IOSR Journal of Environmental Science, Toxicology and Food Technology (IOSR-JESTFT)
e-ISSN: 2319-2402,p- ISSN: 2319-2399.Volume 14, Issue 7 Ser. III (July 2020), PP 28-36
www.iosrjournals.org

Review of Silver nanoparticles in Freshwater fish "*Cyprinus carpio*"

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Abstract: *The nanoparticles accumulate in different organs like gill, liver, intestine, kidney and muscle in fish Cyprinus carpio. The acute, chronic toxicity in the body through absorption by the gills and the glucose and glycogen content in the liver were affected and imbalance occurs in the hormone levels. Silver nanoparticles (AgNPs) are used widely in applications. Human exposure to AgNPs has been increased in recent years. AgNPs are translated into blood streams and accumulated in organs and it is confirmed as organ toxicity and cause eventually death. Metallic and soluble silver compound when exposed occupationally affects the potential antimicrobial pathogens and cause numerous changes in the skin colour. For the optimum function of body immunity, everyone needs nano-silver circulating in their bloodstream. The intensive ingestion and inhalation of silver compounds create various toxic effects on the living organism in the environment, especially in fishes.*
Keywords*: Fish Cyprinus carpio, Bioaccumulation, Bioassay, Histopathology, Biochemical studies.*

Date of Submission: 16-07-2020 Date of Acceptance: 31-07-2020

I. Introduction

Nano-technology is a valuable science evolved recently in science and technology. Silver to 100 nm breaks to silver nanoparticles. In early day's silver were plentiful in its metallic form in ground water. Silver acts as a natural immune system in human body. Silver is a rarely occurring element in earth's crust and associated with other elements deposited at much higher concentrations. Silver has special properties with a wide variety of applications and is used in high electrical and thermal conductivity. Due to its antibacterial properties silver and variety of products, including clothes, food packaging, washing machines, children toys and medical equipments increasingly incorporate silver nanoparticles (Lee and Jeong, 2005, Ben and Westerhoff, 2008). The metal silver nanoparicles plays an important role in aquatic organisms. Silver nanoparticles are naturally occurring precious metal. In the aquatic environment silver nanoparticles is estimated to about 0.01 μgL^{-1} enhanced different changes in physically and biochemically (Tiede *et al*., 2009). Silver nanoparticles increase in the aquatic environment from leaching, mining and anthropogenic sources in jewellery, monetary, currency and photography (Chen and Schluesener, 2008) The intensive ingestion and inhalation of silver compounds create various toxic effects on the living organism in the environment.

For the optimum function of body immunity, everyone needs nano-silver circulating in their bloodstream. The silver nanoparticles in the aquatic environment are formed due to the release of free Ag^+ in water (Navarro *et al*., 2008). The nanoparticles accumulate in different organs like gill, liver, intestine, kidney and muscle in fish *Cyprinus carpio*. The acute, chronic toxicity in the body through absorption by the gills and the glucose and glycogen content in the liver were affected and imbalance occurs in the hormone levels. Silver and silver nanoparticles (AgNPs) are used widely in applications. Human exposure to AgNPs has been increased in recent years. AgNPs are translated into blood streams and accumulated in organs and it is confirmed as organ toxicity and cause eventually death. Metallic and soluble silver compound when exposed occupationally affects the potential antimicrobial pathogens and cause numerous changes in the skin colour. Under case study data from a 59-years old man, who was suffering from skin colour change, it was revealed that he had ingested colloidal silver two or three times a year whenever he felt 'cold'. The man believed that colloidal silver had antibiotic properties. However, it leads to hypertension, hyperlipidemia, diabetes gastroesophageal reflux disease along with this skin colour change. One of the most toxic metals is silver mainly effects the disturbance of osmoregulation (Bianchini *et al*., 2002) cause injuries and reduce survival in freshwater fish.

