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Impact of Fluazifop-P-Butyl on Histological Features and Kidney Functions of the Catfish, *Clarias gariepinus*

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ABSTRACT

Fluazifop-P-butyl is a commercial herbicide commonly used in agricultural practices for controlling grass weeds. The present work aimed to detect and compare the deleterious changes that may occur in the kidney of the African catfish, *C. gariepinus* under the different concentrations of fluazifop-P-butyl, as well as studying the histopathological changes in the kidney of exposed fishes to different levels of the selected pollutant. Fish were exposed to different concentrations (1.72 & 0.57 mg/L) of fluazifop-P-butyl for different periods (14 and 28 days). At the end of the exposure time, the levels of uric acid, creatinine and urea were measured in the blood serum to determine kidney functions. In addition, a histopathological examination of the kidney was performed to assess the impact of fluazifop-P-butyl on its tissue structure. The results showed that exposure of catfish *Clarias gariepinus* to fluazifop-P-butyl led to a significant increase in the levels of uric acid, creatinine, and urea in the serum, indicating impairment in kidney functions. The histological examination revealed pathological changes in the kidney structure, including degeneration of renal cells, atrophy of renal tubules and interstitial fibrosis. The findings of this study highlighted the importance of considering the potentially toxic effects of fluazifop-P-butyl on aquatic organisms upon using this herbicide in agricultural practices.

INTRODUCTION

Chemical pollutant substances of industrial and agricultural activities find their way into water bodies at excessive levels capable causing harmful to living organisms **(Sekar *et al*., 2009)**. The agricultural runoff has cumulative negative impacts on water quality, which is considered the main environmental factor controlling the state of health and disease in both cultured and wild fishes **(Fathi & Flower, 2005**; **Omar *et al*., 2013)**. Xenobiotics sometimes find their way into the human system through the food chain. Pollution of aquatic systems by herbicides residues becomes a major threat and a serious problem to living aquatic organisms all over the world **(Firat *et al*., 2011)**.

Fluazifop-P-butyl is a post emergence phenoxy-herbicide; it is absorbed rapidly via leaf surfaces and quickly hydrolyzed to fluazifop acid. The latter accumulates in the meristems, where it disrupts the synthesis of lipids in susceptible species **(Erlingson, 1988; Inyang *et al*., 2016)**.

Fluazifop-P-butyl inhibits acetyl Co-A carboxylase, an enzyme that catalyzes an early step in fatty acid synthesis in organisms. Such xenobiotic can pass into fish tissues and is

highly toxic to the other aquatic organisms **(Extonet, 1996; Inyang *et al*., 2016)**. This herbicide is highly soluble in water and can persist in the environment for extended periods. Fluaxifop-P-butyl is highly toxic to aquatic animals such as fish when compared to toxicity level to mammals and avians. Several studies have reported the toxic effects of fluazifop-P-butyl on various aquatic organisms including fish. Exposure of different fishes to fluazifop-P-butyl causes changes in the levels of creatinine, urea and uric acid as biochemical markers of kidney functions **(Jiao *et al*., 2010)**.

*Clarias gariepinus*is an omnivorous species feasting on any food material aside from plants and fishes. The fish species inhabits almost all inland freshwaters including flooding plains and swamps **(Iheanacho *et al*., 2018)**. Fishes are sensitive indicators of environmental contaminants because of their consistent responsiveness to dilute pollutant exposure, many of which measurably disrupt physiological and biochemical mechanisms **(Islam *et al*., 2021)**. Therefore, the use of fish as biomarkers of the effects of pollution has gained an increasing importance and can permit early detection of aquatic environmental problems **(Lopez-Barea, 1995; Van Der Oost *et al*., 2003; Elias *et al*., 2020)**.

Kidney plays a vital role in the maintenance of an organism's internal environment, being the key to the regulation of volume of extracellular fluid and composition as well as acid-base balance. The toxic chemicals affect the kidney and disrupt its functions and cause temporary or permanent derangement of homeostasis **(Miller *et al*., 2002; Al-Otaibi *et al*., 2019)**.

