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Original Article

Biomarkers of Cypermethrin (Synthetic Pyrethroid) Toxicity - Biochemical alterations in Cyprinus carpio, a freshwater edible fish

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ABSTRACT

Pesticides are one of the most potentially harmful toxicants introduced into the aquatic environment. Aquatic ecosystems that run through agricultural areas have high probability of pesticide contamination by runoff and leaching. Synthetic pyrethroid pesticides are preferred above organophosphates, carbamates and organochlorines as these have high efficiency, low mammalian toxicity and easy biodegradability. Type II pyrethroids such as cypermethrin are more effective, available as emulsifiable concentrates which keeps it in solution longer and are usually 2-9 times more toxic than the technical grade forms, most likely due to synergistic interactions. Due to its indiscriminate use, cypermethrin makes their entrance into natural water bodies and ultimately affects the several nontarget aquatic organisms such as fish by inhibiting growth, metabolism, histopathology, hematology and thus adversely affects its meat quality and population. Fish responding to the changes in their environment with greater sensitivity, can be used as biomarkers of acute ad chronic toxic effects of various pollutants. Biochemical changes are better indices of damage by pollution than the conventional pathophysiological changes. Changes in biochemical parameters point to the development of sublethal abnormalities, which limit potential of an animal population in effectively coping with the normal stress and strain for survival. In this paper we have reviewed the toxic effects of cypermethrin on various biochemical indices in a non-target organism, fish which provide a base line data for further research investigations and future environmental management programmes.

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INTRODUCTION

Biochemical markers are measurable responses to the exposure of an organism to xenobiotics as well as very suitable biosensors of aquatic pollutants. Aquatic pollution can easily be detected through biomarkers, as enzymes provide one of the most reliable means of assessing the degree of exposure of animals to pollutants. Some of the biochemical alteration occurring in the body gives the first indication of the stress in the organism and hence effect on the part of the pollution [1]. The biochemical studies are good parameters which help to see the effects of toxicants on metabolism of fish [2]. Biochemical tests are routine laboratory tests useful in recognizing acute or chronic toxicity of these insecticides [3] and can be a practical tool to diagnose toxicity effects in target organs and to determine the physiological status in fish. Fish occupy a prominent position in the field of tocicity studies. They are continued to be an extremely reliable component of an aquatic ecosystem, serve as best bioindicators of water pollution and are the inhabitants that cannot escape from the detrimental effects of these pollutants [4]. Toxicological investigations conducted on various fish species proved that the biochemical alterations at the level of whole animal, organs, tissues and sub cellular organelles, are better indices of damage by pollution than the conventional pathophysiological changes. Against this broad background, the present review attempts to provide a comphehensive data available on the biochemical biomarkers of cypermethrin, a type II pyrethroid.

Cypermethrin induced biochemical alterations were studied by various authors in various fish species such as Catla catla [5, 6], Channa orientalis [7, 8], Channa punctatus [9, 10, 11, 12, 13], Channa striatus [14, 15], Cirrhinus mrigala [16, 17, 18, 19, 20, 21, 22, 23, 24, 25], Clarias batrachus [26, 27, 28, 29, 30], Clarias gariepinus [31, 32, 33, 34], Colisa fasciatus [35], Cyprinus carpio [36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49], Heterobranchus bidorsalis [50], Heteropneustes fossilis [51], Labeo rohita [52,53, 54, 55, 56], Lepidocephalichthys guntea [57], Oncorhynchus mykiss [58, 44, 59, 60, 61], Oreochromis niloticus [62, 63], Rhamdia quelen [64], Sebastes schlegeli [65], Solea senegalensis [66], Tilapia mossambica [67, 68].

