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Histological Changes in *Tilapia* Exposed to Bisphenol A (BPA) Compound

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Abstract

Present investigation deals with the effect of the *Tilapia* fingerlings were exposed to single concentration of Bisphenol A for 28 days. Observations were made from 7-28 days to study the structural, behavioural and internal pathological conditions. Analyses of different parameters were carried out in the fish exposed to SLC of toxicant on 7^{th}, 14^{th}, 21^{st} and 28^{th} day of experimentation. Analyses of histopathological studies were carried out from 7-28 days of treatment in the different experimental groups concerned. The results of observations and analyses are given below in detail.

Keywords: Tilapia, Bisphenol A, histopathology

1. Introduction

Waterbodies are a major sink for industrial, domestic and other anthropogenic compounds (Canli *et al*., 1998). The aquatic pollution has far reaching impacts on organisms in the recipient environment. In recent years, BPA is extensively used for aquatic toxicity testing because of its adverse effects on wild life, especially fish. Fish are extensively used to determine the health of aquatic systems because their biological responses serve as biological markers of environmental pollution. Bisphenol A ($C_{15}H_{16}O_2$), an organic compound having two phenol functional groups is used to make polycarbonate polymers and epoxy resins, along with other materials employed to make plastics. The final products of bisphenol A has been found in some of the domestic materials such as adhesives, protective coatings, powder paints, automotive lenses, protective window glazing, building materials, compact disks, optical lenses, thermal paper, paper coatings, as a developer in dyes, encapsulation of electrical and electronic parts (US Environmental Protection Agency, 1986). The chemical structure of bisphenol A is similar to the estrogenic compound thus raising concerns in recent years. BPA issued in the production of epoxy resin lining of food and beverage containers (Staples *et al*., 1998), polycarbonate plastic (Vom *et al*., 2009), as a constituent of dental sealant (Olea *et al*., 1996; Vandenberg *et al*., 2009), as a flame retardant precursor and also used in the production of thermal papers and carbonless copy (Suzuki *et al*., 2000; Debenest *et al*., 2010). Several studies suggest that BPA cause acute, short-term and sub-chronic toxicity (Tyl *et al*., 2002; Tyl, 2008). Bisphenol-A cause tissue injury by forming reactive oxygen species (Kabuto, 2004; Hassan *et al*., 2012; Aboul *et al*., 2015) Grass carp (*Ctenopharyngodon idella*) is a cosmopolitan species. Bisphenol A is one of the highest volume chemicals produced worldwide and its demand is increasing due to the ever-increasing demand and production of plastic products. Bisphenol A is a multipurpose compound that has been widely used in almost all modern industries. It was first synthesized in 1891 and now the current production is estimated at about 4 billion kilograms per year globally (Environment Canada Report, 2009). The chemical structure of bisphenol A is similar to the estrogenic compound diethylstilbestrol and its potential therapeutic estrogenic property was first investigated in 1930s. Bisphenol A, an environmental contaminant have been widely used as a monomer in the manufacture of polycarbonate plastics and epoxy resins where it has also been incorporated into a variety of everyday domestic materials. Ongoing debates in both scientific and common community about the potential harmful effect of bisphenol A and its bioaccumulation in human. One of the literatures clearly demonstrates that bisphenol A likely bio accumulates to some degree in humans where it retains in adipose tissue and excrete a little through sweat and urine mechanism by which humans are exposed to bisphenol A is through leaching from plastic products. In one of the multi-generation breeding studies on medaka fish, showed that incorporation of bisphenol A into adult fish found rapid excretion of the compound but on the other hand there was no such mechanism to excrete the incorporated bisphenol A from the eggs (Takao *et al*., 2008). One of the studies in our laboratory have proved that bisphenol A exposure increased production of oxygen free radicals and destruct the normal architecture of gill in Oreochromis (Chitra

and Sajitha, 2014). Although numerous literatures has considered the effects of anthropogenic pollutants on different fish behaviours, interbreeding and hyperactivity

1.1 Histopathology

Fish as inhabitant of aquatic system cannot avoid the inimical effects of the pollutants. A set of biomarkers is generally used to evaluate the biological effects of pollutants. Such biomarkers act as an early warning of a specific detrimental biological endpoint. Oxidative stress and histopathologic biomarkers are used in ecotoxicology (Pandey *et al*., 2003). Histopathology of fish tissues is a reliable monitoring tool, which allows the assessment of the environmental stressor's effects. It is one of the most reliable indicators of the health impairment induced by the anthropogenic stressors in aquatic organism (Fernandes *et al*., 2008; Leonardi *et al*., 2009). The liver is associated with detoxification and biotransformation processes, and due to these functions combined with its location and access to the blood supply, it is one of the organs most affected by water contaminants (Camargo and Martinez, 2007; Mohamed, 2009). Fish liver is a good indicator of aquatic environmental pollution, where one of the important functions of the liver is to clean the pollutants from the blood coming from the intestine. Also, it is the organ most affected by environmental contaminants in water, leading to histopathological changes in liver. However, kidney is a vital organ of body and its function is to maintain the homeostasis. It is not only involved in removal of wastes from blood but it is also responsible for selective reabsorption, which helps in maintaining volume and pH of blood and body fluid and erythropoieses. Since a large volume of blood flows through the kidney, hence, it is a suitable organ for histological examination where lesions found in this organ can be useful as signs of environmental pollution. Sublethal concentration of Chlorpyrifos produces large histopathological alternations in the kidney of treated fishes (Nazia Khatun *et al*., 2016). Gills are sensitive organs which are easily damaged by numerous pollutants, even at low concentrations (Karlsson, 1983). The histological results observed in all the tissues of *C. carpio* in the present study indicate that sub lethal concentrations of Pb caused moderate to severe alterations in gills structure, which are an important organs performing vital function like respiration, detoxification, osmoregulation, etc. The exposure of fish to various biotic and abiotic stressors during several years through their lifespan can cause remarkable anomalies especially hyperplasia and related lesions like fusion of adjacent lamella (Mabika and Barson, 2013). Fish muscles are commonly analyzed for bioaccumulation of such toxic metals and pathological changes caused by it. These studies have been done for various reasons; many of them concerning food safety and public health interests where muscle tissues are generally the major edible portion of the fish. following bisphenol A exposure was well studied in zebrafish (Saili *et al*., 2012).

Histological study of muscle tissue of catfish (*C. batrachus*) exhibited prominent alterations like degeneration of muscle fibres and many dystrophic changes alterations in muscle tissue of *C. batrachus* may probably be due to significantly high concentration of chromium and their accumulation beyond the prescribed limit in the muscle tissue (Kaur *et al*., 2018).