The mechanism behind nano silver toxicity demonstrates that nano silver reducement, may likely due to impaired respiration, which leads to respiratory toxicity in fishes (Handy and Shaw, 2007) and is particularly vulnerable to nanoparticles. Fish gills are sensitive to nanoparticles in recent studies. In aquatic organisms the silver nanoparticles accumulate in different organs. At first the toxicant enters through the gills and reaches the muscles and hepatic cells and affects the cells in the liver and automatically the glycogen level is decreased. Then the toxicant moves to the stomach and intestine, where the digestive juices are decreased and digestion prolongs to slow process. Next the toxicant enters the kidney and the interstitial cells and the renal tubules are affected. Consumption of food containing the chemicals taken up by either an organism directly from exposure to a contaminated medium and it can be defined as the net accumulation of a metal in a tissue or a whole organism. Metal bioaccumulation is influenced by multiple routes of exposure (diet and solution) and geochemical effects on bioavailability. As metals are not metabolized, bioaccumulation of metals and metalloids is of particular value as an exposure indicator. Similarly, bioaccumulation is often a good integrative indicator of the chemical exposures of organisms in polluted ecosystems (Sung *et al*., 2008).

The acute (short-term test) and chronic (long term test) causing 50% mortality in the fish is calculated as lethal concentration LC50. Median lethal concentration (LC50) which kills 50 percent of test organisms in a fixed time according to Sprague (1969). In natural ecosystem acute toxicity is determined after 24 hours or 48 hours of exposure in tests and in some cases after 96 hours depends upon the development, growth and reproduction (Rand and Petrocelli, 1985) on the basis of regulatory guideline. The researches over toxicological effect of nanoparticles (NPs) are limited, only a few studies are on the acute toxic effects of NPs in aquatic animals (Lovern *et al*., 2007). The mode of toxic action of substance and information on doses with target-organ toxicity and lethality can be used in setting dose levels for repeated dose studies. Thus, it provides information for comparison of toxicity and dose-response among members of chemical classes and help in the selection of organisms and their materials for further work (Hedayati et al., 2010).

The Sublethal effect by pollutants is a long term process. Sublethal toxicity causes physiological disturbances in fish and this toxicity affects in fishes allows us to define and understand the potential danger of pollutant inputs (Oilva *et al*., 2009). The toxicity in the aquatic environment using sublethal level may inflict stress mechanism and changes may occur in physiological, biochemical and behavioural processes, which leads to imbalance physiological state in vital function. The changes by vital functions viz., nerve and muscle functions, respiration, circulation, immune defence, osmoregulation and hormonal regulation. In the ecosystem, toxicity testing is the monitoring or predicting the effects of single compounds, populations, elements or mixture on the short and long term health of individual organism and this is the ultimate goal of toxicological studies. In aquatic organism normal growth, development and attainment of reproduction depends upon the potential hazard of silver nanoparticles and this process is the long term referred as chronic or full interfere with an aquatic organism, is recognised as an understanding and evaluation in the concentrations produce chronic effects and chronic toxicity (Zhou *et al*., 2008).

Changes by impairment of vital functions takes place in the biological systems due to external stimuli referred as biomarker. Biomarkers are defined as exposure or effects of contaminant in biological system in fish. Biological systems are contaminated by the contaminants and are highly toxic to fish. This affects the behavioural process and changes occur in physiology and molecular level where toxic effects of pollutants are determined (Agrahari and Gopal, 2009). Recently in polluted ecosystems the biomarkers monitors both the environmental quality and health of organisms such as serum levels of metabolites, ion (Martinez and Souza, 2002), levels of hormones, such as thyroid (Van *et al*., 2006) and biochemical variables, such as glucose and glycogen are commonly used as stress indicators (Firat and Kargin, 2010), bioaccumulation (Tilak *et al*., 2001). In *Cyprinus carpio*, the physiology and ecology of an organism provides a perspective linking behaviour in its environment (Little and Brewer, 2001). Behaviour is a sequence of quantifiable actions, operating through the central and peripheral nervous system (biochemical and physiologic processes). It is essential to life for feeding, reproduction and predator avoidance. In order to meet the challenge of surviving in a changing environment, behaviour allows the fish to adjust to external and internal stimuli. Adaptations to environmental variables are constantly adapting through direct interaction in the fish *Cyprinus carpio*. The stability for reproductive success efficiently exploit resources and define suitable habitats (Little and Brewer, 2001).