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2. Cypermethrin induced biochemical alterations in fish

2.1. Carbohydrate Metabolism

Carbohydrates are considered to be the first among the organic nutrients to be depleted and degraded in response to stress conditions imposed on animals. Carbohydrates are important, since these provide the energy for the animal required for performing different processes [69, 70]. Alteration in carbohydrate metabolism is prone to have deleterious effect on the survival of the animal [71]. Cypermethrin induced alterations in carbohydrate metabolism were studied by various researchers [67, 31, 5, 33, 18, 57, 52, 19, 62, 27, 63, 68, 51, 64, 46, 59, 65].

2.2. Protein Metabolism

The physiological and biochemical alterations observed in an animal under any physiological stress can be correlated with the structural and functional changes of cellular proteins. Proteins occupy a unique position in the metabolism of cell because of the proteinaceous nature of all the enzymes which mediate at various metabolic pathways [69, 70]. Various authors studied cypermethrin induced alterations in protein [67, 5, 31, 8, 33, 18, 57, 52, 19, 62, 43, 15, 44, 35, 68, 63, 26, 12, 13, 64, 23, 46, 24, 30, 29, 65, 47, 60, 56] and free amino acid levels [36, 31, 52, 19, 20, 43, 35, 29, 65, 47, 56] in different fish species.

2.3. Lipid Metabolism

Lipids are the most important source of energy in the absence of carbohydrates and also serve as energy reserves to meet the metabolic demand for more energy to mitigate toxic stress. Toxicants are known to induce severe impairment in lipid transport and metabolism which may lead to change in lipid composition in fish tissues. Cypermethrin induced lipid metabolism was studied by several researchers [67, 7, 33, 57, 62, 35, 68, 64, 29, 65, 49].

2.4. Nucleic Acids (DNA & RNA)

Cellular enlargement and active protein synthesis are dependent on DNA and RNA content. The changes in DNA, RNA ratio results in eventual losses of cell structure, proliferation and formation of new tissue and tissue degradation with a total loss of cellular control mechanism [40]. Studies of various researchers [37, 40, 18, 9, 52, 35, 14, 26, 12, 13, 55] proved the toxic effects of cypermethrin on nucleic acid content of different fish species.

2.5. Enzymes

Enzyme analysis of organs such as muscles, kidney, liver, heart and gills in fish can provide important information about the internal environment of the organism [72]. Changes in the enzyme activities disrupt physiological and biochemical processes. [73]. These biochemical changes try to maintain equilibrium in the presence of contaminants. A shift in the activities of enzymes from the control is also used as a relevant stress indicator. A major biochemical response to the effect of a toxicant in fishes is the inhibition of a number of enzymes [74]. Cypermethrin induced variations in Transaminases [16, 38, 39, 41, 33, 34, 52, 50, 62, 44, 22, 28, 64, 75, 24, 29, 59, 65, 47, 60, 61], Phosphatases [17, 34, 42, 52, 50, 62, 44, 51, 64, 46, 59, 65, 54, 55, 60, 61], Dehydrogenases [38, 39, 34, 62, 44, 35, 22, 28, 46, 59, 54, 55, 60, 61, 48, AChE [31, 52, 35, 53, 11, 54], ATPases [66, 21, 45, 27, 54, 55], Oxidases [52], Protease [36, 31, 20, 52, 29, 47] and Catalase [58] were extensively studied in different varieties of fish.

Neelima et al., 2015a [36] observed that Cyprinus carpio, exposed to sublethal concentrations (5, 10, 15 and 20% 96hLC50) of cypermethrin (25% EC) for 2, 4, 6 and 8 days caused statistically significant, time and dose dependant increase in the free amino acid levels and protease activity. In Cirrhinus mrigala same sublethal concentrations altered the activity levels enzymes aspartate amino transferase and alanine amino transferase in gill, muscle and liver which showed the increased activities of both the transaminases [16].