2. Materials and methods

2.1 Fish stock selection, feed preparation and feeding

Tilapia fingerlings of the same size of a given season, and relatively of uniform size in the range of 10 to 12 cm and weighing 6-8 gm were procured from kurattur lake, chennai. The fish, after conditioning, were oxygen packed in tins and brought to the lab. They were slowly released into tanks, half filled with bore water and seasoned over night. These were maintained in stocking tanks, where the fish were quarantined and acclimatized for four day**.** The fish feed was prepared with rice bran, groundnut oil cake, tapioca powder and mineral mixture (Radhaiah, 1982). Groundnut oil cake was soaked in enough distilled water and minced thoroughly before mixing with rice bran, tapioca powder and mineral mixture. After thorough mixing, the contents were steam cooked in autoclave at 15 psi for 15 minutes, so as to sterilize the mixture. Pellets were prepared by using a hand mincer and shade dried at room temperature (31^0C-33^0C) for 24 hr and later, in a hot air oven at 60^0 to 80^0C for 48 hr. After enough drying, the pellets were stored in air tight containers. The fish were fed daily with pelleted feed at 5% body weight in two split doses, in the morning and evening. Feeding was started one day after the fish were stocked and stopped 24 hr prior to experiment.

2.2 Maintenance of fish

All the fish were maintained in the glass aquaria of the size 1'L x 2'B x 1'H throughout the period of experimentation. The tanks were disinfected with potassium permanganate thoroughly, before and after use. These tanks were filled with known volume of water per fish (30 litres for 10 fish) and covered with nylon mesh to prevent the mosquitoes breeding in the tanks and also to restrain the fish jumping out. During the period of experimentation, the room temperature fluctuated from 30-32^0C. The water used for the experiment had dissolved oxygen content of 4.4 – 4.8 ml/l and salinity of 0.82 – 0.84ppm. The pH of water was in the range of 7.2 to 7.4.

2.3 Experimental fish

Healthy fish without any observable pathological symptoms were chosen for the experiments. Fish were divided into two groups of ten, where one group as control and another group exposed with Bisphenol A

with the concentration of 1mg/L. The Bisphenol A treatment level was based on the 96hr LC_{50} of the former compound in *O. mossambicus*, which was previously determined to be 10mg/L by Chitra and Sajitha (2014). The following parameters have been studied in the untreated control fish, as well as the different experimental groups of fish treated with the toxicants. For biochemical studies, four different tissues muscle, liver, brain and kidney were dissected out carefully and weighed using K-Roy Single pan electrical balance. The dissected tissues were kept in an ice box till taken out for homogenization. Biochemical studies were observed in 7^{th}, 14^{th}, 21^{st} and 28^{th} days.

2.4 Histological studies

Generally, most of the histological studies are made on the dead cells or tissues. For microscopical studies, cells or tissues have to pass through the process such as fixation, dehydration, embedding, sectioning and staining (Gurr, 1959).

2.5 Fixation and embedding

The term fixation means to immobilize. The fixing solution performs the following functions. It prevents bacterial decay and autolysis of the cells, renders the component of the cell stable, reduces the visibility of different cellular components and prepares the cells for staining. In the present study, on 7^{th} day, fish were taken out, sacrificed and the tissues of gill, liver, kidney, muscle and brain were excised out. After cutting them into small pieces they were transferred immediately to the fixative. In the process of embedding the material was embedded in certain supporting media of sufficient hardness for cutting thin sections on the microtome. Paraffin wax was used in the process of embedding. The embedding process involves soaking of the tissue in molten wax at a standard temperature, coinciding with the melting point of the embedding medium used.

2.7 Block making and section cutting

After embedding the tissue with wax, it was cast into a block of paraffin. This process is known as block making or casting of block. The mould of 'L` pieces were adjusted to accommodate the object. The mould was filled with molten paraffin wax. The impregnated tissue was placed in the mould according to the plane of section needed. Immediately, warm tip of needle was moved in the molten wax on all the slides of the tissue. This was done to remove the air bubbles. The label carrying all the details of the tissue was fixed on one side of the mould. Gently the air was blown on the mould; the wax forms a thin layer on the surface. The mould was gently immersed in cold water as to cool the wax rapidly. When the block became solid, it was removed from water. The prepared block was trimmed into correct shape for section cutting. The trimmed block was attached to a holder and inserted into the jaws of microtome. The attached trimmed block was cut into thin sections of desired thickness of the microtome.

2.8 Mounting and spreading the ribbon and labelling

For mounting the material, glass slides were used. The slides were smeared with adhesive Mayer's albumin because the section should remain fixed to the slide while staining subsequently. A small piece of ribbon was placed on a slide and floods it with water by dropper. Then the slide was placed on hot plate to heat the water, thereby the paraffin ribbons begin to stretch. Soon after the ribbon was completely stretched the slides were removed from the hot plate and the water was drained off allowed to dry. By using a diamond pencil, the slides were labelled after the slide was completely dried.

2.9 Staining process

The slide was kept in xylene for 30 minutes to 1 hour to deparaffinise. Then the slides were passed through the down grade series of 100%, 90%, 80%, 70%, 50% and 30% ethyl alcohol and water. First the slides were stained in haematoxylin for 2 to 5 minutes and then they were washed in water. After that the slides were dehydrated by passing through ascending order alcohol series up to 70% alcohol. Secondly, the slides were stained with eosin for 2 quick dips and then washed in fresh 70% alcohol. Dehydration was done through ascending grades of 80%, 90% ethyl alcohol and absolute alcohol I and II for 5 to 10 minutes. The slides were allowed in absolute alcohol for complete dehydration. Then the slides were transferred into xylene I for clearing. One or two changes of xylene were given and then finally mounted in DPX mountant. The tissues were dissected out from the fish and fixed in 10% formalin for histological preparation. They were treated by normal procedures of dehydration, clearing, impregnation, embedding, sectioning and staining with Haematoxylin and Eosin. The sections were observed under microscope for the histological studies. Photographs of the conditions in the different tissues were taken using standard photomicrography tools and the histological sections of different tissues have been composed in the form of plates.

3. Results

The Tilapia fingerlings were exposed to single concentration of Bisphenol A for 28 days. Observations were made from 7-28 days to study the structural, behavioural and internal pathological conditions. Analyses of different parameters were carried out in the fish exposed to SLC of toxicant on 7^{th}, 14^{th}, 21^{st} and 28^{th} day of experimentation. Analyses of histopathological studies were carried out from 7-28 days of treatment in the different experimental groups concerned. The results of observations and analyses are given below in detail.