Histopathological studies help establishing causal relations between contaminant exposure and various biological responses and have proven to be a sensitive tool used in detecting direct effects of chemical compounds on target organs of fish in laboratory experiments **(Altinok & Capkin, 2007; Capkin *et al*., 2009; Boran *et al*., 2012; Somdare *et al*., 2015)**.

Hence, the principal objective of the present work was to detect and compare the deleterious changes that may occur in the kidney of the African catfish, *C. gariepinus*, under different concentrations of fluazifop-P-butyl, as well as studying the histopathological changes in the kidney of exposed fishes to the different levels of the selected pollutant. In addition, it aimed to investigate the physiological changes of the kidney functions (uric acid, creatinine and urea levels) which lead to a better understanding of some biological aspects like slow growth rates, high mortality, as well as the productivity of the selected fish species commonly found in the Egyptian freshwater bodies.

MATERIALS AND METHODS

1.Collection and maintenance of experimental fish

A total number of thirty- six *Clarias gariepinus* individual, with an average body weight of 230±50g at the beginning of the experiment were procured in May 2020 from ELshakhloba Fish Farms, Kafer El-Sheikh Government (Egypt), forming the material for the present study. After collecting, fishes were transported to the laboratory in the animal house, Zoology Department, Faculty of Science, Al-Azhar University in May 2020. Fish specimens were treated with 0.05% potassium permanganate solution for 2 minutes to prevent any dermal infection and kept in glass aquaria aerated with air pump (Rina, Italy) at temperature of 26.6 ± 6°C, supplied with dechlorinated water with natural photoperiod (8- 16h light- dark cycle). Six fishes were placed in each glass aquaria (60×25×40 cm) and acclimatized to the laboratory conditions for two weeks. During this period, fishes were fed at 2% of body

weight twice daily with experimental fish fodder (30% protein floating pellets). The water was continuously aerated and changed completely every two days to minimize oxygen depletion.

2. Acute toxicity study (LC_{50})

Acute toxicity was carried out according to OECD NO (203) estimation median lethal concentration of fluazifop-P-butyl formulations. Five concentrations of fluaziphop-P-butyl (10,15, 22.5, 33.75, and 50.63 mg/L) were used for estimating LC_{50}. Mortalities, visible abnormalities and the behavior of fish samples were recorded, and the concentrations killing 50% of the fish (LC_{50}) were determined according to the study of **Weil's (1952)**.

3. Experimental design

Fish were randomly distributed into three treatment groups, with 36 fish per group. Each treatment group was further randomized into triplicate experiments of 12 fish per replicate. The fish in group "1" served as control group. Fish in groups"2 and 3" were exposed to 1/10 and 1/30 mg L^{-1} of fluazifop-P-butyl formulations, respectively, based on the determined LC_{50} of the herbicide formulation. Fish samples were fed twice daily at 2% of the body weight. The experiment was carried out by using plastic aquaria containing 50L of water. The water was continuously aerated using air pump. Both water and fluazifop-P-butyl formulations were changed every day to avoid pollution from uneaten food and metabolic wastes, as well as maintaining the toxicant concentration. The physicochemical characteristics of water were temperature 26.7 ± 0.6OC; pH, 7.3 ± 0.03; dissolved oxygen, 6.6 ± 0.2 mg L^{-1}; conductivity, 246 ± 2.27 μScm^{-1}; hardness, 162 ± 1.64 mg L^{-1} and alkalinity 92 ± 0.86 mg L^{-1} [$CaCO_3$]. After 14 and 28 days of treatment, blood samples were collected for estimating the renal biomarkers (urea, creatinine and uric acids).

4. Blood sampling collection

Fish were individually anesthetized by clove oil (50 μ/L) before sample collection to facilitate handling, and blood was collected by tail ablation. The tail ablation was done using a single stroke from a heavy, sharp seizure. The blood was then transferred to cleaned Eppendorf for centrifuge to get the separated serum that was stored in −4°C prior to biochemical estimations of kidney functions.