Cyprinus carpio exposed to sublethal concentrations of cypermethrin (5, 10, 15 and 20% of 96hLC50 value) of cypermethrin for 5, 10 and 15 days showed decreased tendency over control was in both DNA and RNA in all the vital tissues. DNA and RNA contents were not altered by cypermethrin at 5 day exposure period, gradually decreased with increased exposure period and the decrease was observed to be directly proportional to increased sublethal concentrations. The reduction in the DNA content is comparatively less in muscle. Maximum percent of decrement in DNA was (17.17%) in liver and minimum was (13.94%) in muscle at the longest exposure period (15 days) and highest sublethal concentration (20% 96hLC50). RNA content decreased significantly in liver (29.90%), muscle (25.53%), brain (23.38%), kidney (21.82%) and gill (20.34%). The decrease was comparatively higher at 15 days exposure period at highest test concentrations. In all the organs studied, the influence of cypermethrin was found to be time and exposure period dependent [37].

Al-Ghanim, 2014a & b [38, 39] reported Cyprinus carpio exposed to acute dose of cypermethrin (7.5µg/l) for 1, 3, 5, 7 and 9 days and sublethal concentrations (1.5µg/l) for 1, 7, 14, 21 and 28 days altered enzyme activities in gill, liver and muscle. Cypermethrin induced time dependent and tissue-specific elevated glutamate dehydrogenase, aspartate aminotransferase and alanine aminotransferase enzymes in all tissues at both lethal and sublethal exposure. El-Elaimy et al., 2014 [66] studied the effect of cypermethrin 1/25th (20µg/l) and 1/10th (50µg/l) of 24hLC50 (500µg/l) on juvenile Senegalese sole, Solea senegalensis for 10 days in gill and liver to assess the expression patterns of different enzyme genes related to toxicity and osmoregulation, namely glyceraldehyde-3-phosphate dehydrogenases 1 and 2, and Na+, K+-ATPase subunits α and β. Enhanced gill GAPDH-1, NKA-α and NKA-β expressions were observed with less prominent hepatic responses. The low dose decreased GAPDH-2 expressions. These results indicate that cypermethrin induced some degree of oxidative stress in Solea senegalensis specimens led to an osmotic imbalance, activating mainly at branchial level-different antioxidant and osmoregulatory enzyme genes. Jipsa et al., 2014 [67] reported sublethal concentration of cypermethrin in Tilapia mossambica decreased the protein, cholesterol and triglyceride level and increased glucose level in the tissues at 24, 48, 72 and 96h. Kannan et al., 2014 [5] investigated the effects of cypermethrin (10% EC) in the concentration of 0.0006 ml/l on Catla catla for 24h and reported a significant ($P<0.01$) increase in glucose and decrease in total proteins. Olalekan, 2014 [31] reported biochemical responses of Clarias gariepinus exposed to cypermethrin (20µg/l) for 5 days. The total protein decreased in liver and muscle. Free amino acid of liver and muscle increased. Levels of glycogen and pyruvate of tissues of the liver and muscle were significantly

(p<0.05) lower while the level of lactate was significantly (p<0.05) higher. Activity of cholinesterase was 1/3rd that of control. In contrast, protease activity was about 2 folds that of control. Omowumi and Joseph, 2014 [32] studied ionoregulatory impairment in Clarias gariepinus exposed to combined stressors of lead and cypermethrin and reported the exposure of C. gariepinus to 0.5µg/l cypermethrin resulted in a significant reduction in plasma Na+ (43% decrease) and Cl− (31% decrease) but a 2-fold increase in plasma K+ concentrations. Sublethal concentration (0.0007µg/l) of cypermethrin caused decrement in protein level, increment in free amino acid level [8] and decrement in lipid content [7] in muscle and liver of Channa orietalis. Vasantharaja et al., 2014 [17] observed notable decrease in values of ACP and ALP in gill, liver and kidney tissues of Cirrhinus mrigala due to sublethal exposures (30µg/l) to cypermethrin.