3.1 Internal pathology

Moribund fish were autopsied to study the condition of the internal organs in the control as well as treated fish. The fish not exposed to any toxicant revealed normal organization of the visceral organs with all the tissues appearing healthy without any symptoms of degeneration

or pathological condition. In contrast to these observations, the experimental fish treated with the polyphenyl compound Bisphenol A revealed severe damage to the visceral organs. The gross pathological conditions observed were petechiae and haemorrhagic patches on the peritoneal wall and cavity. The liver was haemorrhagic or pale. Brain, kidney, spleen and liver showed degree of degeneration quite distinctly different from the normal tissues. Gills were clubbed and haemorrhagic with oedematous condition in the head kidney.

3.2 Histopathology

Tissues like Muscles, Liver, Brain, Kidney and Gill from the normal Tilapia fingerlings and those exposed to the toxicants were chosen for histological studies. The sections of the different tissues were observed for the pathological conditions with respect to the cell types in the toxicant treated fish.

3.2.1. Muscle (Fig 1)

Histological study of muscle tissue of the control tilapia showed various layers i.e. epidermis, dermis, myo-epithelium and normal myotomes with equally spaced muscle bundles which indicated the fish to be in unstressed conditions. Muscle tissue showed normal architecture in both control tissues and compact muscle fiber and spindle nucleus. After treated with Bisphenol A was observed with split, thinned and shortened muscle bundles were the degeneration increased in time-dependent manner. The pathological findings included degeneration in muscle bundles with aggregations of inflammatory cells between them and focal areas of necrosis. Also, vacuolar degeneration in muscle bundles and atrophy of muscle bundles were observed. Oedema between muscle bundles and splitting of muscle fibers were seen.

3.2.2 Liver (Fig 2)

The organ which is associated with the detoxification process and biomarker process is the liver. Histological observation of liver from control fish in the present study showed normal homogenous mass of hepatocytes with no abnormalities. Sinusoids and central vein were systematically arranged. Lesions were predominantly observed in liver. Liver of fish exposed to SLC of BPA showed Lesions, Oedematous condition, vacuolization, marked degeneration and constriction of the sinusoids appeared in the parenchymatous tissue. Blood vessels were damaged and infiltrated with lymphocytes. Hepatocytes revealed swelling and necrosis. Peri vascular oedema around portal area was marked.

3.3.3 Brain (Fig 3)

Brain revealed generalized congestion and dilation of meningeal vessels along with infiltration of mononuclear cells. Other pathological changes observed in the brain of exposed fish include atrophy, necrosis and dissolution of nissel bodies, swelling of the axon and vacuolization of the myelin sheath of the nerve fibres and melanomacrophages aggregation submeningeal haemorrhage with diffuse gliosis and neuronal degeneration, diffuse malacia with satellitosis as well as neuronophagia .

3.3.4 Kidney (Fig 4)

Photomicrograph of Tilapia kidney from control group showed normal slightly spherical glomeruli with proper bowman space. Brush border of proximal tubules and lumen of distal tubules showed normal structure. In treated group of fishes, histological observation of kidney showed severe lesions. Hyperplasia and necrosis were noticed in the tubular epithelium. Parencymatous cells revealed marked oedema, enlargement of renal tubules, desquamation of epithelial lining, hypertrophied nuclei, dilation of renal tubules, severe necrosis, pyknotic nuclei, vacuolization, disorganized blood capillaries in glomerulus and congestion of the sinusoids. Renal tubules presented hypertrophy and reduced inter tubular spaces. Mild infiltration of tubular and round cells was observed.

3.3.5 Gills (Fig 5)

Gill histology of control fish had both the primary and secondary gill lamellae intact with normal epithelial cells. Figure shows gills from control group, with primary lamellae having chondrocyte skeleton and parallel thread-like secondary lamellae. Secondary lamellae comprise of pillar cells with a protective covering of mucous cells. Several undifferentiated basal cells were noted in gills of fish from control group. Fingerlings exposed to toxicants revealed extensive damage in their gill architecture. Variable damages in the primary and secondary lamellae with loss of epithelial cells were evident. Primary gill filaments were bulged and the secondary gill filaments curled. The pillar cell nucleus showed necrosis and the secondary gill epithelial cells had developed vacuolization. Shortened and clubbing of ends of secondary gill lamellae, fusion of adjacent secondary gill lamellae, necrosis in primary lamellae, hyperplasia and hypertrophy of nucleus were the other gross pathological changes observed in the histological sections of gills of the fingerlings treated with toxicants. Severe histopathological lesions and cellular alterations were observed in major target organs (Muscle, liver, Brain, kidney and Gill) of market fish which could be attributed to the significant accumulation of BPA in these tissues beyond the prescribed limits of WHO/FAO.

4. Discussion

Bisphenol A (BPA) is a vital compound mostly utilized underway of epoxy tars and polycarbonates, and is particularly inexhaustible in PVC plastics (Vandenberg *et al*., 2009). It is likewise present in paper coatings, dental sealants, glues, reusable containers (e.g., infant bottles), nourishment and refreshment bundling, fire retardants, added substance in different plastics and building materials (Staples *et al*., 1998). BPA is one of the most noteworthy volume synthetic concoctions