5. Kidney functions biomarkers

Uric acid and creatinine levels in addition to blood serum urea nitrogen (BUN) were determined according to the methods described in the studies of **Barham and Trinder (1972)**, **Newman and Price (2001)** and **First (2003)**, respectively, by using a commercial kit purchased from the Bio-diagnostic Company, Egypt.

6. Histopathological studies

Fish samples were sacrificed after 28 days and the recovery period (14 days post the end of treatment). The fish were dissected, and the kidney were rapidly and carefully excised and washed with saline solution and fixed in 10% neutral formalin for 48hr. They were dehydrated in ascending grades of ethyl alcohol, cleared in xylene and embedded in paraffin wax blocks. Serial sections were cut at 3- 5μm using microtome (Leica RM2125, Leica Bio systems Nussloch GmbH, Germany). Afterwards, the sections were stained with hematoxylin and eosin for general histological features **(Bancroft & Gamble, 2002)**. The stained tissue-slides were mounted with DPX and covered with cover slips. All slides were examined using a light microscope (Olympus BH-2, Olympus, and Tokyo, Japan).

7. Statistical analysis

The statistical package for social sciences SPSS/PC computer program (version 20) was used for statistical analysis of the results. Data were expressed as mean ± S.E and analyzed using one-way analysis of variance (ANOVA). Differences were considered statistically significant at $P< 0.05$.

RESULTS

1. Median lethal concentration

Results showed that the calculated 96h-LC_{50} value of fluazifop-P-butyl for *C. gariepinus* was 17.17mg/ L according to the data presented in Table (1).

Table 1. Mortality percentage in fish samples according to different concentrations of fluazifop-P-butyl

Concentrations of FPB (mg/L)	No. of fish	dead fish	Mortality (%)
10	6	0	0%
15	6	1	17%
22.5	6	5	83%
33.75	6	6	100%

2. Renal biochemical markers

Results indicate that serum urea can be used as a good biomarker in the catfish *C. gariepinus* (Table 2). Fluazifop-P-butyl increased the urea concentration only at high concentrations after 14 days of exposure. Data showed that, urea level in the serum of fish exposed to fluazifop-P-butyl increased continuously after the recovery period at the different concentrations, with an indication of an accumulation of herbicides for a longer time. On the othr hand, urea level did not significantly change in the serum of catfish after treatment with the low concentration of fluazifop-P-butyl.

Table 2. Impact of different concentrations of fluazifop-P-butyl on serum urea (mg/dl) of *C. gariepinus* after 14 and 28 days and the recovery periods

Treatment / Exposure period	Control	High	Low
14 days	13.30±0.41	15.26±0.41*	12.35±0.49
28 days	14.01±0.34	14.07±0.39	13.49±0.42
Recovery (14 days)	14.29±0.13	18.36±0.43*	15.92±0.37*

Data explained that, serum creatinine was as a specific renal biomarker in the catfish, *C. gariepinus*, exposed to different concentrations of fluazifop-P-butyl. The data showed non-significant increase after all periods of treatment, except at low concentration after 14 days of exposure period (Table 3).

Table 3. Impact of different concentrations of fluazifop-P-butyl on serum creatinine (mg/dl) of *C. gariepinus* after 14, 28 days and the recovery periods

Treatment / Exposure period	Control	High	Low
14 days	0.45± 0.01	0.52± 0.03	0.55± 0.02*
28 days	0.40± 0.04	0.48± 0.03	0.45± 0.02
Recovery (14 days)	0.43± 0.01	0.49± 0.04	0.56± 0.05

Results rvealed that uric acid is a good renal biomarker in the serum of catfish, C. *gariepinus.* A significant increase was recorded in the concentration of uric acid in fish treated with sublethal concentration of fluazifop-P-butyl, compared to the control after exposure periods (14, 28 and recovery), except at the low concentration of fluazifop-P-butyl after 14 days of exposure (Table 4).