Gowri et al., 2013 [40] studied the effect of sublethal concentrations cypermethrin for 7, 14 and 21 days in Cyprinus carpio. DNA and RNA content decreased at 14 and 21 day significantly in brain, gills and liver. However, the decrease was more in 21 day. The reduction in the DNA and RNA content in cypermethrin exposed fishes is comparatively less in liver when compared to the brain and gills. Kakoolaki et al., 2013 [58] observed oxidative stress in rainbow trout and reported in fish brains, catalase activity decreased ($P \leq 0.001$) and malondialdehyde (MDA) level increased ($P \leq 0.001$) in cypermethrin treated group compared to control group. In cypermethrin+propolis-treated group CAT activity increased ($P \leq 0.001$) and MDA level decreased ($P \leq 0.001$) compared to cypermethrin group. Cyprinus carpio exposed to sublethal concentrations i.e. 5, 10, 15 and 20% of 96hLC50 (3.31µg/l) of cypermethrin (25% EC) for 2, 4, 6 and 8 days showed increased activity of ASAT and ALAT in gill, muscle and liver in which dose as well as exposure period depended and statistically significant (P>0.05) alterations were observed [41]. Ojutiku et al., 2013 [33] studied the effect of acute toxicity of cypermethrin in Clarias gariepinus using the following concentrations; 0.025mg/l, 0.050mg/l, 0.075mg/l, 0.100mg/l, 0.125mg/l and 0.000mg/l for 24h and observed biochemical alterations which showed significant higher values (P<0.001, 0.01) for alanine aminotransferase, cholesterol, triglycerides, and total protein. Aspartate aminotransferase and glucose showed a significant reduction (P<0.001) with no significant difference (P>0.05) in alkaline phosphatase as compared to the control. Veeraiah et al., 2013 [18] reported Cirrhinus mrigala exposed to lethal and sublethal concentration (96hLC50 i.e. 2.28ppm and 1/10th of 96hLC50) of cypermethrin (10% EC) for 96h showed decrease in total glycogen, proteins and nucleic acids over control.

Gabriel et al., 2012 [34] observed the effects of sublethal concentrations of cypermethrin (0.05, 0.10, 0.20 and 0.25ml/l) on metabolic enzymes i.e. ASAT, ALAT, ALP and LDH in gill, kidney, liver and muscles plasma of Clarias gariepinus for 10 days in renewal bioassay. The enzyme activities in all the organs were inhibited at all the concentrations, with ALP activity being mostly affected. The highest ALP activity was observed in the kidney, while the lowest ALP in the gill. The activities of the enzymes in all the organs showed a concentration dependent activities which decreased significantly (P<0.005) with the increasing concentration of cypermethrin. Variations in the activities of acid and alkaline phosphatases were evaluated by Gopala Rao et al., 2012 [42] in different tissues of Cyprinus carpio under sublethal toxicity of cypermethrin. The results revealed that, the activities of ACP and ALP are decreased in all the tissues studied irrespective of the concentration of the toxicant and exposure period. This decrease was directly proportional to the concentrations of the pesticide and duration of the exposure period was statistically significant ($p \leq 0.05$). Maximum inhibition of ACP and ALP activity was observed in the intestine of test fish at highest test concentration (20% of 96hLC50) and longest exposure period (15 Days). Patil and Patole, 2012 [57] reported significant fluctuation in protein, decrease in glycogen and lipid over the control in Lepidocephalichthys guntea exposed to sublethal concentrations (1/4th and 3/4th of LC50) of cypermethrin for 96h.