The behaviour and physiologic state of plasma and serum reflect in animals because they are the products of intermediate metabolism (Firat and Kargin, 2010). For metabolic activity energy precursor like protein, carbohydrates and lipid play a major role in fish practicably and quantitatively. In carbohydrate metabolism the serum glucose and glycogen utilization are affected by toxicant. This toxicant affects the tissue release and uptake of carbohydrate level and used as biomarkers under toxicant stress. The stress in fish due to toxicant appeared to be a sensitive indicator in the uptake of blood glucose and glycogen level in aquatic environment. Many investigators have reported alternations in blood glucose and tissue glycogen content under the stressful conditions may be of handling, forced exercise, thermal shock and contact with xenobiotics (Martin Deva Prasath and Arivoli, 2008). In aquatic toxicology, biomonitoring biochemical parameter is commonly used as a diagnostic tool for measurement. The exposure of nanoparticles affects the physiological and biochemical reactions and affects the endocrine tissues. These tissues incur by exposure of chemical stressors and maintain homeostasis for the growth of organisms. The growth of organisms by the measurement of hormonal concentrations in the blood may be used to gauge the impact of contaminants on metabolism, growth and reproduction. The ability of endocrine tissues responds to plasma hormone levels to their appropriate releasing factor. The hormones, the thyroid hormones such as thyroxine (T4) and triiodothyronine (T3) are most extensively studied group of stress-related hormones in fish (Brown *et al*., 2004). The regulation of endocrine organs in fish experiencing stress related, mainly with two principle neuron endocrine axes. Chromaffin cell axes with the catecholamines in the sympathetic hypothalamus, epinephrine and nor epinephrine as end products and the inter renal axis in pituitary hypothalamus–with hormone is its end product. Hormone influences an array of physiological parameters including carbohydrate, metabolizing and mobilization of amino acid and fatty acids from cellular stress, gluconeogenesis and plasma protein production (Van der Ven *et al*., 2006)

The physiological functions like growth, development and metabolism of vertebrates play an important role in ion regulation, energy metabolism, growth and reproduction (Bres *et al*., 2006, Powers *et al*., 2011). Silver nano particles affect the level of thyroid hormones and its level are demonstrated to be decreased (Deane *et al*., 2001) (Van der Ven et al., 2006). To assess thyroidal hormone status and for growth of fish thyroid hormones Triiodothyronine (T_3) and Thyroxine (T_4) in the plasma of fish has been used as suitable biomarkers. After exposures of silver nanoparticles to freshwater fish gill epithelium disrupts, thus epithelium permeability increases and hyperosmosis takes place in the surrounding water, and thus lead to a final significant decreased of ion concentrations, protein and plasma osmolality. In fish *Cyprinus carpio* exposure of silver nanoparticles causes significant alterations in plasma hormone concentrations and has been reported (Lavanya *et al.,* 2013).

Histopathology is an important biomarker in fish commonly observed in studies involving Ag NPs, with high ionic strength particularly when diluted in media (> 10 mM). This histology agglomerates the rate of degradation or cell uptake, and affects their bioavailability and internalizes the cell variables. The most important experimental parameters in vivo toxicological studies depend upon the source and type of AgNps in variation in particle size, shape and surface chemistry impacts on toxicity. It's necessary to analyze silver and AgNPs makes significant temporal changes during experimental trial. Kelly and Janz (2009) reported that histopathological lesions to cells and tissues reflect the concerted effects of multiple different mechanisms of action rather than only a few, as is typically the case with biochemical endpoints. Silver nanoparticles discharge in freshwater ecosystem through the routes of synthesis, production, transferring goods. Silver nanoparticles have been modelled differently along with the routes of silver (Blaser *et al*., 2011).