Table 4. Impact of different concentrations of fluazifop-P-butyl on serum uric acid (mg/dl) of *C. gariepinus* after 14, 28 days of exposure and the recovery periods

Treatment / Exposure period	Control	High	Low
14 days	0.83± 0.04	1.71 ± 0.10*	0.94± 0.06
28 days	0.72± 0.04	1.25± 0.08*	1.28± 0.04*
Recovery (14 days)	0.77± 0.05	0.52 ± 0.06*	1.24± 0.08*

3. Histological study

3.1. Histological structure of the kidney

The urinary system consists of two elongated thin kidneys, lying quite close to the vertebral column. They are mostly fused along their entire length and appear to form a continuous mass. Posteriorly, there comes out from each kidney a very short mesonephric duct. The two ducts unite shortly after leaving the kidneys to form a common mesonephric duct, which opens to the outside on the summit of urinogenital papilla. Nearly mid-way, the common duct dilates giving rise to a small urinary bladder. Posterior kidney of *Clarias gariepinus* showed normal renal tubules with normal hematopoietic tissue in between normal glomeruli with well-distinguished Bowman's capsule, provided with normal blood vessels (Fig. 1).

3.2. Histological changes in the kidney of C. gariepinus after 28 days of treatment

Result exhibited that, fish samples treated with the lowest concentration (0.57 mg/L) of fluazifop-P-butyl for 28 days showed fibrosis of hematopoietic tissues, with accumulation of melano-macrophage patches in mesonephric kidney. Furthermore, renal tubules exhibited atrophied glomeruli with wide space in Bowman’s capsule and a destructed glomerulus. In addition, vacuolated in renal tubules and destruction of renal tubules were clearly observed (Figs. 2, 3).

Microscopic examination for treated fish with the highest concentration (1.72 mg/L) of fluazifop-P-butyl for 28 days showed a marked fibrosis area of hematopoietic tissues and highly destructed glomeruli with undistinguished Bowman’s space. In addition, massive

fibrotic areas with non-coordinating of hematopoietic tissues were observed. Moreover, destruction and extreme vacuolation in the renal tubules were clearly detected (Figs. 4, 5).

3.3. Histological changes in the kidney ofClarias gariepinus after recovery period

Histopathological studies of *C. gariepinus* (Fig. 6) exhibited little fibrosis of hematopoietic cells, destruction of renal tubules and destruction of glomeruli after the recovery of the lowest concentration of fluazifop-P-butyl for 14 days. The recovery period of fish treated with the highest concentration of fluazifop-P-butyl for 14 days; however, exhibited a little fibrosis of hematopoietic tissue and vacuolated in renal tubules with wide space in Bowman's capsule of glomeruli (Fig. 7).

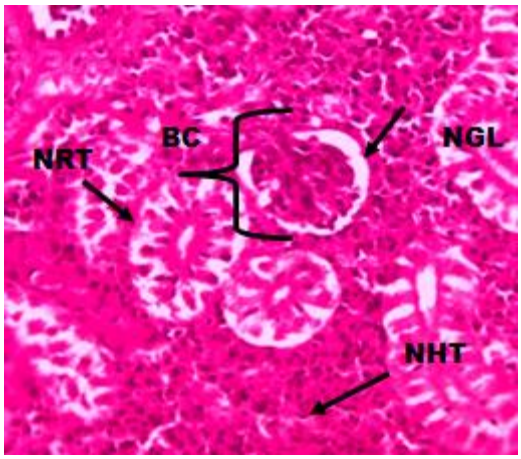

Fig. 1. Photomicrograph of the normal kidney of the catfish, *C. gariepinus*, showing hematopoietic tissue (NHT) with normal nuclei, normal renal tubules (NRT) with normal glomeruli (NGL) and Bowman's capsule (BC)(H&E x400)