created around the world. Worldwide BPA creation limit in 2003 was 2.2 million metric tons (more than 6.4 billion pounds), with a 6– 10% development sought after expected every year (Burridge, 2003). With the expanding interest for polycarbonates and epoxy tars the market for BPA has been developing and worldwide interest has developed from 3.9 million tons in 2006 to around 5 million tons in 2010 (Tsai, 2006). The harmfulness of any contamination is either actue or constant. Despite the fact that toxicants adjust the metabolic and physiological exercises of the living beings, physiological examinations alone don't fulfill the entire comprehension of neurotic states of tissues under harmful pressure. Thus it is helpful to break down the histological viewpoints moreover. The degree of tissue harm is an outcome of the centralization of the toxicant and is time subordinate. The seriousness of harm relies upon the poisonous possibility of a specific compound or pesticide accumulated in the tissue. Histopathological examination is a valuable apparatus for deciding impacts of various anthropogenic poisons on living beings. Histopathological biomarkers mirror the general wellbeing status of population in a biological system (Khoshnood *et al*., 2010). Different anthropogenic squanders are discharged in water bodies unfavorably influencing aquatic life, particularly fish. Histopathological changes in excess of one tissue are constantly instructional in appraisal of the natural impacts of a toxicant and take into account analyses of the observed changes (Adeyemo, 2008). Lethal capability of a toxicant is specifically related with seriousness of harm, it causes. Bisphenol A is an anthropogenic endocrine upsetting compound. Already, studies have been directed to illustrate the impacts of different anthropogenic toxicants on fish liver, kidneys and gills (Osman *et al*., 2007). The accessible writing rattles off the histopathological changes caused by the contaminations on various essential organs like liver, kidney, gill and brain because of pesticide presentation in tilapia (Radhaiah and Rao, 1992; Thangavel *et al*., 1994; Inbamani and Srinivasan, 1998; in *rohu* (Das and Mukherjee, 2000; Sahoo *et al*., 2001), in *mirigal* (Kaur and Toor, 1997; Susan and Tilak, 2003) and in *catla* (Tilak *et al*., 2005), The outcome demonstrated that the level of bending of the gill, liver was corresponding to the introduction time frame and grouping of the metals was observed to be measurement and time subordinate in new water angle Clarias batrachus presented to Mercury and Cadmium (Selvanathan *et al*.,2013). Additionally, the impact of metals causing extreme neurotic changes in liver, kidney and gill were examined by Bengeri and Patil (1986, 1986), Ghosh and Chakrabarthi (1993). Different examinations on histopathology of fish incorporate the impact of chlorine on tilapia (Ramalingam and Murabai, 2002), antigen on *rohu* (Vardhni and Gowri, 2002) and tannery emanating on regular carp (Rani *et al*., 2004). Histopathological changes in excess of one tissue are constantly instructional in appraisal of the organic impacts of a toxicant and take into consideration findings of the watched changes (Adeyemo, 2008). Fish muscle is imperative important and prescribed human nourishment having cardio protactive impact because of the low substance of fat and high substance of proteins, minerals and ideal unsaturated fats. Muscle of control bunches indicated typical design made out of stretched muscle filaments held together by connective tissues with specherical core. In the present investigation of Bisphenol A indicated dynamic harm in the structure of muscle with expanding term of introduction. Shortening and thickening of muscle strands, incorporate partition and diminishing of muscle filaments have been noted. In this manner the degeneration of muscle strands could be due to the consumption of glycogen or atropy of muscle with the dangerous impacts of Bisphenol A. The consequences of present examination on showcase carp are certified by the discoveries of Abbas and Ali, 2007, who noticed a few histological varieties, for example, decimation and vacuolation in the muscle cells of *Oreochromis* species, following introduction to chromium. The perceptions on histopathology in liver, muscle and kidney of freshwater cyprinid, *Labeo rohita* treated with substantial metal incorporated a few hepatic injuries viz. cytoplasmic degeneration, extreme corruption, melano-macrophage focuses, invasion of leukocytes, pyknosis and atomic degeneration. Shortening and stretching of muscle packs were all around set apart in muscle tissue. Histological investigation of muscle tissue of the control cyprinid indicated different layers i.e. epidermis, dermis, myo-epithelium and typical myotomes with similarly dispersed muscle packs which showed the fish to be in unstressed conditions. Conversely, muscle tissue of market cyprinid (*L. rohita*) showed unmistakable changes like shortening of muscle groups, edema and rot. Stretching of muscle groups was likewise watched. Renal adjustments included edema, unpredictable widths, degeneration and decay of renal tubules (Kaur *et al*., 2018). Moreover, Patnaik *et al*. (2011) concentrated the histology of *C. carpio* presented to sub-deadly centralizations of lead cadmium. The creators detailed stamped thickening and partition of muscle groups with intracellular edema. So also, degeneration of muscle packages alongside the accumulation of incendiary cells between them, central zones of rot, vacuolar degeneration in muscle packages and decay of muscle groups have been accounted for in angle presented to various poisons (Fatma, 2009). A few histopathological changes were additionally instigated by Cauvery stream toxins in muscle tissue of *L. rohita* which included shortening of muscle packs, serious intra solid edema and rot of muscle groups. Every one of these progressions demonstrated the fish under profoundly distressing conditions because of more dirtied area getting effluents from modern complex (Dhevakrishnan and Zaman, 2012). Fish liver is the primary organ for

detoxification of xenobiotics, including BPA. In the present investigation, tilapia presented to BPA indicated changes in typical engineering of liver, widened veins and sinusoids, clog of focal vein, expanded vacuolization and rot. Blood streams from hepatic entry vein and hepatic conduit into the focal vein, blockage in the focal vein makes stream of blood troublesome. Cell degeneration and putrefaction might be because of the clog of focal vein. Subsequently, the adjustments in liver of oceanic fauna, for example, fishes are intelligent of amphibian contamination of their living space. Liver histology is exceedingly delicate and is a precise method to evaluate the impact of any contamination on angle. (El-jawaher 2012) watched comparable changes in hepatocytes of *Oreochromus spilurus* presented to nonylphenol (endocrine upsetting concoction). Change in typical liver design with expanded sinusoids might be because of loss of auxiliary proteins. (Abdelaziz *et al*. 2006) watched strange liver design of Siganus rivulates presented to overwhelming metals. Vacuolation of hepatocyte is a nonspecific reaction of fish because of harmful conditions (Roberts, 1978). The vacuolization of hepatocytes may show an irregularity between the rate of combination of substances in the parenchyma cells and the rate of their discharge into the course (Gingerich, 1982). Present investigation revealed that BPA caused cytoplasmic degeneration and burst of focal vein. Radhaiah and Rao (1992) revealed hepatocyte degeneration, cracked blood vessels, vacuoles development, and pyknotic cores in liver of *Tilapia mossambica* presented to the bug spray, fenvalerate. Comparable changes were seen in the liver of tilapia presented to the organophosphate bug spray, chloropyrifos (Tilak *et al*., 2005). The histopathological appearance of liver of *Tilapia zillii* presented to aluminum likewise demonstrated cytoplasmic vacuolization which was contemplated (Hadi and Alwan, 2012). Vacuoles in cytoplasm of liver tissue of *Oncorhynchus mykiss* was additionally watched (Velisek *et al*., 2009) after exposure to bifenthrin. Appearances of macrophages were additionally watched. Doaa and Hanan, 2013 revealed macrophages collection in lead treated liver of *Oreochromis niloticus*. The macrophages more often than not take up scrounger atoms. Scrounger materials are corrupted inside the vacuoles of macrophage and reused in the combination of new substances (Agius and Roberts, 2003; Passantino *et al*., 2005). In the present examination BPA prompted degeneration of hepatocyte in the liver of *Oreochromis mossambicus*. This finding is in concurrence with Muthukumaravel *et al*. (2013) who considered histopathological effect of monocrotophos on the liver of *Labeo rohita*. Deteriorating hepatocytes were likewise revealed by Ahmed *et al*. (2011) in cadmium chloride treated liver of *Clarias batrachus*. Stringy tissue attacked with some incendiary cells was additionally seen in the present investigation. As indicated by Kadry *et al*. (2012) atrazine likewise brought about comparable neurotic adjustment in the liver of *Clarias gariepinus*. Degeneration of hepatocytes and stringy tissue attacked with some provocative cells were additionally seen in malathion treated liver of *Heteropneustes fossilis* (Barbhuiya Hasina Begum and Dey Mithra, 2015). In the current examination, epithelial lifting and hyperplasia was seen in gills presented to a slope of BPA fixations. The gills of fishes play bunches of fundamental exercises including respiratory, osmoregulation and discharge capacities; moreover the gills have close contact with the encompassing condition and prevalently fragile to changes in the nature of the water, thusly, they are viewed as the essential focus of the contaminants (Ahmed *et al*. 2014; Pereira *et al*. 2013).The first change in the gills under intense introduction to the toxicant included lifting of the lamellar epithelium. Comparative epithelium lifting was seen by (Muller and Lloyd, 1994) and (Heath 1995) in fish gills presented to oils, smelling salts, cleansers, acids, and metals like mercury, and phenols. Fusion and clubbing of auxiliary lamellae were seen in fish gills presented to 2ppm of BPA. Fish gills are essential organ for breath and ionic control and on account of their high penetrability and contact zone with water, gills are thought to be an effective instrument for bio-observing potential effects of pollutants (Zeeman and Brindley, 1981; Schwaiger *et al*., 1997; Vigliano *et al*., 2006). In the present study, gills of fish in the control aggregate demonstrated ordinary structure, while BPA exposed fish groups indicated degenerative changes in their gills. Seriousness of harm expanded with expanding centralization of BPA. Gill peculiarities of fish presented to BPA included hyperplasia, combination, clubbing and inspiring of auxiliary lamellae and degeneration of essential lamellae. (Tietge *et al*., 1988) detailed that hyperplasia (increment in cells of the auxiliary lamellae) and epithelial lifting (height of the outer layer of the lamellar epithelium) are defensive systems of fish towards contaminations. Comparable changes in fish gills were recorded as a reaction to copper by Arellano *et al*.(1999), effluents from a dying paper process (Pacheco and Santos, 2002) and sewage from an auxiliary treatment plant (Coutinho and Gokhale, 2000). Figueiredo-Fernandes *et al*. (2007) clarified that combination of some optional lamellae causes decrease of the branchial shallow region that is in contact with the outside condition and this combination is a case of barrier system. At the point when presented to higher groupings of BPA, gill cells experienced degeneration and rot. Mazon *et al*. (2002) had noted comparative changes in gill epithelium of crisp water angle, Prochilodus scrofa, when presented to copper. Gill degeneration and putrefaction reflects coordinate impact of poisons on angle wellbeing (Garcia-Santos *et al*., 2007). Compositional bending of the gill tissue to the chlorpyrifos treated tadpole hatchlings of Asian basic amphibian, *Duttaphrynus melanostictus* was accounted for in the investigation of Bandara *et al*., (2012). Hypertrophy of lamellar epithelium, devastation of gill