The sublethal concentration of cypermethrin (0.00078µl/l) for 24, 48, 72 and 96h showed reduced levels of DNA and RNA. RNA/DNA ratio was also changed at different exposure periods as compared to control [14]. Thakur and Kakde, 2012 [9] reported DNA, RNA and RNA/DNA ratio in muscle of Channa punctatus under the influence of sublethal concentrations of cypermethrin (0.00078µl/l) for 24, 48, 72 and 96h and observed a decreased trend in DNA, RNA levels. While the RNA/DNA ratio significantly changed respectively at different periods. Laboratory evaluation of cypermethrin toxicity made by Tiwari et al., 2012 [52] revealed sublethal doses of cypermethrin (0.129µg/l, 0.258µg/l for 24h and 0.082µg/l, 0.164µg/l for 96h exposure period caused significant (P<0.05) alterations in protein as well as carbohydrate metabolism of the fingerlings of Labeo rohita in both liver and muscle tissues. Total protein, nucleic acids (DNA and RNA), glycogen, and pyruvate levels were significantly reduced (P<0.05) while total free amino acids and lactate levels were significantly enhanced (P<0.05) in liver and muscle at sublethal doses. Activities of acid, alkaline phosphatases, AChE, and CyO were significantly (P<0.05) reduced while activities of enzymes proteases, ALAT, ASAT were significantly enhanced (P<0.05) in liver and muscle tissues after exposure to sublethal doses. Vani et al., 2012 [6] reported reduced total adenosine triphosphatase, sodium-potassium adenosine triphosphatase, and magnesium adenosine triphosphatase activities in the gills of Catla catla exposed to sublethal concentrations of cypermethrin. Vasantharaja et al., 2012 [19] studied acute toxicity of cypermethrin (30µg/l) and its impact on biochemical alteration in Cirrhinus mrigala for 24, 48, 72, 96 and 120h. Dose dependent alterations in the level of total protein, free amino acid and glucose were observed.

Heterobranchus bidorsalis exposed to cypermethrin (0.005, 0.0075, 0.010, 0.125 and 0.0150ppm) for 23 days showed enzymatic alterations in the gill, kidney, liver and muscle tissue [50]. In gill, activity of ALAT was lowered (P>0.05) at 0.005 and 0.010ppm were lower, whereas elevated at the other concentrations. ASAT activity was elevated (11.36-22.45% above the control) at all the concentrations. ALP activity was inhibited and the highest inhibition (40.46%) at 0.010ppm. In kidney, ALAT

activities were elevated 33.33% and 66.67% above the control at 0.005-0.010ppm and 0.0125-0.0150ppm respectively at all the exposure concentrations. ALAT and ASAT activities in the liver were inhibited. ALP activity was inhibited at 0.0075 (44.12%), and 0.0150ppm (23.53%), but elevated at the other concentrations with a peak, 33.83% at 0.010ppm. In the muscle, 12.68% and 23.94% elevation were recorded at 0.0125 and 0.0150ppm respectively, for ALAT with a decrease in the lower concentrations. There was excitation of ASAT activity at 0.0050, 0.010 and 0.015ppm and inhibition at 0.0075 and 0.0125ppm relative to the control value. There was a general inhibition of ALP activity in the muscle except at 0.010ppm. Sublethal concentrations of 5, 10, 15 and 20% 96h LC50 (3.31µg/l) for 2, 4, 6 and 8 days resulted dose as well as exposure period depended ($p \geq 0.05$) increase in free amino acid levels and protease activity in Cirrhinus mrigala. Maximum elevation of free amino acids and protease activity was observed in liver, followed by muscle and gill [20]. Firat et al., 2011 [62] studied the effect of cypermethrin (0.05µg/l) for 4 and 21 days on serum enzyme activities, metabolites and ion levels in Oreochromis niloticus. ALAT and ASAT activities increased at both the exposure periods. While elevations in ALP and LDH activities and in cholesterol level were observed. Fish showed an increase in cortisol and glucose levels at 4 days followed by a return to control levels at the end of the exposure period, their levels elevated at both the exposure periods. Total protein levels decreased at 21 days. Na+ and Cl- levels decreased at both the exposure periods. An elevation in K+ level was also observed at the end of the exposure period. Acute toxicity experiments conducted by Neelima et al., 2011 [20] revealed that sublethal concentrations (5, 10, 15 and 20% 96hLC50) of cypermethrin for 2, 4, 6 and 8 days to the fish Cirrhinus mrigala caused dose as well as exposure period depended ($p \geq 0.05$) increase in free amino acid levels and protease activity. Maximum elevation of free amino acids and protease activity was observed in liver, followed by muscle and gill. Srinivasa Rao et al., 2011 [43] investigated cypermethrin induced protein and free amino acid alteration in the tissues of Cyprinus carpio through HPLC and insignificant protein alterations were observed at the end of 24h suggesting fish resistance to the sudden stress for shorter duration and later significant decrease in protein content was observed with a maximum depletion in head (26.33%) followed by gill (24.8%), digestive system (21.78%), liver (15.65%) and muscle (11.42%). Tantarpale, 2011 [15] observed sublethal concentration of cypermethrin (0.00078µl/l) for 24, 48, 72, and 96h decreased total protein level in Channa straitus. Total protein was found to decrease 58.99, 41.12, 38.11, 21.81mg/l in muscle and 23.62, 20.77, 19.17, 12.67mg/l in liver tissues at different exposure periods.