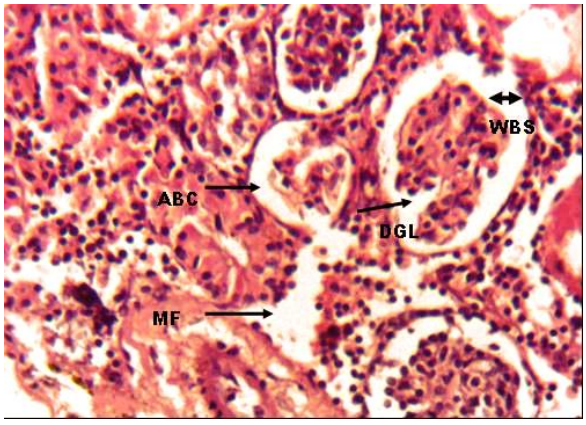

Fig. 2. Photomicrograph of the kidney of *C. gariepinus* after exposure to the lowest concentration of fluazifop-P-butyl after 28 days, showing marked fibrosis of hematopoietic tissues, atrophied Bowman's capsule (ABC) with destructed glomeruli (DGL) and wide Bowman's space (WBS)(H&E x400).

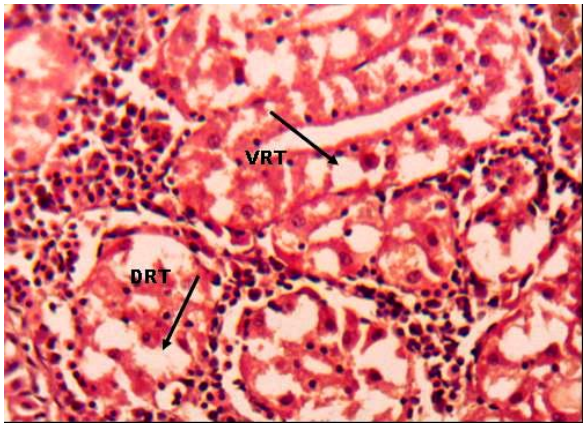

Fig. 3. Photomicrograph of the kidney of *C. gariepinus* after exposure to the lowest concentration of fluazifop-P-butyl after 28 days, exhibiting vacuolation (VRT) and destruction of renal tubules (DRT) (H&E x400).

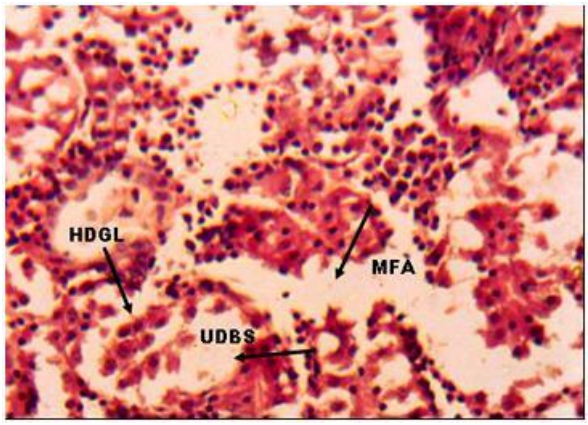

Fig. 4. Photomicrograph of the kidney of *C. gariepinus* treated with high concentration of fluazifop-P-butyl after 28 days, showing massive fibrotic areas (MFA) of hematopoietic tissue and highly destructed glomeruli (HDGL) with undistinguished Bowman's space (UDBS)(H&Ex400).