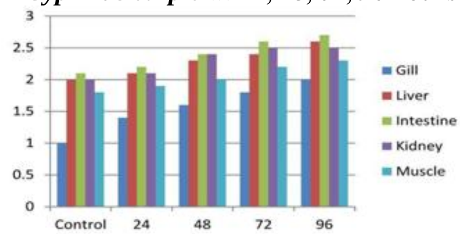
Ag NPs have noticeable toxicity against several cell lines as well as a number of aquatic organisms, but the mechanistic basis of these toxic effects is now an area of active research. To the people of India fish are the chief source of protein, for the survival of fish, water is an important component. The changes in water quality depends upon the extensive use of chemicals, organic enrichment of surrounding water by nutrients and solid wastes, current aquaculture practices, higher stocking densities into the system are the marked problems in water (Matos *et al*., 2006). Toxicity of silver nanoparticles in fishery water is the matter of investigation and it is a proven fact that how much amount can be used in fishery water depends upon the health and quality of cultured fish, it is worth asking whether the chemicals used in aquaculture practices, as well as the contaminants present in the surrounding waters, have a negative impact on fish health (Fernandes *et al*., 2008). Silver particles in aquatic environment is increased especially for the nonmaterial's concerned and only little data's are available on fish *Cyprinus carpio* relating silver nanoparticles. In ecotoxicity monitoring, the measurement of the mortality response after the exposure to nanoparticles could provide useful data for aquatic monitoring as a bioindicator. In the current study, exposure of silver nanoparticles on fish *Cyprinus carpio* may provide insights to the potential toxic effects of AgNPs on aquatic environments and introduce most toxicants material and the conventional median lethal concentration tests were conducted. The ecotoxicity of nanomaterials in fresh water ecosystems could be valuable in relation to aquatic nanoecotoxicology of fish *Cyprinus carpio*.

II. Materials And Methods

1. Bioaccumulation studies by the method APHA, 1998.
2. Bioassay Static flow methods APHA, 1985.
3. Glucose by O-Toluidine method (Cooper and Mc Danial, 1970).
4. Glycogen by Anthrone method (Samseifter *et al*., 1949).
5. Thyroid hormone by Thyroxine (T_4) Triiodothyronine (T_3) - (ELISA of hormones) using kits.
6. Histopathological studies by pears (1968), Roberts (1978) and Humason (1979) were followed for gill, liver and kidney.

III. Results

Fig 1. Represents the accumulation of silver nanoparticles in *Cyprinus carpio* at 24, 48, 72, 96 hours' concentration.



LC50 of silver nanoparticles for 24 hrs

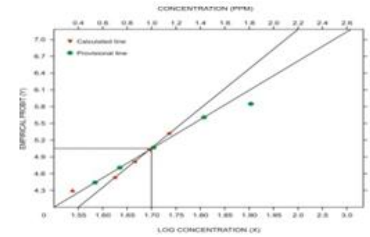
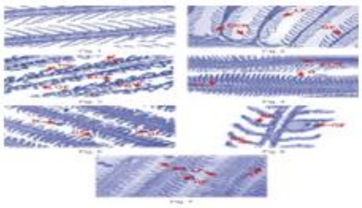
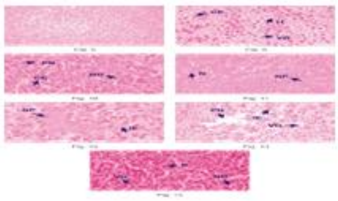


Fig 3. Effect of gills due to silver nanoparticles **Fig 4. Liver** **Fig 5. Kidney**





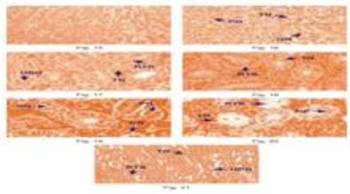


Fig 6. Plasma thyroxine (T4) exposed to AgNPs

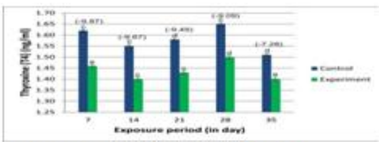


Fig 7. Plasma triiodotyhronine (T3) exposed to AgNPs

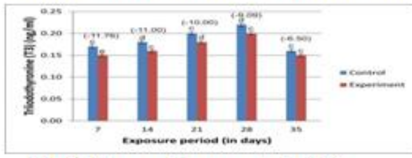


Fig 8. Plasma glucose to AgNPs

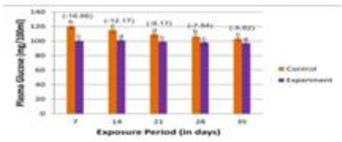
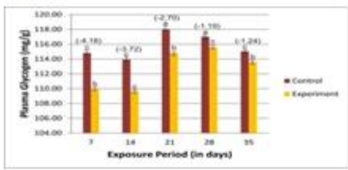