lamellae and blood blockage was accounted for in cadmium chloride treated fish Ophiocephalus (Channa) striatus (Bais and Lokhande, 2012).

Fish kidneys are the major hematopoietic and osmoregulatory organs. Changed fish histology is a decent marker of natural contamination in light of the fact that biggest extent of post-branchial blood goes to angle kidneys (Cengiz, 2006). Numerous examinations utilized histological qualities of kidney as a pointer of contamination (Faheem *et al*., 2016; Srivastava *et al*., 1990; Banerjee and Bhattacharya, 1994; Ortiz *et al*., 2003; Cengiz, 2006). Results from present work revealed histological changes in tilapia kidneys after introduction to BPA were corruption, hypertrophy of glomerulus, degeneration and separation of renal tubules and Bowman's case, expansion in the renal tubule and haemopoieatic tissue, shrinkage of glomerulus, pyknosis, widened vein, crack of Bowman's container, and annihilated Bowman's space. Comparable outcomes were accounted for in fishes after introduction to different toxins (Cengiz, 2006; Khidr and Mekkawy, 2008). Extremely restricted writing is available in regards to the histological impacts of BPA on fish tissues. Hence, the outcomes got and revealed here are the first for this EDC on tilapia and will be valuable for future work in clarifying the point by point impacts of BPA. With similarity to our present work histology of kidney of market cyprinid showed decay of renal tubules, conglomeration of fiery cells, loss of cell uprightness of renal tubules and degeneration of renal tubules . Different modifications, for example, unpredictable measurements of renal tubules, couple of necrotic territories and invasion of edematous liquid between renal tubules were likewise noted (Saravpreet Kaur *et al*., 2018). Similar histopathological changes i.e. development of renal tubules, desquamation of epithelial coating, hypertrophied cores, edema, widening of renal tubules, serious rot, pyknotic cores, vacuolization, confused blood vessels in glomerulus were incited in kidney of *Channa punctatus* following presentation to sublethal concentration of zinc (Gupta and Srivastava, 2006). The authors recommended that high gathering of zinc in kidney would most likely brokenness the detoxification system of renal tissue and cause histopathological variations from the norm in it. Different changes, for example, gentle edema, decrease in cell measure, serious harm and further degeneration of renal tubules, complication of renal tissue and corruption were seen when *T. mossambica* was presented to sub-deadly centralization of cadmium sulfate for 20 days under research facility conditions (Jalaludeen *et al*., 2012). Moreover, Rana *et al*., 2015 noted different changes, for example, collection of incendiary cells, expansion in fine containers of renal tubules and hemolysis in kidney of *C. carpio*, following presentation to chromium at sublethal concentrations. The brain tissue of treated fishes in the present investigation revealed blockage of cerebral and meningeal veins, perivascular edema and melanomacrophages collection , submeningeal drain with diffuse gliosis and neuronal degeneration, diffuse malacia with satellitosis and also neuronophagia seen in comparable examination with the Influence of phenol contamination on Nile tilapia, *Oreochromis niloticus* (Anisa *et al*., 2007). These discoveries were credited to phenol neurotoxicity (Viccellio, 1993) and were in concurrence with Devi and Sastry (1987) in Java tilapia. Yacobu (1999) announced swelling of the axon, decay, corruption and pycnosis in the fish. *Ctenopharyngodon idellus* under fenvalerate poisonous quality and the seriousness of harm is more in deadly exposures than in sub-lethal exposures. In the present study, investigations of histopathology clearly show that the neurotic convergences of the toxicants, age of the fish and well being profiles of the life form add to the seriousness of the side effects. As such, in some random natural conditions, initital response to the pressure factors is more articulated and the intrinsic versatile highlights may add to recapturing regularity by compensatory metabolic marvels.

