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CADMIUM INDUCED HISTOPATHOLOGICAL ALTERATIONS AND IN *CLARIAS BATRACHUS* OF MEERUT REGION

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ABSTRACT

The present work is conducted to evaluate to pathological effect of heavy metal cadmium sulphate in liver of edible fish, *Clarias batrachus*. Preliminary toxicity tests were conducted to figure out the suitable ranges to be used in the final trials of lethality test. Static bioassays were conducted in the laboratory for 96 hours to determine the median lethal dose of toxicant. The (96-h) Lc-50 for Cadmium sulphate was calculated to be 13.8 mg/l for the present study. $1/10^{th}$ (1.38 mg/l) of this concentration was used for toxicity tests concentrations . Oedema of hepatocyte with blood congestion in sinusoids was observed after 15 days of chemical exposure. Cytoplasmic vacuolization, pyknotic nuclei, dilation and congestion in blood vessels were noted after 30 days of exposure period, while 45 days of exposure period showed degeneration in the hepatocytes with focal areas of necrosis pyknosis, karyolysis, karyorrehexis with portal tract revealing marked degenerative changes. 60 days of exposure period showed increase in hepatocyte cytoplasmic, pyknosis and hypertrophy of Kupffer cells.

KEYWORDS: karyolysis, pyknosis, karyorrehexis, vacuolization, cadmium sulphate, *Clarias batrachus.*

INTRODUCTION

Fish is consumed as food for human being not only in India even for the whole world. This is considered second most important food in the world after rice as it is most nutritious protein

source for human being which fulfill approximate all the nutritious demand. Increasing level of pollution day by day affects the aquatic ecosystem, production and health of the important food fishes, so it becomes too important to maintain their safety and quality at proper interest to retain the health and production of fish. According to the report of FAO, 2020 global fish production is cited to be 179 million tonnes in 2018. Of the total production around 156 million tonnes were used as human food consumption which is about an average of 20.5 kg per capita.

In India increased activities of industrialization such as textile, chemicals, synthetic goods, petrochemical and pesticides etc. discharge their chemical hazardous wastes in the rivers and sea which affect the life of important edible fishes. Heavy metal such as Lead, Mercury, Arsenic and Cadmium are the most hazardous metals that are poisoning the aquatic ecosystem. These are very toxic that get stored, and assimilated by the living organism through the food chain by the process of biomagnifications resulting in the pathological alteration and cause damage of the tissue **(Pigott and Tucker1990; Ruiter 1995).** Heavy metals gets dissolved in water and therefore absorbed by the aquatic organism and get transfered to higher animals through the food chain by the process of bioaccumulation altering the normal physiological process and causing damage to the tissue of organism **(Malik and Maurya 2014).**

Cadmium, which is a blue- tinged, silver-white, lustrous metal having melting point 321°C with boiling point 765°C, its atomic number 48 with 112.4 atomic weight is insoluble in water but it is seen its Sulphate and Chloride salt are freely soluble in water **(Windholz *et al.*, 1976)**. Natural and anthropogenic sources such as volcanic activity, forest fires, usage of phosphate fertilizer, Cigarettes smoking, use of paints, plastics, Nickel-Cadmium batteries and automobiles industries etc. have contributed to the entry of Cadmium into the animals and food chains **(WHO 1992; Okada *et al.*,1997; Kumar *et al.*, 2007)**. In unpolluted water natural Cadmium concentration generally is less than 1µg/l or 1 part per billion (ppb) **(Nordberg *et al.*, 2007). Nida *et al.*, 2018** studied that the Cadmium pollution in aquatic water which is found higher than the WHO permissible limit in some western region of U.P. Comparative study of acute toxicity test of 63 heavy metals, Cadmium is the most toxic metal in unpolluted water, it's concentration is generally less than 1µg/l or part per billion (ppb) **(Nordberg *et al.*, 2007; Borgmann *et al.*, 1999).** Cadmium gets biomagnified in the food chain and can accumulate in the human. It enters the fresh water due to various anthropogenic

activities and it is uptaken by the phytoplankton and Zooplankton and gets passed through the food chain and accumulates in their gills, liver and kidney of the fishes **(Eisler 1985; Nordberg *et al.*, 2007; ATDSR, 2008).**

Fishes are the main target organism to study the implication of chemical on aquatic pollution for any toxicological study because of its direct exposure to water bodies as it is easily connected to humans in the form of food chain **(Au 2004).** In aquatic ecosystem fishes are the important biological indicators of aquatic pollution. Alterations of antioxidant and biochemical changes are important parameters for toxicity study **(Bashir and Zuhair 2008).** Cadmium accumulates in the kidney, liver and gills of fresh water fish in the presence of Cadmium binding molecules called M\etallothioneins (**Chowdhaury *et al.*, 2004; Dallinger *et al.*, 1997).**

EXPERIMENTAL DESIGN

Present investigation was conducted on catfish, *Clarias batrachus*. Experimental protocols were divided into following heads.

