrated by the change in circulating values of these pituitary hormones.

The foregoing review of literature reveals the environmental stress causes disturbances in the homeostasis of fish. The role of pituitary hormones like T_3 and T_4 from inter renal cells under mercury toxicity is well documented. However literature on the impact of toxicity on primary stress response like hormonal levels in Indian major carps are scanty. Thyroid hormones regulate a wide range of biological processes associated with development, somatic growth, metabolism, energy provision. Thyroid hormone axis poses a significant hazard to human and wildlife health from interference of exogenous salts. The need for development and valid, ion of an in vivo assay for detection of thyroid system disrupting chemicals arises from concern that a considerable number of compounds have the potential to interact with different species of thyroid function and thyroid hormone action. The majority of studies on endocrine control functions have concentrated on the suppression of immune response by decreased secretion of thyroid hormone in response to environmental

stress.The major goal of the present study were to investigate the response of triiodothyronine and thyroxin as biomarkers of mercury induced health effect.

Reference

[1] AndersonLL, FederJ, BohnkerCR. Effect of growth hormone on growth in immature hypophysectomized. *J. Endocrin*. 68-345. 1986.
[2] AndersonDP. Environmental factors in fish health: Immunological aspects. In: ''The fish Immune system. *Organ. Patho.Environ* (Eds.), 289-310. 1996.
[3] AposhianHV. Water soluble antidotes for heavy metal poisoning. *Annual Review of Pharmaco. Toxico*.23, 193–215. 1983.
[4] APHA. Standard methods for the examination of water and waste water (20th EDS). American Public Health Association, Washington, DC. 1998.
[5] BerlinM, ZalupsRK, FowlerBA. Mercury, Handbook on the Toxicology of Metals. 3rd edition. Chapter 33. New York, NY, USA.*Els*. 2006.
[6] BernhoftRA. Mercury Toxicity and Treatment. A Review of the Literature.J EnvironPub Health.1- 10, 2011.
[7] BleauH, DannielC, ChevalierG, VantraH, HontelaA. Effects of acute exposure to mercury chloride and methyl mercury on plasma cortisol, T3, T4, glucose and liver glycogen in rainbow trout, Oncorhynchus mykiss. *Aquat. Toxicol*. 34, 221-235.1996.
[8] BrownDJA, SadlerK. Fish Survival in acid waters. In ''Acid Toxicity and Aquatic Animals'' *CambridgeUniversityPress*, *Cambridge*, pp.31-44. 1989.
[9] BrownJA. Endocrine responses to environmental pollutants. *Fish Ecophysio*. Chapman and Hall, London, New York, pp.276-296. 1993.
[10] BuckmanAH, FiskAT, ParrotJ, SolomonKR, BrownSB. PCB scan diminish the influence of temperature on thyroid indices in rainbow trout (*Oncorhynchusmykiss*). *AquatToxicol*., 84, 366-378. 2007.
[11] CamargoJA, AlonsoA. Mercury toxicity to aquatic animals, a review with new data for freshwater invertebrates. *Chemo.* 58, 1255-1267.2002.
[12] CharlemagneJ, FellahJS, De GuerraA, KerfournF, PartulaS. T.Cell receptors in ecotothermic Vertebrates. *Immunol.Rev*. 167, 81-100. 1998.
[13] ClarksonTW, MagosL, GreenwoodMR. The transport of elemental mercury into fetal tissues. *Biol Neo.*21(3), 239–244. 1972.
[14] ClarksonTW, MagosL. The toxicology of mercury and its chemical compounds. *CritRevToxicol*, 609-620. 2006.
[15] CoimbraAM, Reis-HenriquesEMA. Tilapia larvae aroclor 1254 exposure: Effects on gonads and circulating thyroid hormones during adulthood. *Bull. Environ. Toxicol*., 79, 488-493. 2007.
[16] CooperRL, KavlockRJ. Endocrine disrupters and reproductive development a weigh-off evidence overview. *J. Endocrinol*., 152, 159-166.1989.