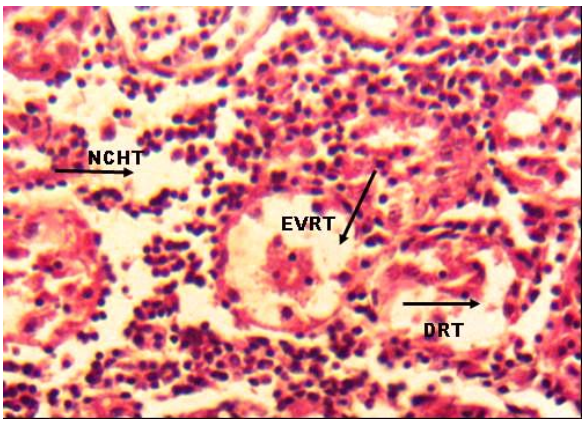

Fig. 5. Photomicrograph of the kidney of *C. gariepinus* treated with high concentration of fluazifop-P-butyl after 28 days, showing non-coordination of hematopoietic tissues (NCHT), destruction renal tubules (DRT) and extreme vacuolation renal tubules (EVRT) (H&Ex400).

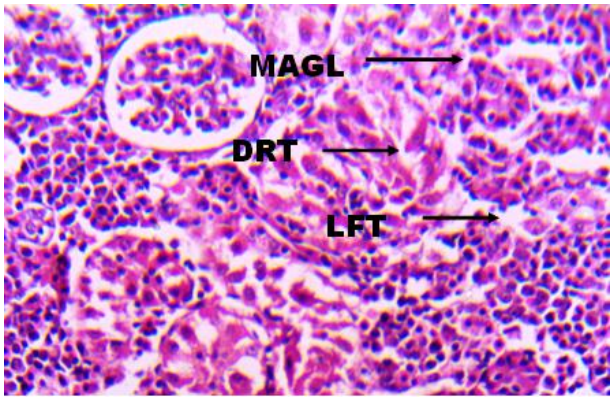

Fig. 6. Photomicrograph of the kidney of *C. gariepinus* after the recovery period from the lowest concentration of fluazifop-P-butyl after 14 days of exposure, showing little fibrosis of hematopoietic cells (LFH), destruction in the renal tubules (DRT) and mild atrophied glomeruli (MAGL) (H&Ex400).

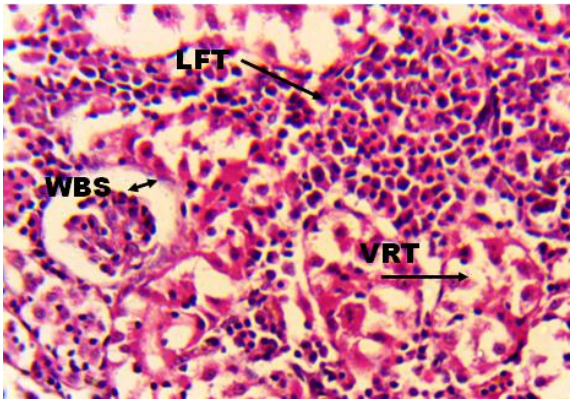

Fig. (7): Photomicrograph of the kidney of *C. gariepinus* after the recovery period from highest concentration of fluazifop-P-butyl after 14 days of exposure, showing little fibrosis of hematopoietic tissue (LFH), vacuolated renal tubules (VRT) and wide Bowman's capsule space (WBS) (H&Ex400).

DISCUSSION

The present study showed several abnormal swimming behavior and increased deformities in fish exposed to sub-lethal concentration of fluazifop-P-butyl during the exposure period. Initial catfish was active swimming; the speed of swimming was directly correlated with the chemical's concentration. *Clarias gariepinus* anxious and irregular behavior also tends to suggest respiratory impairment, which is probably caused by the chemical's impact on the gills. Fish directly contacted with the environment **(Hlavek &**

Bulkey, 1980), making them extremely vulnerable to any physicochemical changes that may be reflected on their blood parameters **(Ndimele *et al.,* 2015)**.The use of plant protection products may pose a danger not only to fish but also to consumer health. This may take place since pesticides bioaccumulated in fish are biomagnified throughout the food chain **(Buah-Kwofie *et al*., 2018)**.

The kidney of exposed fish is considered the first organ adversely affected by water contamination **(Thophon *et al*., 2003)**. Therefore, histological feature can be used a good indicator of environmental pollution **(Ortiz *et al*., 2003)**. Whereas, kidney receives large amount of blood as a target organ for some filtration and its prime route of excretion **(Cengiz, 2006; Oropesa *et al*., 2009)**.