Acute exposure to cypermethrin resulted in a significant ($P<0.01$) lower concentration of ALP and significant ($P<0.01$) higher concentration of NH3, ASAT, LDH, CK, and LACT in rainbow trout. In common carp cypermethrin resulted in a significant ($P<0.01$) lower in TP, ALB, GLOB, NH3, LDH, and ALP, and a significant ($P<0.01$) higher in GLU, LACT, and CK levels compared to controls [44].

Sublethal concentrations of cypermethrin caused an increase in gill Na+, K+-ATPase activity in Cirrhinus mrigala [21]. Singh et al., 2010 [35] reported toxicological and biochemical alterations of cypermethrin against Colisa fasciatus at different seasons. Cypermethrin after 96h exposure significantly altered the levels of total protein, total free amino acid in muscle and liver tissues, nucleic acids in gonadal tissues and the activity of enzyme acetylcholinesterase, lactic dehydrogenase and succinic dehydrogenase in nervous tissue of the fish in time and dose dependent manner. A significant ($P<0.05$) dose dependent decrease in total protein levels in liver and muscle tissues was observed. Suvetha et al., 2010 [45] studied the effects of acute and sublethal toxicity (1.86ppm 24hLC50) of cypermethrin on plasma electrolytes (Na+, K+ and Cl-) levels and gill Na+/K+-ATPase activity in Cyprinus carpio. During acute exposure, cypermethrin caused hyponatreima, hypokalemia and hypochloremia and inhibition of gill Na+/K+-ATPase activity. In sublethal exposure (0.186ppm for 35 days), plasma Na+ was decreased throughout the exposure period except 7th day whereas plasma K+ level was increased up to 28th day, then declined. However, plasma Cl- level was decreased. Likewise, gill Na+/K+-ATPase activity was decreased as the exposure period extended.

Begum, 2009 [27] reported cypermethrin-challenged Clarias batrachus showed significant inhibition of the activities of total, Mg+2, and Na+-K+ ATPase enzymes, while it increased the levels of glycogen phosphorylase, thereby suggesting that these enzymes had the potential to be used as biomarkers of cypermethrin exposure in fish. Korkmaz et al., 2009 [63] observed marked decline in protein and glycogen level in different organs of Nile tilapia (Oreochromis niloticus) exposed to cypermethrin for 10 days. Cypermethrin showed positive correlation between concentration and inhibition/ alteration of AChE activity in Channa punctatus and the inhibition of AChE activity in brain was significantly higher than muscle followed by gill [11]. Logaswamy and Remia, 2009 [68] reported that cypermethrin significantly altered various biochemical constituents such as protein, glucose, cholesterol and triglycerides. Significant decrement was observed in protein, cholesterol and triglycerides while hyperglycemic condition was observed under sublethal concentrations at 24h exposure period. Marigoudar et al., 2009 [53] studied the effects of cypermethrin at 1/7th (0.57mg/l) and 1/12th (0.33mg/l) of the lethal concentration (4mg/l) for a period of 1, 7, or 14 days and allowed to recover for a further 7 days and observed inhibition in acetyl cholinesterase (AChE) activity. Maximal inhibition was found in brain followed by muscle, gill, and liver on day 14 at both the sublethal concentrations. Recovery showed a rise in AChE activity but significantly decreased compared to controls. Saha and Kaviraj, 2009 [51] studied the effect of cypermethrin (0.3-0.5µg/l) on Heteropneustes fossilis and observed an increase in glucose level with simultaneous decline in the level of glycogen as well as the activity of acid and alkaline phosphatases.