5. Conclusion

In conclusion, the present results show that sublethal exposure to bisphenol A, firstly, caused an induction of antioxidant activities indicating the activation of the detoxification pathways and the antioxidant defenses. Histopathological alterations in tissue may be used as a rapid method to evaluate the toxic effects of chemicals in different tissues and organs. However, treatment disrupted the morphology of the liver resulting in an impaired total antioxidant capability. Continued bisphenol A overuse should be considered a serious threat to aquatic ecosystem and to endemic and cultured species of fishes such as *tilapia*.

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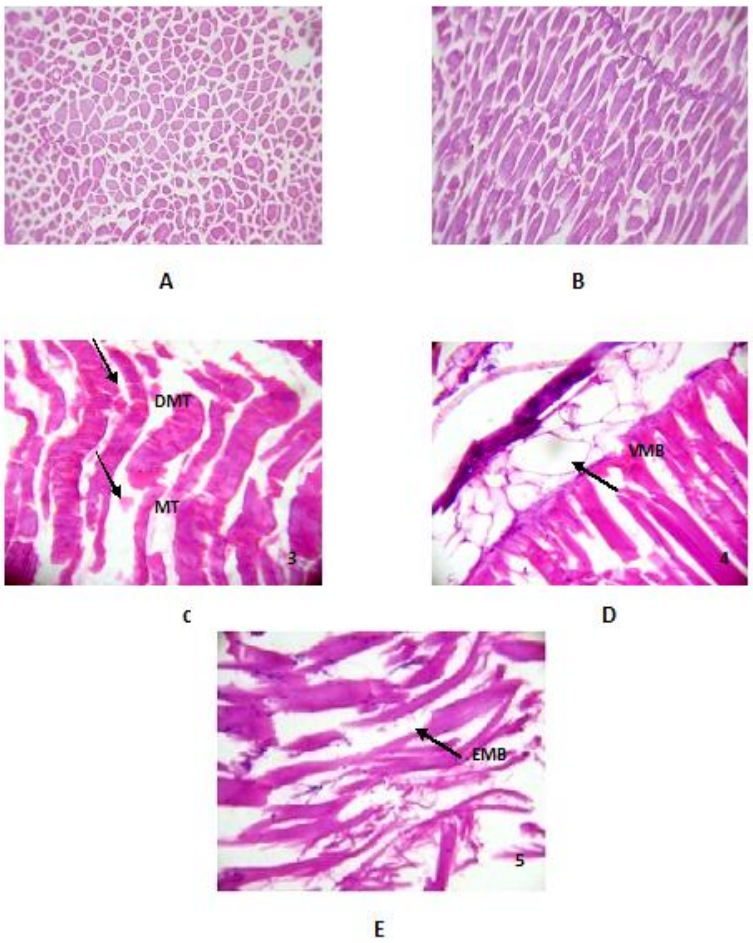

A- showing Normal Muscle Fibres (MF)
B- showing Spliting of Muscle fibres (SPF)
C- showing Disintegrated myotomes (DMT) and Myotomes (MT)
D- showing Vacoluzation in muscle fibres (VMB)
E- showing Edema of Muscle bundles (EMB

Fig : 1Changes in the Muscles of *Oreochromis mossambicus* exposed to lower sub lethal concentration (µg/L) of Bisphenol A for 7, 14, 21 and 28 day

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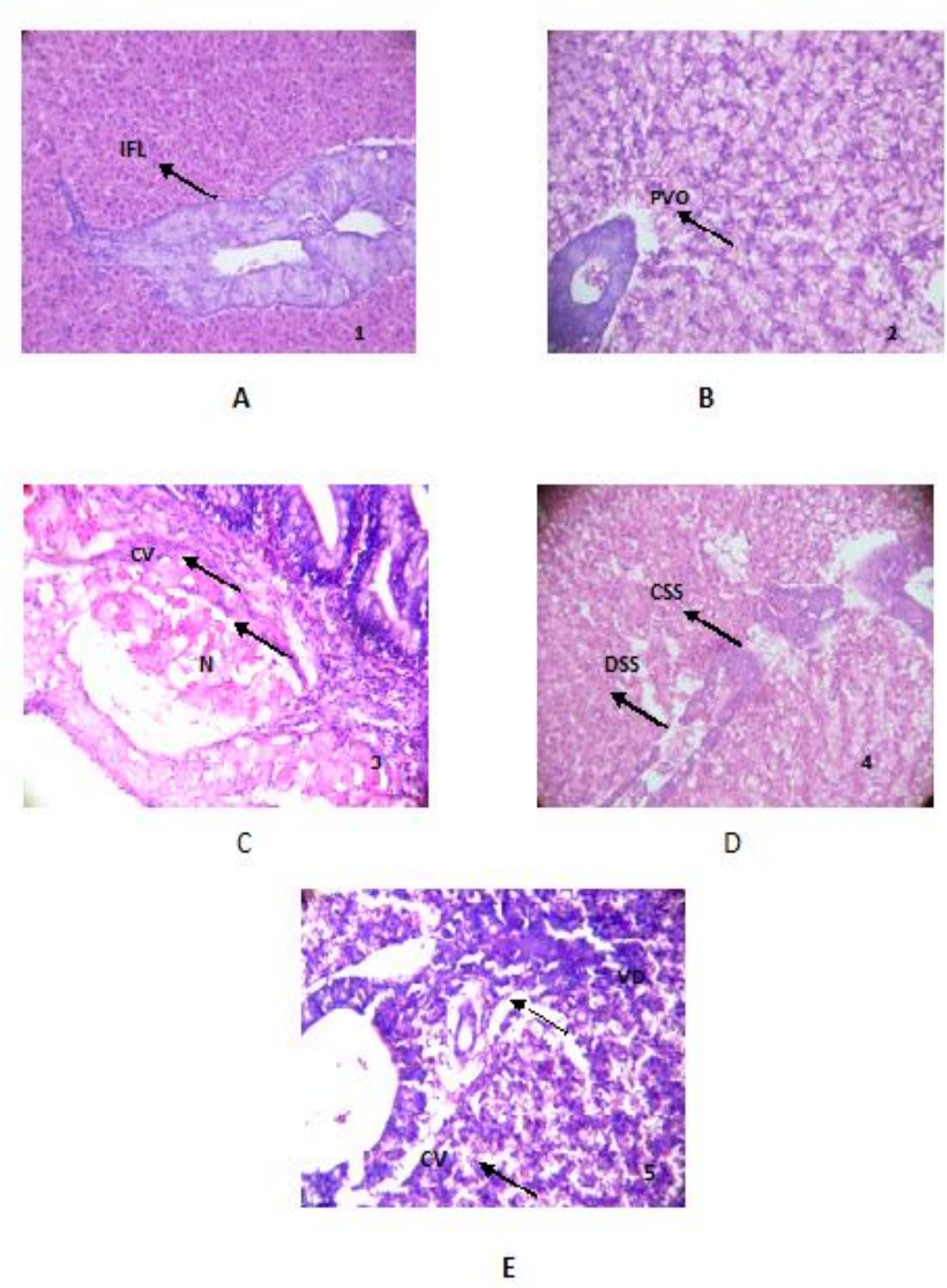