Urea, creatinine and uric acids' levels are indicators for kidney functions, and they are important variables predicting to which limit the kidney is adversely affected **(Shalaby *et al*., 2007)**. Urea is a product of the deamination of glycogenic amino acid in the liver usually under conditions that the system requires energy generation to overcome any physiological stressor **(Okonkwo *et al*., 2013)**. Moreover, urea and creatinine (indicators of kidney functions) are nitrogenous waste products that are eliminated by the kidney of vertebrates, whereas excretion is suppressed in renal insufficiency **(Lall *et al*., 1997; Ajeni & Solomon, 2014)**.

Results revealed that, serum urea and creatinine are considered as specific renal diagnosis in the catfish, *C. gariepinus* exposed to different concentrations of fluazifop-P-butyl. Data showed a significant increase in the concentration of urea and creatinine after 14 and 28 days of exposure period, compared to the control one. This may be due to reducing the glomerular filtration as first step of kidney dysfunction. These results match with those of **Shalaby *et al.* (2007)**, **Bakhshwan *et al.* (2009)**, **Harabawy and Ibrahim (2014)**, **Sharafeldin *et al*. (2015)** and **Fathy *et al*. (2019)**. An increase in serum urea and creatinine of fish exposed to pendimethalin herbicide may be attributed to the action of pendimethalin herbicide on the glomerular tissues as well as deficiency of oxygen reducing the glomerular filtration rate, which causes pathological changes in the kidneys due to the accumulation of herbicide in the organ **(Parums, 1996**; **Abdel-Daim *et al*., 2020)**. Similar observation recorded a significant increase in urea and creatinine levels in the serum, suggesting nephrotoxicity after exposing *Clarias batrachus* to carbofuran and *O. niloticus* to sublethal concentration of atrazine **(Mekkawy *et al*., 1996; Kaur *et al*., 2012)**.

Biochemical parameters are fundamental in the physio-pathological evaluation of animals, with identification of the target organs of toxicity; for example, nephrotoxicity manifests as renal failure with a rise in serum uric acid levels **(Khaled *et al*., 2015; Mahmoud *et al*., 2019)**. The increase in uric acid concentration indicates disorders in the excretion of nitrogen metabolite. Therefore, they provide useful information about the health status of the kidney **(Bojarski1 & Witeska, 2020)**.

The present study indicates that, there is a significant increase in the concentration of uric acid affected by sublethal concentration of fluazifop-P-butyl, compared to the control after exposure periods of 14 and 28 days. These results agree with those of **Kumari (2015)**, **Kovacik *et al*. (2019)**, **Mahmoud *et al*. (2019)**, and **Bayili *et al*. (2020)**. Whereas, they differ with the findings of **Ogamba *et al*. (2011)**, **Mekkawy *et al*. (2020)** and **Mohamed *et al*. (2021)**. The increasing level of uric acid may be attributed to the action of the herbicide on the glomerular tissues of kidney, causing pathological changes due to the accumulation of herbicide **(Jacobs *et al*., 2002; Shalaby *et al*., 2005; Abbas *et al*., 2007)**. High levels of used chemicals indicate malfunction of the kidney **(Giordano *et al*., 2015; Noureen *et al*., 2017)**. From another viewpoint, uric acid elevation refers to the disturbances in the kidney and

necrosis of endothelial cells **(Fischer-Scherl *et al*., 1991)**. **Sharafeldin *et al*. (2015)** reported an increase in the level of uric acid related to an increase in protein catabolism.