[17] DeaneEE, LiJ, WooNYS. Hormonal status and phagocytic activity in sea bream infected with vibriosis. *Comp.Biochem. Physiol*. B.129, 687-693. 2001.
[18] DeaneEE, Lij, WooNYS. Hormonal status and phagocytic activity in sea bream infected with vibriosis. *Comp. Biochem. Physiol*. B, 129, 687- 693. 2007.
[19] De Oliveira RibeiroCA, BerlgerPelletierL, RouleauC. Histopathological evidence of inorganic mercury and methyl mercury toxicity in the arctic charr (*Salverlinusalpines*). *Environ. Res*., 90, 217-225. 2002.
[20] DickhoffWW, PierceAL, ShearerKD, BakerDM. An autumn profile of growth regulatory hormones in Chinook salmon (Oncorhynchus tshawytscha). Biomedical Life Science. *Fish Physiol Biochem*. 83-88. 1997.
[21] EalesJG, BrownSB. Measurement and regulation of thyroidal status in teleost fish. *Rev. FishBiol. Fisher*. 3, 299-347. 1993.
[22] EL-Moselhy, KhM. Bioaccumulation of mercury in some marine organisms.*Egyptian* J.*Aqu. Res*., 32, 124-134. 2006.
[23] EnglerR. Technology out of control. *TheNation* 240. 1985.
[24] EPA. Health Effects of Mercury and Mercury Compounds.349 pp. 1997.
[25] FolmarLC. Effects of chemical contaminants on blood chemistry of teleost fish.*Environ. Toxicol. Chem*., 12, 337-375. 1993.
[26] GrandiM, GuzziG, CattaneoC. Dental amalgam and mercury levels in autopsy tissues: food for thought. *Amn J Foren Med Pathol*. 27(1), 42–45. 2006.
[27] HadleyME. Endocrinology, Fourth ed. Prentice Hall, *NewJersey*. 1996.
[28] HansenJD, StrassburgerP, ThorgaardH, YoungWP, Du papsquierL. Expression, linkage and polymorphism of MCH-related genes in rainbow trout, *Oncorhynchus mykiss. J. Immunol.* 163, 774-786. 1991.
[29] HiggsDA, FagerlundUHM, EalesJG, BrideJR. Application of thyroid and steroid hormones as anabolic agents in fish culture. *Comp. Biochem. Physiol*. B, 73, 143-176. 1982.
[30] HoglandE, BalmPHM, WinbergS. Skin darkening, potential social signal in subordinate artic chart *Salvelinus alpines*. The regulatory role of brain monoamines and pro opiomelanocortin-derived peptides. *J.Exp.Biol*. 203, 1711-1721. 2000.
[31] HooleD, SchuwerackMM, LewisJW. Cadmium-induced celluler and immunological responses in *Cyprinus carpio* infected with the blood parasite, *Sanguinicola inermis*. *J.Helmin*. 77, 341-350. 2003.
[32] IshiharaA, NishiyamaN., Sugiyama, Yamauchi. The effects of endocrine disrupting chemicals on thyroid hormone binding to Japanese quail transthyretin and thyroid hormone receptor. *Gen. Comp. Endocri.* 134, 36-43. 2003.
[33] KurrogiJ, LidaT. Social stress suppresses defense activities of neutrophils in *Tilapia*. *Fish. Pathol*. 34, 15-18. 1999.
[34] LamTJ. Thyroxine enhances larval development and survival in *Sarotherodon* (*Tilapia*) *mossambiocusRuppell*. *Aquacul*. 21, 287-291.1980.
[35] LarssonM, PatterssonT, Carlstorm, A. Thyroid hormone binding in serum of 15 vertebrate species: isolation of thyroxine-binding globulin and prealbumin

analogs. *Gen. Comp. Endocrin*., 58, 360-375. 1985.
[36] MarcAM, QuentelC, SevereA, LeBailPY, BoeufG. Changes in some endocrinological and non-specific immunological parameters. During seawater exposure in the Brown trout. *J FishBiol*., 46, 1065-1089. 1995.
[37] MillerNM, TrippMR. The effect of captivity on the immune response *Killi fish, Fundulus heteroclitus. J.Fish.Biol*. 20, 301-308. 1982.