A- showing Normal Infiltrated Lymphocytes (IFL)
B-showing Perivisceral Oedema (PVO)
C- showing cytoplasmic vacuolation (CV) and Necrosis (N)
D- showing congestion and dilation of sinusoid (CSS and DSS)
E-showing Vascular Dilation (VD)

Fig : 2Changes in the liver of *Oreochromis mossambicus* exposed to lower sub lethal concentration (µg/L) of Bisphenol A for 7, 14, 21 and 28 day

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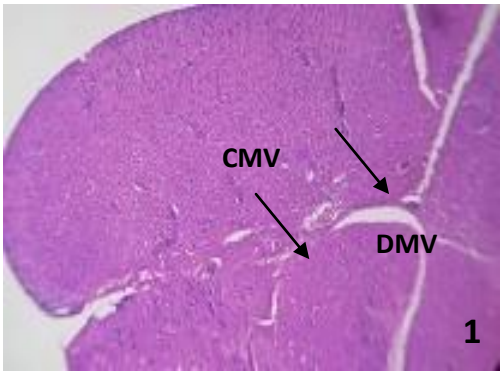
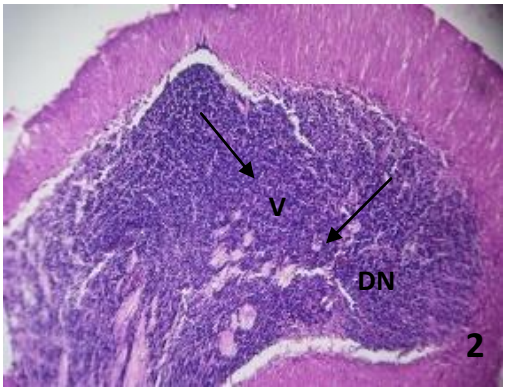


A



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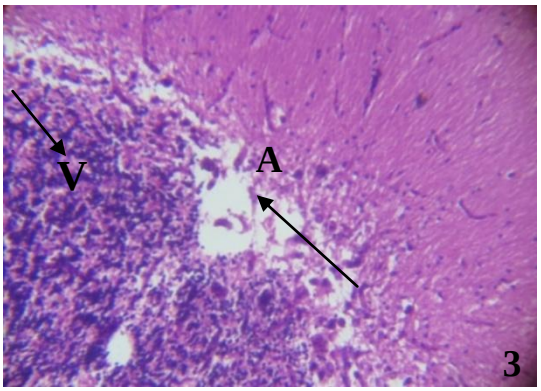

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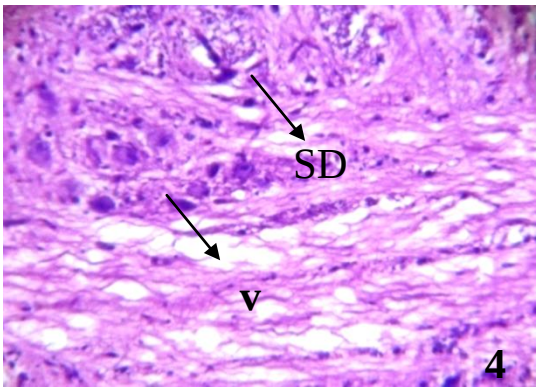

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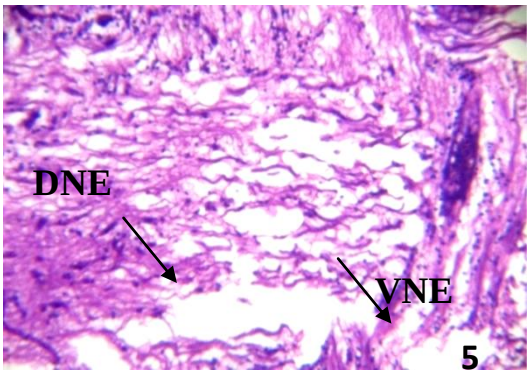

E

A- showing normal Congestion and dilation of Marginal Vessels (CMV & DMV)
B- showing Vacoulazation (V) and Atrophy (A)
C- showing Structural degeneration i.e. degeneration of nucleus
D- showing Degeneration of Neurons cells (DNE)
E- showing Vacoluzation in Neuron cells (VNE)

Fig : 3Changes in the brain of *Oreochromis mossambicus* exposed to lower sub lethal concentration (µg/L) of Bisphenol A for 7, 14, 21 and 28 day