Fig 9. Plasma glycogen to AgNPs



IV. Discussion

In this study in all the parameters the experimental values were decreased when compared to the control except bioaccumulation studies. The nanoparticles accumulate in different organs like gill, liver, intestine, kidney and muscle and the changes were observed in fish *Cyprinus carpio* and this is due to disturbance of osmoregulation that cause injuries and reduce survival in freshwater fish. The bioassay determines the static flow methods were the acute, chronic studies are observed, the changes were noted and it is due to excess mucous all over the surface of the body, rapid opercular movements, floating upside down, and finally death occurs. In biochemical studies the glucose level decreased due to induction of hypoglycemia in the fish and glycogen content were evaluated and decreased due to the absence of metabolite named plasmatic pyruvate in liver and in hormone level the changes in the thyroid hormone such as triiodothyronine and thyroxine were observed and this is due to suppression of immune response. The histopathological changes in aquatic organisms especially in fish *Cyprinus carpio*, the effect of metal silver nanoparticles in the cells of gill, liver and kidney were observed and this were due to epithelial lifting, hyperplasia and hypertrophy of epithelial cells in gills, and in liver it might be due to distinctive lesions and the severity of the lesions, changes in hemopoietic tissues resulting severe necrosis in kidney..

Nanotoxicology is a branch of bionanoscience which deals with the study of nanomaterials and their impact on living organisms' threat to the environment and to human beings. Nanoparticles are small sized particles. In the aquatic environment nanoparticles depends on different types of factor such as organic matter, pH, composition and ionic strength. These small sized particles leads to a high volume surface ratio metals and other compounds which in turn leads to a lot of binding sites (Moore 2006). Accumulation of nanoparticles enters through the membrane and accumulates inside the cell and causes damage to the cell (Choi *et al*., 2008). Silver nanoparticles have been reported to have an effect on accumulation, DNA and development, reproducibility. In this study fresh water fish *Cyprinus carpio* showed effects on survival, embryonic growth and pigmentation at high concentration of AgNP which affects the swim bladder and larval swimming at low concentration of AgNP. Due to the exposure of silver nanoparticles neuro behavioral changes occur and this is the end points and those changes are different from Ag^+ (Powers *et al*., 2011).

The heavy metal silver nanoparticles accumulate in fishes in different organs. The term bioaccumulation is defined as the chemicals taken up by an organism either directly from exposure to a contaminated medium or by consumption of food containing the chemical. Accumulation of metals and metalloids is of particular value as it acts as an exposure indicator since metals are not metabolized. At some bioavailability all trace metals are toxic. Bioavailable toxic metal may come under selection for changes in one or more physiological processes, thus aquatic organisms are exposed to the rate of efflux of detoxification of accumulated metal into a relatively processing level. Half of the body surface areas comprise fish gills with an epithelial lifting in the environment. As results of this close association between the water and blood, the gills are strongly affected by environmental pollutants. Due to accumulation of these metals in gills alterations like epithelial lifting, hyperplasia and hypertrophy of epithelial cells, oxygen uptake is impaired (Fernandes and Mazon, 2003). Liver and intestine causes the metabolic problems. Bile is affected and digestion stagnation occurs in the liver and intestine. The accumulation of pollutants in bile indicates damage to the hepatic metabolism (Fanta *et al*., 2003).

In aquatic environment, many heavy metals are present in water. The toxicity of heavy metal poisoning is defined as, "functional or morphological change in the body is due to ingested, injected, inhaled or absorbed drug, chemical, or biological agent". The toxicity of metal silver is influenced by many factors like solubility, binding specificity to a biological site. Among metals, silver is considered as an important metal where silver to 100µm breaks to silver nanoparticles, used for treatments like argyrosis, curing of oncogenic gene cells. More than 1.0ppm of this metal is toxic to aquatic organisms especially to fishes. Silver particles in aquatic environment are based on their potential toxicity. In contrast, the affinity of silver for membrane and neuronal structures and the deposition of silver in an insoluble compound (Ag_2S) leads to the progression of clinical diseases like generalized argyria. Bluish-black pigmentation is observed in a tissue resulting from the deposition of an insoluble albuminate of silver is referred as argyrosis. It is a pathologic disease. In bulk form silver cause cronic toxicity to fish (Gulbranson, *et al*., 2000).