Prashanth and Neelagund, 2008 [22] studied the effects of cypermethrin on aspartate amino transferase, alanine amino transferase and glutamate dehydrogenase in the gill, liver and muscles of fresh water fish, Cirrhinus mrigala. Exposure to lethal

concentration (5µg/l) for 1, 2, 3, 4 days and sublethal concentration (1µg/l) for 1, 7, 14, 21 days caused an increase in the activities of ASAT, ALAT and GDH in all the tissues with increase in exposure time. But in sublethal concentration at 14 and 21 day, a decreasing trend was observed in all the tissues exposed to cypermethrin.

Exposure to cypermethrin causes increased levels Na+, K+, Mg2+, P, urea, glucose, cholesterol, creatinine, ASAT and ALP, whereas total protein, triglyceride and ALAT levels are reduced in silver catfish, Rhamdia quelen [64]. Begum, 2007 [28] observed 10 days of exposure to cypermethrin caused marked increase in the activities of transaminases and GDH in different organs of Clarias batrachus. Kumar et al., 2007 [13] observed increasing effect on DNA and RNA profile of gill, brain, liver and kidney of Channa punctatus treated with cypermethrin (40-60µg/l). Prashanth, 2007 [23] reported significant alterations in the levels of ammonia, urea and glutamine in Cirrhinus mrigala due to cypermethrin treatment.

Dobsikova et al., 2006 [46] reported that Cyprinus carpio exposed alimetrin 10EM in the concentration of 29.1µg/l corresponding to 29.1µg/l of cypermethrin for 96h caused a significant ($P<0.01$) increase in glucose and lactate concentration and creatine kinase activity, and a significant ($P<0.01$) decrease in total proteins, albumins, total globulins, ammonia, lactate dehydrogenase and alkaline phosphatase in blood plasma of exposed carp compared to the control group. Induction of proteolysis as a result of elevated protease activity reflecting in the decrease of the protein levels and elevation in the levels of free amino acids of different tissues of C. mrigala exposed to cypermethrin was reported [24]. Tripathi et al., 2006 [30] reported increase in protein content in liver, heart, kidnay and gill of Clarias batrachus exposed to cypermethrin (0.002ppm) for 72h. Velisek et al., 2006 [59] reported that in rainbow trout cypermethrin caused significant decrease in concentration of ALP and significant increase in concentration of ammonia, ASAT, LDH, CK and lactate in blood plasma. Higher values ($P<0.01$) of plasma ammonia, aspartate aminotransferase, lactate dehydrogenase, creatine kinase, lactate and significantly lower ($P<0.01$) values of alkaline phosphatase were recorded. Cypermethrin induced hyperglycaemia was also recorded.