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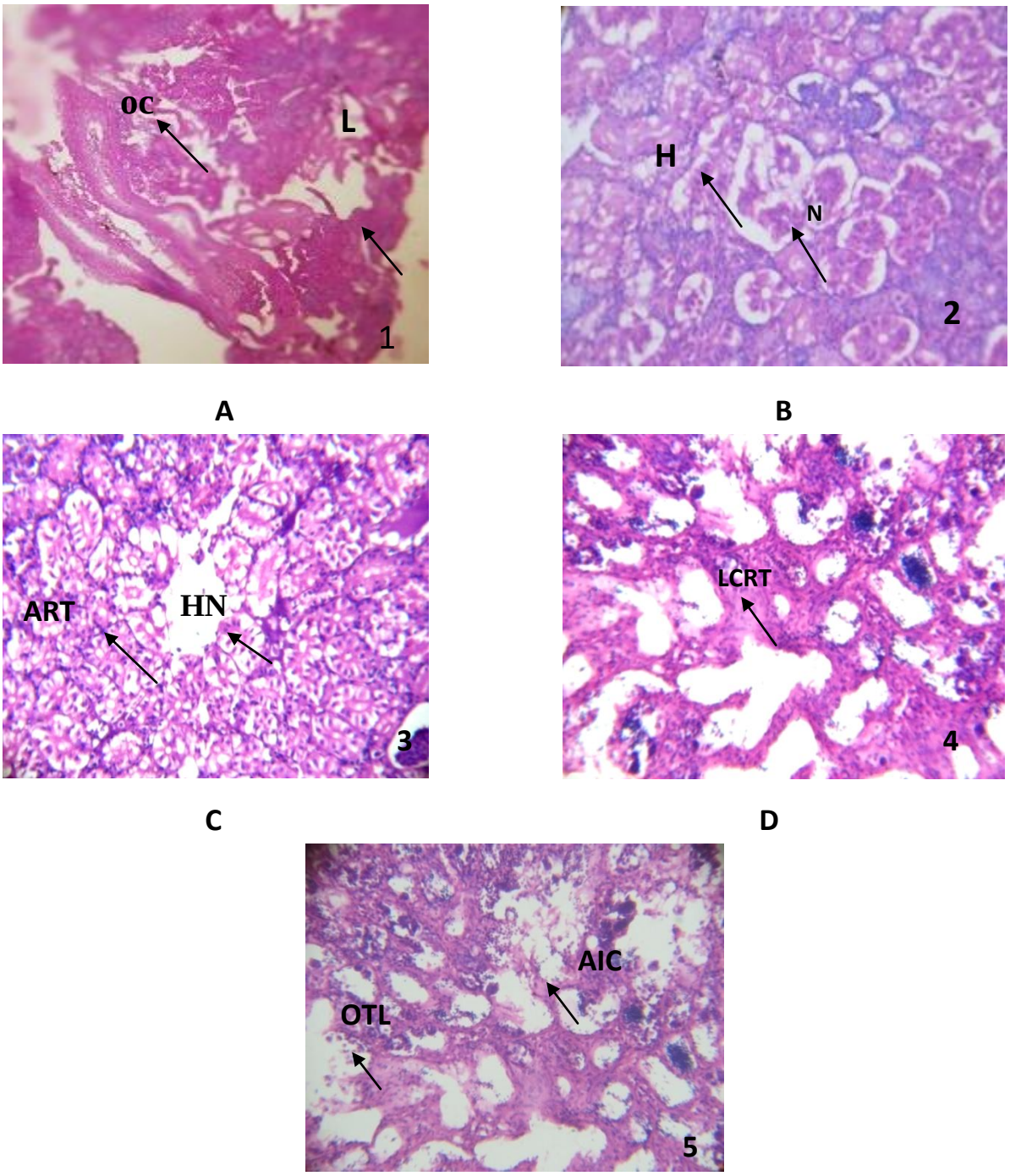

A- showing normal Odema (OD), Congestion (c) and Lesions (L)
B- showing Aggregration of integrated cells (AIC)
C- showing Aggregration of Renal Tubules (ART)
D- showing Loss of cellular integrity of renal tubules (LCRT)
E- showing Occlusion of the tubular lumen and cloud swelling degeneration (OTL)
F- showing Hypertrophied nucleus with tubule cells (HN)

Fig : 4Changes in the Kidney of *Oreochromis mossambicus* exposed to lower sub lethal concentration (µg/L) of Bisphenol A for 7, 14, 21 and 28 day

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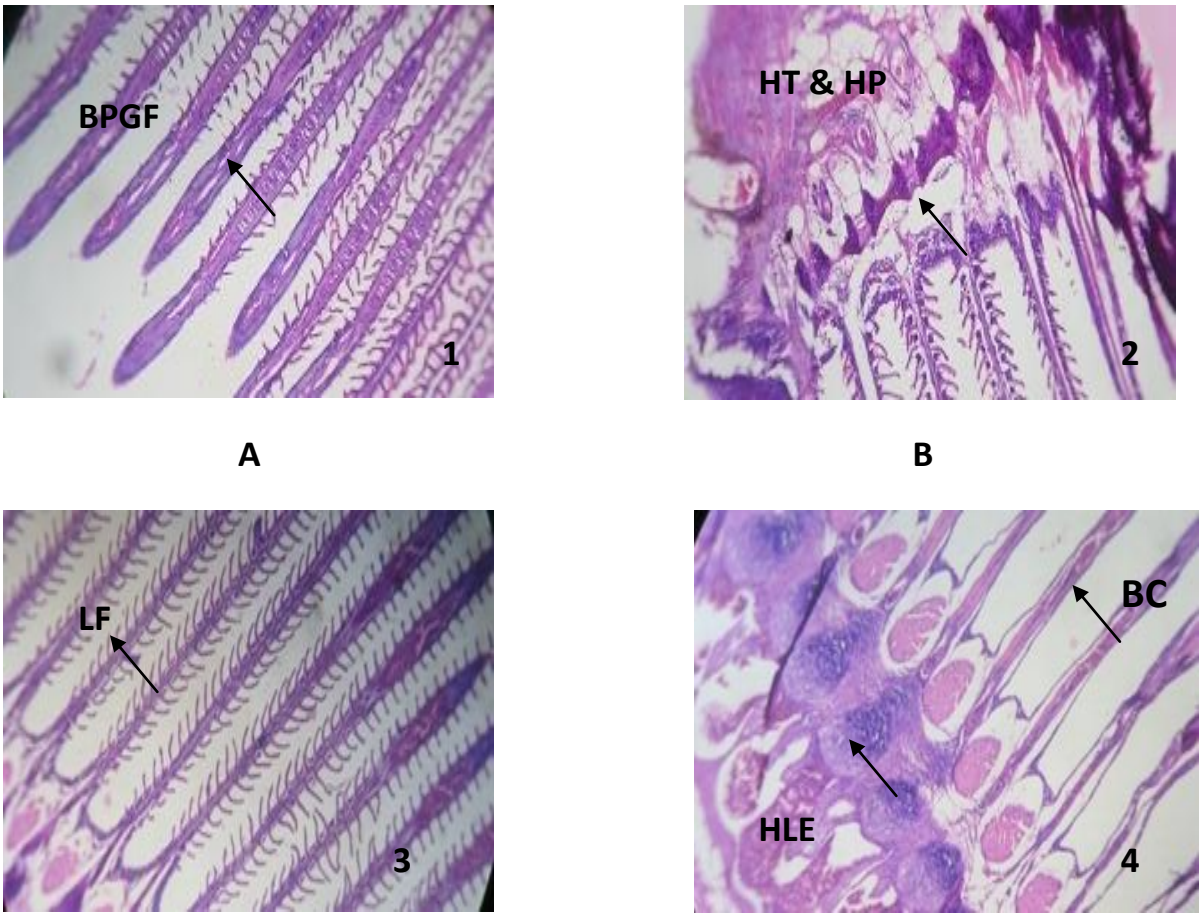

A- showing Bulged primary Gill Filament (BPGF)
B- showing Hyphertrophy and Hypherplasia (HT & HP)
C- showing Laminar fusion (LF)
D- showing Hypertrophy of the laminar epithelium (HLE)
E- showing Lamellar aneurysm (LA)
F- showing Blood congestion (BC)

Fig : 5Changes in the Gills of *Oreochromis mossambicus* exposed to lower sub lethal concentration (µg/L) of Bisphenol A for 7, 14, 21 and 28 day