Bioassay studies are accepted as standard methods for assessing toxicity of chemicals (APHA *et al*., 1985). The aim of using bioassay in monitoring of environmental pollution is to establish a relationship between toxicity and concentration of pollutant being studied in the biotope; the toxic effects can be classified viz., effects that occur very quickly after a brief exposure to a chemical agent (acute) and those that appear only after repetitive exposure to the substances (chronic). Since fish are the chief source of protein to the people of India, Indian aquaculture plants are used for higher fish production by minimizing the area of cultivation and water usage. Toxicity of silver nanoparticles to fish is a proven fact but how much amount can be used in fishery water is the matter of investigation. Regarding the health and quality of cultured fish, it is worth asking whether the chemicals used in aquaculture practices, as well as the contaminants present in the surrounding waters, have a negative impact on fish health. In *Cyprinus carpio* the 24-hour nanosilver LC_{50} value has been found to be 1 mg/L^{-1} exposed to metal. Accordingly, it is clear that silver nanoparticles of various sizes and with or without different stabilization agents possess different levels of toxicity in different organisms, under different exposure times and conditions.

The recent study demonstrates that, nanosilver particles reduces swimming activity in fish, may be due to impaired respiration. AgNPs cause respiratory toxicity in fishes and are particularly vulnerable to nanoparticles. Fish internal organs are sensitive to nanoparticles (Sung *et al*., 2008). In the aquatic environment, the concentration of silver nanoparticles from consumer products is predicted to be about 0.01 ng L-1 (Tiede *et al*., 2009). The expected extensive uses of nano silver undoubtedly increase the discharge of nano silver to the aquatic environment. Respiratory disturbance is caused by various nanoparticles, Titanium dioxide nanoparticles in rainbow trout (*Oncorhynchus mykiss*) (Federici *et al*., 2007), Single walled carbon nanotubes elevated ventilation in rainbow trout and surface ventilation is induced by silver nanoparticles exposure in *Cyprinus carpio* (own observations). The nanoparticles of copper also act on the gills in *Zebra fish* (Griffitt *et al*., 2007). The high percentage of silver metallic form characterizes nano-silver products. It is noticeable that ionic silver becomes silver chloride in the stomach or blood stream and the solubility of silver chloride is low. The silver chloride is less effective when compared to metallic silver. The metallic particles can survive in the body and the hydrochloric acid of the stomach to remain effective inside the body. On aquatic systems like ocean, lakes, rivers, ponds silver has adverse toxic effects unexpectedly. In fresh water fish, the acute toxicity of silver appears to be caused solely by ionic Ag^+ interacting in the gills, affecting basolateral Na^+, K^+, -ATP ase activity. Active Na^+, and cl^- uptake is inhibited by disruption of this enzyme and osmoregulation by the fish. It is indicated that silver may be adversely affecting the health of the estuarine fish by recent studies with macro invertebrates.

Most of the silver is in the form of metallic silver nanoparticles and the remaining silver is in ionic form. The total surface area of the silver exposed in solution is minimized because of the small size of the particles, resulting in the highest possible effect per unit of silver (Alt *et al*., 2004). A very small concentration of silver in nanosilver provides greater effectiveness inside the body than silver solutions in the colloidal form. A potential cytotoxic effect can be showed by silver nanoparticles on mammalian germ line stem cells. The cytotoxic effects of silver nanoparticles on mammalian germ line stem cells were investigated in the experimental case study of Braydich – Stolle *et al*. (2005). The effect on cell morphology, mitochondrial membrane and function leakage was taken into consideration. In this study silver nanoparticles at 10 ng/ml, and above concentration showed dramatic changes like necrosis and apoptosis of cells. The mitochondrial function and cell viability was drastically reduced by silver nano particles at 5-10 ng/ml. In the literature of Drake *et al*. (2005), it was mentioned that colloidal silver protein had been used for allergy cold medication in eydrops to alleviate soreness (Loeffler and Lee, 1987) and for the treatment of various ailments. Discoloration in the finger nails, octuar agyrosis and generalized argyria is caused by the prolonged usage of this silver protein.