Experimental fish: *Clarias batrachus*

Experimental chemical- Cadmium Sulphate

All these parameters were evaluated after control, 15, 30, 45 and 60 days of exposure period according to experimental design.

Experimental groups: The fishes were feed with basal and supplemented diet @ 10% of body weight in control and treated group of fishes. Healthy living 30 specimens of teleost, *Clarias batrachus* were collected from local fish market of Meerut, Hastinapur and nearby areas.

HISTOPATHOLOGICAL STUDIES

After the completion of experimental exposure time, the fishes were dissected and liver, gills and kidney were removed immediately from control and treated groups for histopathological studies. All the tissue were wiped thoroughly by using the blotting paper to remove excess amount of blood and other body fluid and fix for 8 hours in alcoholic Bouin's fluids. Gills were decalcified with 8% Formic acid and Sodium Citrate solution for six hours. After the fixation the tissue were dehydrated with different grade of alcohols and cleaned with xylene. The tissue were embedded in the paraffin wax at 60°C and prepared the block by using the

"L" piece. 5mm section was cutting and stained with the Eosine and Haematoxylene as per protocol. Histopathological slides were examined under light microscope and the microphotographs were taken at high magnification for comparative study among the groups.Group I served as control and experimental the fish, *Clarias batrachus* feed with basal diet. Histopathological changes in T.S. of Liver of control fish *Clarias batrachus* (Fig. No.1) The liver of the fish *Clarias batrachus* in control group showed normal polygonal shaped hepatocytes. Each hepatocyte has a well shaped nucleus with central neucleolus and granulated cytoplasm. T. S. of liver of the normal fish form a rather cord like pattern which are arranged around tributaries of the hepatic vein. A large number of well arranged blood sinusoids were observed which separates the hepatic cord from one another. Bile caniculi between the two layers of cells form network of the ducts eventually draining into canal of herring which entered in portal canal and merged into fine branches of bile duct the surface of the liver is covered by peritoneal layer of mesothelium. The layer is underlined by dense connective tissue layer called Glisson capsule. The portal tract consists of one portal vein, hepatic artery and bile duct. The wall of the sinusoids consists of endothelial cell with distinct nucleus. Histopathological changes in T.S. of Liver of fish, *Clarias batrachus* after 30 days of post treatment period treated with Cadmium Sulphate and basal diet (FigNo. 2) In fish exposed to cadmium sulphate showed marked swelling of hepatocyte swelling with blood congestion in sinusoids after 15 days of chemical exposure. Cadmium induced hepatocyte swelling was the prominent alteration noted at this stage. Histopathological changes in T.S. of Liver of fish, *Clarias batrachus* after 30 days of post treatment period treated with Cadmium Sulphate and basal diet (FigNo. 3) After 30 days of post treatment period, treated with Cadmium Sulphate, liver of the fish, *Clarias batrachus* showed some pathological alteration such as infiltration of leucocyte around the central vein and deshaped hepatocytes. A large amount of cytoplasmic vacuolisation was noted in the hepatocytes after this period of time. Hepatic cells suffered from fatty acid degeneration, enucleation in the hepatocytes with cellular degeneration were observed in the liver of fish. The Inter hepatic blood vessels were dilated and congested with blood. After this exposure of period hepatocytes showed inflammation with cellular oedema.

Histopathological changes in T.S. of Liver of fish *Clarias batrachus* after 45 days of post treatment period treated with Cadmium Sulphate and basal diet. (Fig.No. 4) After 45 days of post treatment period hepatocytes were showed degenerative changes like vacuolisation with enucleation. A large number of cells were noted with the pyknosis of nuclei. After 45 days of

post treatment period with Cadmium Sulphate, degeneration of the hepatic cells and nucleus were observed. Pyknosis, Karyolysis and Karyorrhexis were also observed in the nucleus of hepatocytes. Dilation of blood sinusoids with focal necrosis, dilation and thrombosis formation in central vein dilation with vacuolar degeneration showed in the hepatocytes with the aggregation of inflammatory cells and cellular oedema.

Histopathological changes in T.S. of Liver of fish, *Clarias batrachus* after 60 days of post treatment period treated with Cadmium Sulphate and basal diet (Fig.No 5) After 60 days of post treatment period with Cadmium Sulphate the T.S. of liver of fish, *Clarias batrachus* noted with the large number of deshaped and degenerated hepatocytes with enucleation. Disorganization of hepatic cord and damaged cell membrane were noted after, 60 days of post treatment period with Cadmium Sulphate. Large number of pyknosis, karyolysis and karyorrhexis were seen in the hepatocytes. Degenerated changes such as cloudy swelling and necrosis were noted in the hepatic cell after this duration of time dilation of blood sinusoids along with hypertrophy of cells were also observed in the liver cells. Nuclei of hepatocytes frequently exhibit necrosis with cellular oedema.