[38] MorgadoI, HamersT, LeoVanderDM. Disruption of thyroid hormone binding to sea bream recombinant transthyretin by ioxinyl and polybrominated diphenyl ethers. *Chemo*. 69(1), 2007.
[39] NagaeM, OgawaK, KawaharaA, YamaguchiM, NishimuraT, ItoF. Effect of acidification stress on endocrine and immune functions in carp, *Cyprinuscarpio*. *Water. Air. Soil. Poll*. 130, 893-898. 2001.
[40] NordbergGF, SereniusF. Distribution of inorganic mercury in the guinea pig brain. *Acta PharmacoToxicol*. 27(4), 269–283. 1969.
[41] OliveraRiberioCA, FlipakNetoF, MelaM, SilvaPH, RandiMAF, RabittoIS, AlvesCostaJR, PelletierE. Hematological findings in neotropical fish *Hoplias malabaricas* exposed to subchronic and dietary doses of methylmercury, inorganiclead, tributylinchloride,. *Environ.Res*. 101, 74-80. 2006.
[42] OliverG, BrackC, Müller-SpahnF. Mercury induces cell cytotoxicity and oxidative stress and increases â-amyloid secretion and tau phosphorylation in SHSY5Y neuroblastoma cells. *JNeurochem*.74(1), 231–236. 2000.
[43] OrtunoJ, EstebanMA, MeseguerI. Effects of short term crowding stress on the gilthead *Sea bream. Fish Physiol* 15-20, 2001.
[44] OlssonPE, KlingP, PetersonC, SilversandC. Interaction of cadmium and Oestradiol 17Bon metallothionein in vitellogenin synthesis in rainbow trout (*Oncorhynchus mykiss*). *Biochem*. 307, 197-203.1995.
[45] Osha., 1998. Update following Karen Wetterhahns death. Fish physiol. 15, 1-62.
[46] ParkKS, SeoYC, LeeSJ, LeeJH. "Emission and Speciation of Mercury from various Combustion Sources". *Pow Tech* 180, 151–156. 2008.
[47] ParkSH, ArakiS, NakataA. Effects of occupational metallic mercury vapour exposure on suppressor-inducer (CD4+CD45RA+) T lymphocytes and CD57+CD16+ natural killer cells. *InArchOccupEnviron Health*.73(8), 537–542. 2001.
[48] PowerDM, LlewellynL, FaustinoM, NowellMA, BjornssonBTH, EinarsdottirIE, CarnarioAVM, SweeneyGE. Thyroid hormone in growth and development of fish. *Comp. Biochem. Physiol*. 130, 447-459. 2001.
[49] PulsfordAL, Laraaire-GonyS, TomlinsonCN, GlynnPT. Effects of acute stress on the immune system of the dab. *Lim comp. Biochem. Physiol*. 109, 129-139.1994.
[50] RosenstreichD, deVosG, AbotagaS, LiaoZ, JerschowE. Selective effect of mercury on Th2-type cytokine production in humans. *ImmunopharmaImmunotox*. 29(3-4), 537–548.2007.
[51] SheperdBS, SakamotoT, NisgiokaRS, RichmanNH, MoriI, MadsenSS, ChenTT, HiranoT, Bern, HA, GrauEG. Somatotropic actions of the homologous growth hormone and prolactins in the euryhaline teleost.*Sparus aurata L*, innate immune response. *Fish. Shell. Fish innate*. 11, 187-197.
[52] Subash peter, LejiJ, BabithaGS, RejithaV, VijayasreeAS.Thyroidal and osmoregulatory responses in tilapia (*Oreochromis mossambicus*) to the effluents of coconut husk retting mechanism of thyroid hormone action. *TrendsEndocrinolMetab*., 5, 65-72. 2007.
[53] SuchiangP. Variation in the plasma levels of thyroid hormones and testicular activity in the male air breathing Catfish (*Clarias gariepinus*) over the annual cycle. 2011.