Several organs of *Cyprinus carpio* fish which was exposed to nanosilver did not reveal nanosilver desposits in the dark field of micoscopy, In the aquatic environment the concentration of nanosilver used in the present study was higher than the estimated concentrations of silver. Due to disruption of membrane transport processes the toxicity of silver is hypothesized, which disturb Osmoregulation, finally lead to cell death. The mechanism of action of silver to adult *Cyprinus carpio* was investigated. This action leads to increase of salinity, cl^-, in water occurred to increase the toxicity. Ag^+ binds to the gill surface and interferes with Na^+/cl^- uptake, might leads to decrease in plasma Na^+ and cl^- concentrations and fluid balance. Silver can be taken up through different ion channels, cell surface and ligands. (Ratte, 1999). Bioaccumulation and uptake rate of silver ions, Ag^+ have been reported to have high bioconcentration factors, (<10.5µg/mL). Low concentration of free Ag^+ ions in water is due to sulphide complexes. In aquatic organisms' up take of silver nanoparticles through gills, epithelia, membrane and surface. At cellular level, intake of nanoparticles occurs via endocytosis. For several aquatic organism's silver ions was found to be more toxic. (Navarro *et al*., 2008.).

Silver ions of the nanoparticle suspension where nanoparticles inherent toxicity. Fish exposed to silver nanoparticles shows extra variations of blood. Increased mucus secretion has been noticed in *Cyprinus carpio.* Through gill the mucus production is increased to trap and transport this toxicant away from the gills. This study proves that silver nanoparticles reduce the ability of fish to take oxygen from the water during progressive oxygen depletion, which leads to increased vulnerability to hypoxia. In the context of biosensing and biological imaging strong optical properties of AgNps can be found useful. This offers good opportunities to study nanoparticles uptake and biodistribution, in vitro as well as in vivo studies (Seok-Jeong oh *et al*., 2014). AgNPs can support a variety of bio analytical sensing and imaging modalities and localized surface plasmons that leads to resonant light scattering and other optical properties (Yi Zhang *et al*., 2014). Recent application of AgNps include the detection of biomarkers in Alzheimer's disease (Chao-Hung *et al*., 2014), the targeted imaging of cancer cells (Liya Guo *et al*., 2013).

The Plasmon-enchanced optical activities of AgNps enable for evaluating their eventual degradation. Cell death through oxidative stress-related mechanisms significantly increases by AgNPs which results in DNA damage in animal cells. In fish embryos, larvae and on adult fishes harmful effects and cytoxicity is showed by AgNps. The toxicity of silver nanoparticles in fish *Cyprinus carpio* species at early-life stages were investigated. The results suggested that AgNPs may have toxic potential toward *Cyprinus carpio* and AgNPs-induced mortality might provoke higher-level consequences, which could comprise a contribution to the knowledge on the aquatic toxicity of AgNPs on aquatic ecosystems. However, further research on the mechanism behind AgNPs-induced damage and mortality based on the ecotoxicity of AgNPs in *Cyprinus carpio*. Based on the obtained results of this study, it is suggested that small-sized nanosilvers are more active to exert toxicological or biological responses and they induce mortality responses by repeated water exposure.

Analysis of blood chemistry by fish physiologists can provide important information about the function of organs in fishes specifically to detect and assess the metabolic disturbances in aquatic environment and aquatic ecosystems. Plasma and serum reflects the physiologic state of animals because they are the products of intermediate metabolism (Firat and Kargin, 2010). Fish physiologists make use of blood chemistry normal value indices for evaluation of fish stress responses, nutritional condition, reproductive state, tissue damage due to handling procedures and health status (Congleton and Wagner, 2006). In blood, hormones are measurable target tissues where silver nanoparticles act on and effects on osmoregulation, ion regulation or water change across gills, kidney intestine and skin in fish and its secretion may be subjected to complex feedback. In fish *Cyprinus carpio*, alterations of plasma thyroid level were observed to environmental nanoparticles (Power *et al*., 2011). Silver nanoparticles disrupts thyroid axis and may seriously compromise normal development, differentiation, growth and reproduction in many fishes. In response to developmental state and age, natural variation in thyroid status and the effect of silver nanoparticles have been demonstrated (Suchiang *et al*., 2001).