DISCUSSION AND CONCLUSION

In our study the liver of control group of fishes showed normal histological structure without any pathological alteration. It is shown that liver is made up of hepatocytes that form cord like structure, separated by sinusoids. Hepatocytes are polygonal in shape with a central spherical shaped, densely stained nucleolus. In group II the liver of Cadmium Sulphate treated fish caused histopathological alteration after 30 days with increased vacuolisation in the hepatic cells. These alterations were more severe after 45 and 60 days exposure of time such as pyknosis in the nucleus of hepatic tissue, dilation of blood sinusoids and enucleation with cytoplasmic degeneration. Similar results have been reported by **Cengiz *et al.*, 2001 and Capkin *et al.*, 2006** in their studies. Hepatocyte vacuolisation is associated with the inhibition of protein synthesis, energy depletion, disaggregation of microtubules or shift in substrate utilisation **Hinton and Lauren 1990**, while cellular swelling occur either directly by volume regulating ATPse or indirectly by disruption of the cellular energy transfer processes required for ionic regulation **Hinton and Lauren 1990.** According to research by Zulkipli et al. (2021), exposure to heavy metals caused a number of pathological changes in different fish livers, including hyalinization, hepatocyte vacuolation, cellular expansion, and blood channel congestion. Hepatic cell degeneration, congestion, and haemorrhages were all

seen during the histopathological analysis of the liver tissues. Cadmium typically accumulates at higher concentrations in internal organs, particularly the gills (the primary site of waterborne uptake) and the kidneys (a major site for detoxification and sequestration) (**Lee *et al.*, 2024; Liu *et al.*, 2021**). While muscles—the edible part of the fish—often show lower cadmium levels compared to organs like the gills or liver, they are still a significant pathway for human exposure **(Helczman *et al.*, 2025; Liu *et al.*, 2021).** Cadmium exposure induces oxidative stress by generating reactive oxygen species (ROS) and suppressing the fish's natural antioxidant defense systems (e.g., superoxide dismutase and catalase) **(Yu *et al.*, 2024**). As fish occupy higher trophic levels, cadmium can biomagnify, posing risks to human consumers **.**Chronic human exposure through the consumption of contaminated fish is linked to serious health conditions, including renal dysfunction, bone demineralization (osteomalacia), cardiovascular disease, and increased cancer risks Cadmium is found accumulated in liver of fishes in high concentrations when the fishes are sacrificed after 45, 60 days and it is noted that the normal colour of liver was lost and it appeared black in colour. Liver is the target organ where accumulation of cadmium occurs.Various pathological changes in liver tissues including engorgement of blood vessels, congestion, vacuolar degeneration of hepatocytes, necrosis and fatty changes in the hepatocytes.

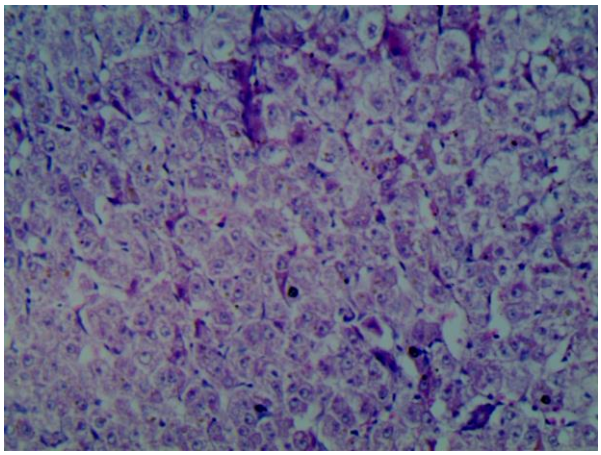

Fig. 1: Microphotograph of T.S. of Liver of control *Clarias batrachus* H.E X 400.