The present study exhibited that, the kidney of *Clarias gariepinus* treated with fluazifop-P-butyl for 28 days exposure and recovery periods for 14 days showed marked fibrosis of hematopoietic tissue and accumulation of melano-macrophage patches in mesonephric kidney. Wide bowman's capsule with moderately distracted atrophied glomeruli, plus moderately vacuolated, destruction, hemorrhage and destructed glomeruli of renal tubules were observed. Blood vessels were congested and dilated with vacuolated epithelium and accumulation of blood cells. Moreover, marked progressive necrosis, sever fibrosis of hematopoietic tissue and marked destruction of renal tubules were observed. These results coincide with those of **Gupta *et al*. (2016)** who reported the degeneration of renal tubules, pyknosis and vacuolation presence of sinusoidal space in addition to tubular necrosis. The recorded damage in the epithelial cells of the renal tubules and an increase of the bowman's space resulted in the glomerulosclerosis in the kidney. Changes have been proposed as markers of renal toxicity for several substances, including pesticides and herbicides **(Abbas *et al*., 2007; Abd El-Rahman *et al*., 2019**; **Sayed *et al*., 2022)**.

Samanta *et al*. (2015) and **Badroo *et al*. (2020)** elucidated that, the degeneration process of the kidney progresses to hyaline degeneration, which is characterized by the presence of eosinophilic granules inside the cells. These granules by reabsorption of proteins that are lost in the urine are formed inside the cells, indicating the corpuscle damage **(Hinton & Lauren, 1990**; **Takashima & Hibiya, 1995)**.

CONCLUSION

Results indicate that, fluazifop-P-butyl at high concentrations could be renal toxic; therefore, further studies are required to evaluate the potential environmental risk of fluazifop-P-butyl. Meanwhile, limiting the use of fluazifop-P-butyl in the rice fields care is recommended. Moreover, the recovery period must be longer than the exposure one to reduce or delete the dangerous effects expected on fish wealth and human health.

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Arabic Summary

تأثير مبيد الحشائش فلوازيفوب بي يوتيل على الخصائص الهستولوجية ووظائف الكلى للقرموط (*Clarias gariepinus*)

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يعتبر مركب فلوأذيفوب - بي- بيوتيل من أكثر مبيدات الحشائش التى يتم إستخدامه على نطاق واسع فى مكافحة الحشائش فى حقول الأرز، التى تشارك المحصول المأوى،الغذاء، والماء والتى يؤدى إنتشارها بصورة كبيرة فى التكلفة وخسارة هائلة فى المحصول. تمت دراسة تأثير فلوأذيفوب- بي- بيوتيل على وظائف الكلى في القرموط (***Clarias gariepinus***) لتحديد السمية المحتملة لهذا المبيد،حيث تم تعرض أسماك الدراسة لتركيزات مختلفة من فلوأذيفوب- بي- بيوتيل لفترات مختلفة (١٤ يوما و ٢٨ يوما). تم قياس مستويات كل من حمض اليوريك، الكرياتينين، واليوريا فى الدم للوقوف على مدى تاثر وظائف الكلى بهذا المركب. كما تم إجراء فحص التركيب النسيجي لأنسجة الكلى لتقييم التأثير المرضي لهذا المبيد على التركيب النسيجى الكُلوي للأسماك.

أظهرت النتائج أن التعرض لمبيد فلوأزيفوب- بى- بوتيل أدى إلى زيادة معنوية في مستويات كل من حمض اليوريك،الكرياتينين واليوريا لأسماك القرموط، دلالة على وجود خلل كبير فى وظائف الكلى لهذه النوعية من الأسماك. كما أظهرت الدراسات الهستوباثولوجية تغيرات مرضية في التركيب النسيجى لكُلى الاسماك موضوع الدراسة تمثلت فى وجود تحلل فى الخلايا الكلوية، ضمور فى الأنيبيبات الكلوية، وتليف فى الانسجة البين خلوية. كما أكدت نتائج هذه الدراسة على أهمية دراسة التأثيرات السامة لهذا المبيد على صحة الكائنات المائية الاخرى والحد من إستخدامه فى الأنشطة الزراعية لتجنب الآثار المدمرة على صحة الأسماك والانسان والحيوان.