They regulate many metabolic processes and are paramount in early development, thyroid hormones play role in growth and reproduction. THS (Thyroid hormone) play crucial role in metabolic process and are essential for normal growth, differentiation and development of vertebrates (Morgado *et al*., 2007). In reproduction and development, TSH implicate in fish. During metamorphosis on larval transition increased levels are reported and high concentrations are present in fish eggs. In homeostasis of plasma THS, THS are lipophylic and can rapidly diffuse into tissue and for this reason binding to transport proteins play an important role. Increased in circulating T_3 were correlated in the T_3 – supplemented fish with a decline in plasma T_4. A decrease of the thyroid gland activity is indicated by this diminution, which might account for a decline in TSH secretion. Moreover, regulation of TSH secretion by the TH has been demonstrated in the *Colo Salmon*. Due to the change in equilibrium between T_3 and T_4 level is elevated and maintained by peripheral monodeiodination processes, causing a backing up of plasma T_4 levels. Another possible explanation is that the very high T_3 levels in elevated measured T_4 filters as a result of interference of T_3 in the T_4 assay. A hyperactivity of the thyroid follicles is induced by silver nanoparticles, which results in a decrease of the T_4 concentrations, the T_3 concentration, which is regulated by the deiodination in peripheral tissues, is not affected in *Cyprinus carpio* (Schitzler *et al*., 2008).

Silver nanoparticles (AgNPs) are commonly used for solar energy absorption, spectrally selective coatings and acts as chemical catalysts especially for antimicrobial sterilization made them one of nonmaterial's in many applications (Pal, *et al*., 2007). Open access literature regarding the toxicity of nanoparticles (Nps) is still emerging and gaps still exist in our knowledge of this area. Biosystem may have serious ecological consequences and affect human and animal health due to the presence of Nps (Handy *et al*., 2012). Chronic inhalation and consumption of Nps are the most dangerous implications (Moore, 2006). This implication of nanoparticles leads to the histopathological changes and aggregation in the aquatic environment. The concentration of various nanoparticles for fish ranged from 100 g L^{-1} to 1 mg L^{-1} , while the lethal concentration of nanoparticles reaches the milligrams per liter range. The concentrations of Nps in surface water range from nanograms per liter to low micrograms per liter which affects the organs like the gill, liver, kidney (Handy *et al.* 2012). Up take of silver ions ruptures the permeability of membrane and destroy cell wall which could cause cell lyses and silver ions also inhibit different important cycles (S, N and P).

Fish exposed to AgNPs showed similar pathological changes: irregular structure and pyknotic nuclei of epidermis, aplasia and/or fusion of lamellae, telangiectasis, epithelial necrosis and lifting of the gills, dilation of sinusoidal space, overfilled blood vessels, and pyknotic nuclei of the liver. The tissues and organs of fish are affected by silver iron exposure leads to a slight increase in mortality. As mortality is the most obvious sign of progression of serious pollutant at the organism level, the impairment role of survival due to AgNPs exposure may be considered a consequence of a serious progression of population mortality. It has been confirmed that AgNPs are translated into blood circulation and accumulated in organs like gill, liver and kidney and causes organotoxicity, and histopathological test were examined and finally death occurs. It was concluded that silver nanoparticles at 10 µg /ml, and above concentration showed dramatic changes like necrosis and apoptosis of cells. The concentrations of nanosilver used in the present study in *Cyprinus carpio* are higher than the estimated concentrations of nanosilver in the aquatic environment. Prolonged usage of this silver protein as a medication caused discoloration in the fingernails, occurs agyrosis and damages the cells.

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Thangam Y, et. al. "Review of Silver nanoparticles in Freshwater fish "Cyprinus carpio"." *IOSR Journal of Environmental Science, Toxicology and Food Technology (IOSR-JESTFT)*, 14(7), (2020): pp 28-36.