[54] TamWH, PaysonPD. Effect of chronic exposure to sublethal pH on growth, egg production and ovulation in brook trout, *Salvelinus fontinali. Canad.J.Aquat.Sci*.43, 275-280. 1986.
[55] ThuvanderA. Cadmium exposure of rainbow trout (*Salmo gairdneri).* Effect on immune functions. *J.Fish Biol*. 35, 521-529.1989.
[56] U.S. 1999. Centers for Disease Control (ATSDR). 1999. "Toxicological Profile for Mercury.'' Environmental Protection Agency, Office of Air Quality Planning and Standards and Office of Research and Development.
[57] USEPA, 1997. Environmental Protection Agency."Mercury Study Report to Congress, Volume II: An Inventory of Anthropogenic Mercury Emissions in the UnitedStates.''
[58] Vander GeytenMolKA, PluymersW, KuhnER, DarrasVM. Changes in plasma T_3 during fasting, refeeding in tilapa (*Oreuchromisniloticus*) are mainly regulate through change in hepatic type II Iodothyronine deiodinases *FishPhysiol. Biochem*., 19, 135-143. 2001.
[59] Vander GeytenS, ToguyeniA, BaroillerJF, FauconneauB, FostierA, SandersJP, VisserTJ, KuhnER, DarrasVM. Hypothyroidism induces type II iodothyronin deiodinases expression in tilapia liver. *Gen, comp.Endocrinol*., 124, 333-342. 2000.
[60] VanderVenLTM, VandenBrandhofEJ, VosJH, PowerDM. Effects of the antithyroid agend propylthiouraci in a partial life cycle assay with *ZebrafishEnviron. Sci. Technol*., 40, 64-81. 2006.
[61] VasserTJ. Pathways of thyroid hormone metabolism. *ActaMed. Austriaca*, 23, 10-16. 1996.
[62] VelmaV, VutukuruSS, TchounwouPB. Ecotoxicology of hexavalent chromium in freshwater fish: A critical review. *Rev. Environ. Hith*. 24, 129-145. 2009.
[63] VutukuruSS, JuveriaV, HimabinduY, AnjaneyulU. Physiological stress responses as biomarkers of sensitivity in *Esomusdanricus* exposed to copper. Asian J. *Microbiol. Biotech. Env. Sci*. 11, 969-975. 2009.
[64] WendelaarBongaSE. The stress response in fish. *Physiol. Rev*. 77, 591-625. 1997.
[65] WilsonM, BengtonE, MillerNW, ClemLW, Du PasquierL, WarrGW. Anovel Chimeric Ig heavy chain from teleost fish shares similarities to Ig. *D. Proc. Natl.Acad.Sci*.USA. 94, 4593-4597. 1997.
[66] WooNYS, ChiuSF. Effects of mercury chloride exposure on growth and Survival of sea bass, *LatesCalcarifer* Fingerlings in different Salinities. *J.*

Appl., *Aquacult*., 4, 45-54. 1994.
[67] XuY, ZhangJ, SchrammKW, KettupA. Endocrine effects ofsublethal exposure to persistent organic pollutants (POPS) on *mercurycarp* (*Hypophthalmichthysmolitrix*). *Environ*. *Pollut*., 120, 683-690. 2002.
[68] YadaT, AzumaT. Hypophysectomy depresses immune functions of the rainbow trout. *Comp. Physiol. Biochem*. 131C, 93-100. 2002.
[69] YadaT, AzumaT, KitamuraS, IkatuK. Dose-Dependent effect of exposure to acidic water on plasma sodium levels in *Rainbow trout. Bull. Nati. Res. Inst. Aquat*. 29, 217-224. 2002.
[70] YadaT, AzumaT, TakagiY. Stimulation of non-specific immune functions in sea water-adapted rainbow trout, *Oncorhynchus mykiss*, with reference to the role of growth hormone. *Comp. Biochem. Physiol*. 1298, 695-701. 2001.
[71] YenPM, ChinWW. New advances in understanding the molecular assay. 1994.
[72] ZapataAG, ChibaK, VarasA. Cells and tissues of immune system of fish. *Organ Path Environ*.1996