T.S of the Liver of the control group fishes showed normal histoarchitecture with the compact hepatic tissue and centrally placed nucleus in the hepatocytes. Cadmium Sulphate treated fishes in Group II showed some histopathologcal alteration as vacuolisation after 15 days of exposure these changes increased with prolonged exposure to heavy metal such as increase in hepatocytes, pyknosis, Karyolysis, karyorrhesis in the nucleus and necrosis in the hepatic tissue after 30 days post treatment period. These histopathological lesions were more

severe depends upon dose and time dependent manner after 45 and 60 days post treatment period Cadmium Sulphate treated fishes.This study is indicated prolonged exposure to heavy metal causes detrimental effets in liver pathology of *Clarias batrachus.*

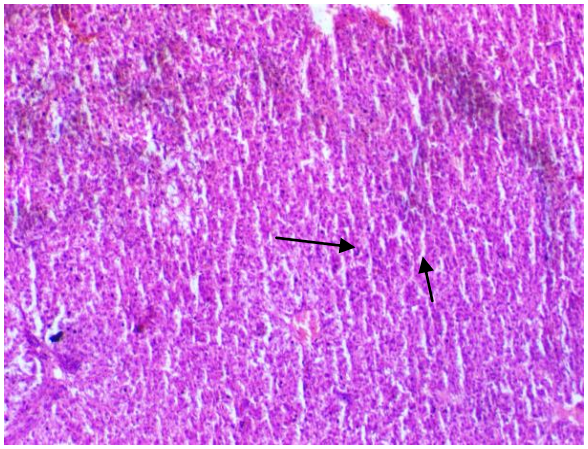

Fig. 2: Microphograph of T.S of Liver of *Clarias batrachus* after 15 days showing (←) nuclear hypertrophy, (→) cellular hypertrophy , (↑) cytoplasmic vacuolisation H.E X 400.

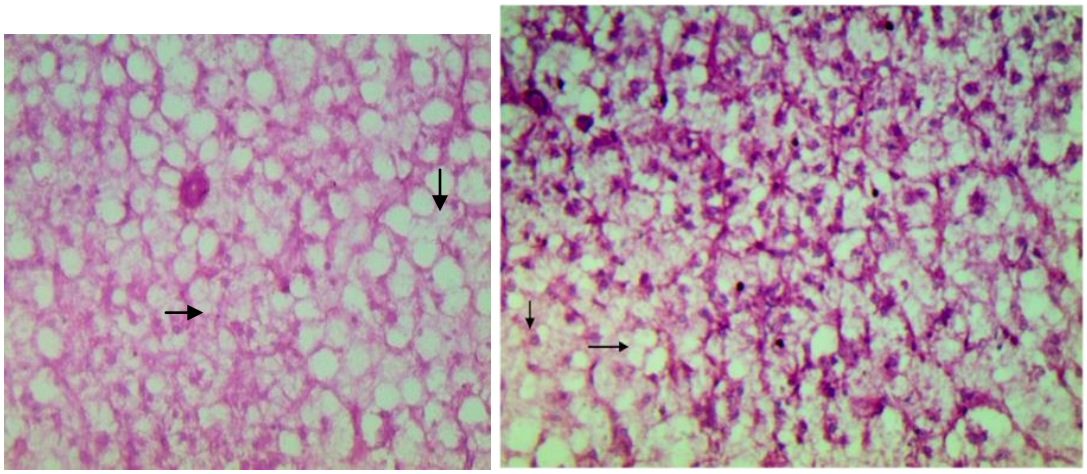

Fig 3: Microphotograph of T.S. of Liver of *Clarias batrachus* after 30 days exposure of Cadmium Sulphate and Basal diet exhibiting cytoplasmic vacuolization(→), karyolysis (↓), pyknosis, cellular degeneration with dilation of sinusoids H.E X 400.

Fig 4: Fig 13: Microphotograph of T.S. of Liver of *Clarias batrachus* after 30 days exposure of Cadmium Sulphate and Basal diet exhibiting cytoplasmic vacuolization(→), karyolysis(↓), pyknosis, cellular degeneration with dilation of sinusoids H.E X 400.

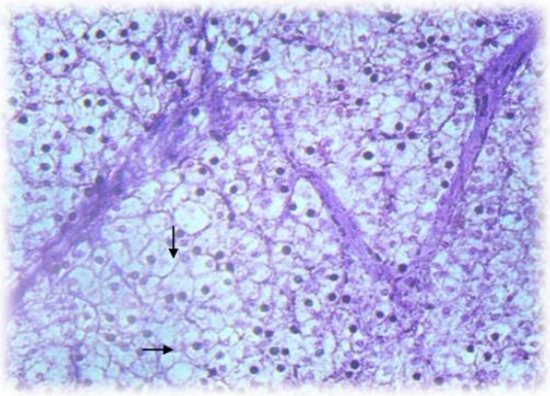

Fig 5- Microphotograph of T.S of Liver of *Clarias batrachus* after 60 days of exposure to cadmium sulphate exhibiting (←) pyknosis, (↑) Karyohexis, (↓) Karyolysis, (→) coagulative necrosis, cytoplasmic vacuolization, necrosis, dialation of blood vessels, hyperplasia and hypertrophy of hepatocytes, H.E X 400.

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