Begum, 2005 [29] observed sublethal concentrations of cypermethrin induced decrease in total proteins and increase in free amino acids, protease, alanine aminotransferase, and aspartate aminotransferase in the liver, and gill tissues of Clarias batrachus. Depletion of hepatic glycogen due to cypermethrin treatment was also observed in the fish. She also documented an elevation in the activity of glutamate dehydrogenase in liver and brain, 30.40% reduction in protein content in liver of Channa punctatus exposed to cypermethrin (0.07mg/l) for 10 days. Jee et al., 2005 [65] found an increase in levels of serum glutamic-acidoxylacetic-acid-transaminase, glutamic-acidpyruvic-acid-transaminase, glucose, and alkaline phosphatase and a decrease in the concentration of plasma total protein, albumin, cholesterol, and lysozyme in Korean rockfish (Sebastes schlegeli) exposed to cypermethrin. Hyperglycemia was also observed.

Adhikari et al., 2004 [54] to 0.139ppm of cypermethrin for 45 days altered enzyme activities. Acid phosphate was unchanged while alkaline phosphatase was depleted. Brain acetylcholinesterase activity was decreased significantly over a period of 45 days. Lactate dehydrogenase and ATPase activities were depleted in brain, kidney and liver. David et al., 2004 [47] studied the effect of the sublethal concentration of cypermethrin on the metabolic profile of Cyprinus carpio and reported a decrease in soluble proteins, while amino acids and activities of protease, aspartate and alanine aminotransferase increased with the administration of the toxicant. They interestingly noted that ammonia content decreased but urea and glutamine increased with the dosage.

Das and Mukherjee, 2003 [55] in Labeo rohita observed cypermethrin induced changes in DNA, RNA, LDH, SDH and ATPase of muscle, liver, brain and kidney. Sublethal exposure to cypermethrin produced a significant increase in the activities of serum ALP and LDH. Hyperglycemia was also observed. Atamanalp et al., 2002a [60] found changes in the concentration of Ca2+ and phosphorus in rainbow trout (Oncorhynchus mykiss) following cypermethrin exposure at three different sublethal doses. After 15 days of exposure, Ca and P decreased, while TP and Na took various values depending on the doses. Significant decrease in the activities of alkaline phospahtase, but a significant increase in the concentration of ammonia, lactate dehydrogenase, aspartate transaminase, creatine kinase and lactate in blood plasma were observed [60, 61]. Durga Prasad and Veeraiah, 2002 [56] worked on effect of cypermethrin on protein metabolism of the fish Labeo rohita observed that the total protein level decreased in all the tissues tested where as the free amino acid levels were increased.

Kamlaveni et al., 2001 [48] studied effects of cypermethrin on the activities of succinate dehydrogenase and glucose-6-phosphate dehydrogenase in Cyprinus cario var communis and found a steady inhibition in SDH activity with concomitant elevation in G6PD which indicated the activation of an alternative pathway of carbohydrate metabolism, viz the hexose monophosphate shunt or pentose phosphate pathway as a biochemical adaptation to overcome the toxic stress. Uner et al., 2001 [49] observed induction of lipid peroxidation in liver and kidney of the freshwater fish Oreochromis niloticus and Cyprinus carpio due to intoxication with cypermethrin.

3. Conclusion

The analysis of data from the present review demonstrated that cypermethrin (a synthetic pyrethroid pesticide) is highly toxic and had a profound impact on biochmecal changes in various fish species in both lethal and sublethal concentrations. No doubt cypermethrin can create a great economic loss by fish mortalities on one hand and rendering them unfit for human consumption on the other hand. If consumed, these fish can create health hazards for those who consume these fish. The present review proved that, cypermethrin is toxic to fish even at minute concentrations and research should be carried in both laboratory and natural condition to determine the safety and permissible limits for

different pesticides in general and synthetic pyrethroids in prticular. The present data can be a tool for documentation of toxic action by the xenobiotic chemical cypermethrin. Thus, cypermethrin in the aquatic medium is a major factor responsible for drastic changes in the fish physiology. However, it would be more rational to mention that alterations in biochemical parameters in cypermethrin exposed fish will provide important information on the general well being of fish. Thus, fish physiology following exposure to cypermethrin is the best suitable biomarker in the field of aquatic toxicology.

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